Allegato 1 – Anlage 1

Progetto di ricerca e cooperazione tecnologica EUREGIO-EFH - Projekt für Forschung- und technologische Kooperation EUREGIO-EFH
(English version only)

EUREGIO: Environment, Food & Health

(EUREGIO-EFH)

The Overweight/Obesity/healthy ageing challenge:

European Region Tyrol-South Tyrol-Trentino as Land of Solutions

INDEX

EXECUTIVE SUMMARY

EUREGIO **E**nvironment, **F**ood & **H**ealth (***EUREGIO-EFH***) deals with the growing socioeconomic challenges of age- and obesity-related chronic disease. It addresses the interface of environment, genetics, metabolome, microbiome, food and health, linked to obesity and ageing. These are important research priorities identified within current European, national and regional research plans. EUREGIO-EFH constitutes an inter-sector (academic, medical, industrial, service providers, tourism), inter- to transdisciplinary (medicine, biology, agriculture, informatics, food and nutrition, chemistry) and trans-regional (Trentino-South Tyrol-North Tyrol, hereafter ***EUREGIO***) partnership to unite and drive regional strengths in a common fight against obesity and age-related diseases. **Our mission is to lay the scientific basis for practical approaches to fight obesity and age-related chronic disease, providing innovative solutions and new products, valorising regional food production chains while safeguarding the natural environment.**

This mission will be implemented using a three-pronged approach:

1) ***Consortium Stakeholder Workshops***: EUREGIO-EFH will organise a series of high level training workshops for stakeholders and decision makers in EUREGIO presenting how food, diet and life-style can be harnessed to reduce the societal challenges of obesity and age associated disease within the constraints of genetic predisposition. This represents a first step towards personalised nutrition/medicine. Participants will include stakeholders from the food industry and agriculture, health care systems, academic institutes and political leaders. The aim will be to foster multidisciplinary thinking to tackle these challenges and provide a cross-societal strategy to implement change in the way we look at the environment, offer new solutions by maximising the nutritional quality of the EUREGIO food chain and improve the impact of public health measures targeting obesity and chronic disease risk.

2) The ***EUREGIO-EFH post-graduate training school*** will bring together EUREGIO academic strengths in environment, food and health to tackle obesity and healthy ageing. We will measure how current land use impacts on the quality of EUREGIO food chain and ecosystem sustainability through interactions with natural biodiversity and aim to improve the security of EUREGIO dairy production systems. We will explore the nutritional potential of local foods, potentially identifying new new nutraceuticals or functional food products. We will explore the health associations of EUREGIO dietary practices and design a new alpine diet to reduce obesity- and age-associated chronic disease risk based on the Mediterranean dietary guidelines but utilizing EUREGIO nutritious foods and food culture. We will define the economic cost of failing to take on healthy eating guidelines and explore the psychology of consumer behaviour and risk perception concerning diet and lifestyle choices. We will conduct a two centre (Trento and Bolzano) dietary and life-style intervention, the FASTMOB study, in obese individuals exploring the therapeutic potential of “fasting mimicking foods”, high in fiber, polyphenols and beneficial fats drawn from EUREGIO foods. This study is designed to mimic the weight loss associated with fasting using foods low in energy but rich in nutrients known to impact on inflammatory and metabolic processes which regulate obesity and the diseases of obesity. We aim to achieve a 5 to 10% weight reduction in 6 months, maintained over 12 months and a significant reduction in chronic disease risk. Taking advantage of state of the art technologies within EUREGIO academia, we will employ a combined *omics* strategy to provide new mechanistic understanding, from the cell to whole organism level, of how the FASTMOB diet impacts on obesity and related inflammatory and metabolic risk. We will provide new cause and effect evidence in support of how diet, through interactions with the gut microbiome may be exploited to reduce the burden of chronic disease and promote healthy ageing. We will provide new technologies, including prediction from genetic profiles and new methods to measure metabolic rates, to assist clinical nutritionists diagnose and better understand the risk of metabolic disease allowing more personalised design of therapeutic dietary protocols. Finally, EUREGIO-EFH will impact on these societal challenges well beyond the lifespan of this current project by training 12 of the next generation of postgraduate professionals working in this area.

3) ***The EUREGIO-EFH scientific research network*** has already brought together internationally recognised experts in the fields of environment, food and health stretching from Trento to North Tyrol under a single working initiative. We aim to build on existing relationships and through the EUREGIO-EFH project construct a strong working partnership to attract inward investment from both public (EU) and private sources into EUREGIO environment, food and health research.

LIST OF PARTICIPANTS

Table 1: List of Participants

Consortium member	Short name	Academic	Non-Academic	Awards Degrees	Region	Dept./ Division/ Laboratory	Scientist-in-charge	Role of Partner Organisation
Fondazione Edmund Mach	FEM	✓			Trento	1. Nutrition & Nutrigenomics Unit (NN), 2. Department of Food Quality and Nutrition (DQAN) 3. Applied Ecology (AE), Department of Biodiversity and Molecular Ecology (DBME) 4.Computational Biology (CB) technology platform	1. Kieran Tuohy 2. Annapaola Rizzoli 3. Urska Vrhovsek 4. Franco Biasioli 5. Claudio Donati 6. Francesca Fava 7. Lisa Rizzetto 8. Matthias Scholz	1. Gut microbiota, nutrition, functional foods 2. Metabolomics, Food quality, food chemistry 3. Ecology, environment and health 4. Computational Biology
Servizio di dietetica e Nutrizione Clinica – Bolzano	ASAA		✓		South Tyrol	Servizio di Nutrizione Clinica, Ospedale di Bolzano	1. Lucio Lucchin 2. Massimo Pellegrini 3. Michael Kob 4. Dept. Of Public Health	Clinical nutrition, obesity, metabolic disease
Azienda Provinciale per i Servizi Sanitari - Provincia Autonoma di Trento	APSS		✓		Trento	Servizio di Dietetica e Nutrizione Clinica, Ospedale di Santa Chiara	1. Carlo Pedrolli 2. Dept. of Public Health	Clinical nutrition, obesity, metabolic disease

Free University of Bozen-Bolzano	UNIBZ	✓		✓	South Tyrol	Faculty of Science and Technology	1. Matthias Gauly	1. Agriculture, Livestock production systems 2. Environment and Applied Botany 3. Environmental Microbiology, antibiotic resistance, metagenomics 4. Food microbiology and metagenomics
University of Trento	UNITN	✓		✓	Trento	1. Dept. Of Physics, NMR Unit 2. C3A (CAFÉ) 3. CiBio	1. Graziano Guella 2. Fulvio Mattivi 3. Nicola Segata	1 & 2 Metabolomics and applied analytical chemistry 3. Metagenomics & bioinformatics
European Academy of Bolzano	EURAC	✓			South Tyrol	1. Institute for Biomedicine (IB) 2. Institute of Alpine Environment (IAE)	1. Francisco Domingues 2. Julia Seeber	1. Bioinformatics, Molecular Medicine, Precision Medicine, Genomics, Epidemiology.
Leopold Franzens University Innsbruck	UIBK	✓		✓	Tyrol	1. Faculty of Mathematics, Computer Science and Physics (MCSP) 2. Institute for Biomedical Aging Research (IBA)	1. Beatrix Grubeck-Loebenstein and Werner Zwerschke 2. Christopher Mayhew (MCSP) 3. Ulrike Tappeiner	1. Chemistry, Physics, PTR-MS, Food Science 2. Ageing research, adipose tissue biology, cell biology 3. PTR-MS, Molecular Physics 5. Ecosystem and landscape ecology
Centro di Sperimentazione Laimburg	LRC	✓			South Tyrol	1. Plant and Fruit Analysis	1. Michael Oberhuber	1. Food science, analytical chemistry, metabolomics

University for Health Sciences, Medical Sciences and Technology	UMIT	✓		✓	Tyrol	1. Department of Psychology and Medical Sciences, RiskLab (PMS) 2. Dept. of Public Health (PH)	1. Bernhard Streicher 2. Uwe Siebert	1. Social and Personality Psychology 2. Assessment of public health nutrition, agrifood, and lifestyle
Gruppo Europeo di Cooperazione Territoriale - L'Euregio Tirolo-Alto Adige-Trentino	GECT		✓		All			WP leader Dissemination & Exploitation
Provincia autonoma di Trento	PAT		✓		Trento			WP5 Dissemination & Exploitation
Autonome Provinz Bozen – Südtirol	APBS		✓		South Tyrol			WP5 Dissemination & Exploitation
Land Tirol	LT		✓		Tyrol			WP5 Dissemination & Exploitation

PROJECT ACTIVITY PLAN

1) *Consortium Stakeholders Workshop or* EXPERT LECTURE SERIES

Organized within the context of the EUREGIO Academia – Highway of Autonomy - roots, challenges and the future, EUREGIO-EFH will offer a **theoretical and practical advanced course on "Food, Nutrition and Health – prevention of chronic disease"**, targeting decision makers within the three territories. A select group of about 45 people who occupy important positions in the context of building the future (decision makers) will be invited to participate in order to build an **inclusive training exercise** designed to cover the analysis of major priority areas and social challenges related to nutrition, specifically overweight / obesity and diseases of old age. The EUREGIO-EFH *Consortium Stakeholders Workshops* will take **a nutritional perspective of the entire food supply chain from production through testing, clinical implications and the impact of lifestyle, and will detail the specific implications for public policy**. Three seminar series will be organized, one in each province, Trento, Bolzano and Innsbruck. In parallel, EUREGIO-EFH will organise PhD training workshops which will provide both subject specific training materials for the EUREGIO-EFH early stage researchers (ESR) and also generic skills for young researcher career development. The aim will be at all

times to foster the ability of young researchers to develop their indpendence as scientific investigators, providing the information and training needed to build successful careers in science and the courage and confidence to meet the challenges of independent postgraduate research training. Finally, at the end of the EUREGIO-EFH project we will organise a major international congress under the working title: "One Health" – EUREGIO model for environment, food & health: investing in a healthy future". The aim will be to maximise dissemination of the EUREGIO-EFH project results, build the international visibility of the EUREGIO partners, provide a space for EUREGIO stakeholders to foster new collaborations and network on the international stage, provide a recruitment networking event for the EUREGIO-EFH ESRs and to consolidate the research network and partnerships forged during the 36 months of the EUREGIO-EFH project.

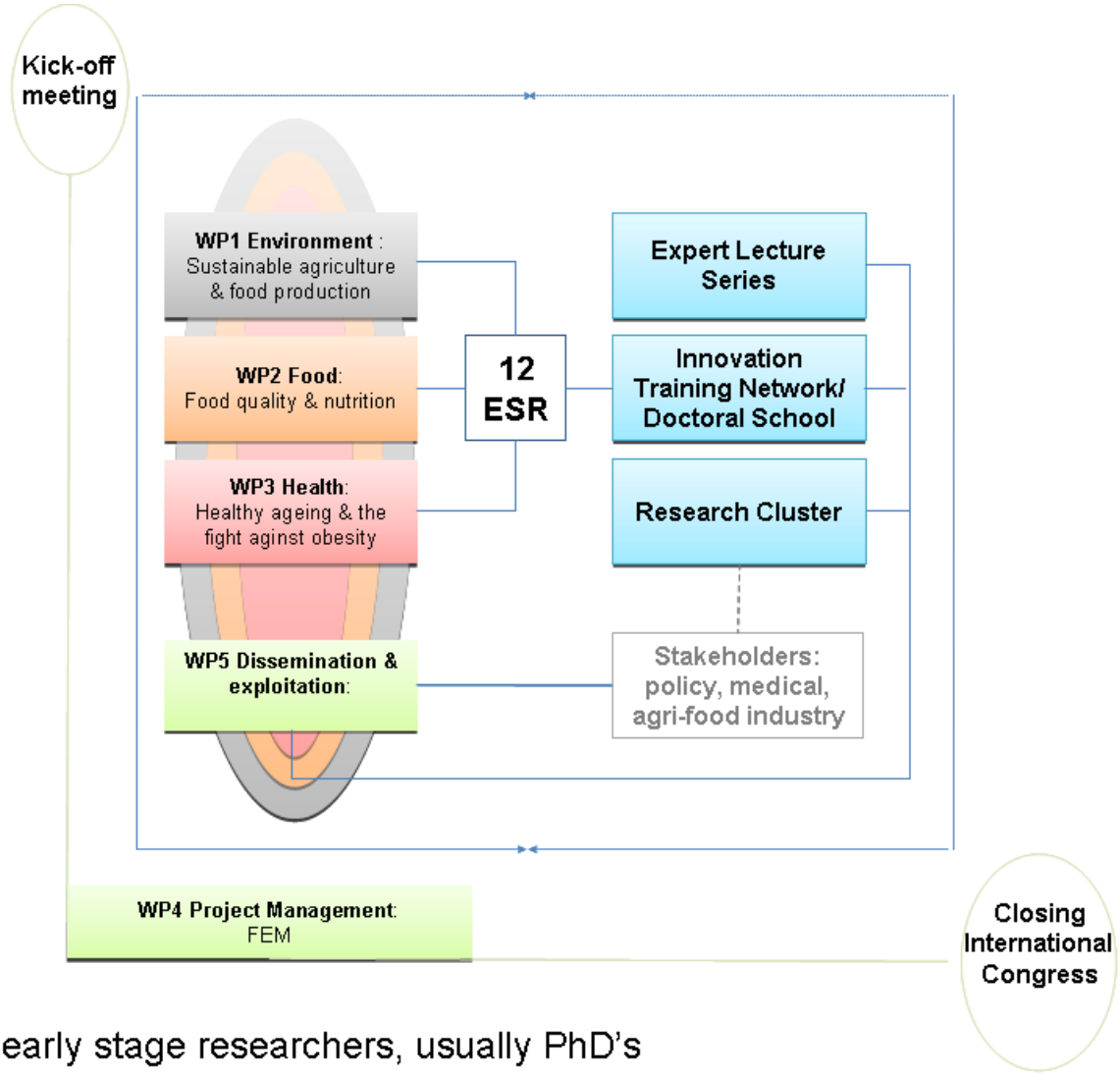
2) INNOVATION TRAINING NETWORK/Doctoral school

EUREGIO-EFH will organize an **integrated doctoral level training network** between the three partner territories comprising approximately 8 three-year training doctorates and in addition two early stage dieticians, one research assistant and one early stage clinician. These positions will split between environment, food/nutrition research and clinical nutrition medical specializations. This collaborative and concerted cross-border innovation training network will operate under the **unifying theme "Obesity and healthy aging: lifestyles, environment, genetics, agriculture, molecules and microbes".** Training provided will cover the various aspects of the relationship between food, nutrition and health and the prevention of chronic diet/age associated disease. Each doctorate should normally receive **co-supervision/training from at least two institutions** based within EUREGIO. The organizational headquarters will be based at FEM-C3A with joint annual progress meetings organized in Trento, Bolzano and Innsbruck.

3) RESEARCH CLUSTER

EUREGIO-EFH represents an ideal opportunity to bring together the regional research and clinical community working on obesity and healthy ageing. The aim of this research cluster will be to **identify project actions strategic to the three partner regions** and integrate multidisciplinary skills to address today's challenges, existing and future research priorities and opportunities. The cluster will provide expert **insight into research developments and challenges** in environment, food production and its clinical implications and provide easy access to information for stakeholders, key decision-makers and the EUREGIO population. The EUREGIO-EFH research cluster will comprise a scientific commission that can produce and edit a **quarterly newsletter** and prepare a **EUREGIO dossier proposing joint strategic actions** within the EUREGIO area. A top priority of this Research cluster will be to identify and collaborate in attracting inward investment in scientific research from both private (e.g. agri-food multi-nationals) and public (European Commission) sources.

Figure 1: EUREGIO-EFH project activity plan.



ESR = early stage researchers, usually PhD's

Table 2: List of EUREGIO-EFH events

EVENT	Location	Main Training Events	Lead Institution	Participants	Audience	Month
1	Trento (FEM/ UNITN)	**EUREGIO-EFH kick-off meeting** (all participants, signing of consortium agreement, election of boards/committees)	FEM	All	All	1
2	Trento (FEM/ UNITN)	**PhD training:** Introduction for PhD students – the journey from student to independent researcher	FEM	All	ESR 1-12	3
3	Tyrol (IBK or Hall)	**Consortium Stakeholder Workshop:** Cost and socioeconomic impact of obesity in EUREGIO – focus on environment, food & health interactions.	UMIT	All EUREGIO partners and invited expert speakers	EUREGIO opinion formers and stakeholders, health, spa and food industries, local ministries for health, economy, environment and tourism, EUREGIO research community, ESR 1-12	3
4	South Tyrol Bolzano	**Consortium Stakeholder Workshop:** The role of nutrition and life-style in obesity and metabolic disease	ASAA	All EUREGIO partners and invited expert speakers	EUREGIO opinion formers and stakeholders, health, spa and food industries, local ministries for health, economy, environment and tourism, EUREGIO research community, ESR 1-12	12
5	Trento	**Consortium Stakeholder Workshop:** Designing the foods of the future – valorisation of EUREGIO food production streams and land use in the fight against obesity/metabolic disease.	FEM	All EUREGIO partners and invited expert speakers	EUREGIO opinion formers and stakeholders, health, spa and food industries, local ministries for health, economy, environment and tourism, EUREGIO research community, ESR 1-12	24
6	Trento FEM/ UNITN	**PhD training:** Career models for research scientists in EUREGIO	FEM	All	ESR 1-17	30

7	Trento	**Consortium Stakeholder Workshop, Scientific conference and recruitment fair:** International congress on "One Health" – EUREGIO model for environment, food & health: investing in a healthy future.	FEM	All	EUREGIO stakeholders, national, international research and industrial leaders	36

Background and Start of the Art

The challenges: Overweight/Obesity and Ageing

Regions all around Europe face the same major health related socioeconomic challenges: an ageing population and an epidemic in overweight/obesity. European Region Tyrol-South Tyrol-Trentino (EUREGIO) is no exception and the economic cost of age- and obesity-related disease at the population level and adverse impact on quality of life at the individual or personal level make these related health challenges important for both regional government and our population. By the year 2060 more than 20% of the EUREGIO population will be over 65 years of age placing considerable economic burden on social provision and health care costs. Similarly, more than 50% of our people are currently overweight and nearly 20% obese (data source APSS). Obesity carries a significant health penalty, with obese people 80 times more likely to develop type 2 diabetes, 2 to 3 times more likely to develop cardiovascular disease (CVD) and are at a 40% increased risk of dying from cancer (Foresight 2007, Tackling Obesity, UK.gov). Unfortunately, obesity, the diseases of obesity and ageing are all related at the biological level, with changes in body composition in old age due to loss of muscle mass driving age-related obesity and the onset of chronic obesity related diseases especially type 2 diabetes, heart disease and diseases driven by chronic inflammation. This "perfect storm" of age and obesity related chronic disease threatens the economic viability of our region and the health and welfare of our people.

The Roots and the Future: European Region Tyrol-South Tyrol-Trentino (EUREGIO) as Land of Solutions

EUREGIO has considerable innate strengths which, if channelled with unified vision, could influence the socioeconomic impact of obesity and age related chronic disease at local, regional and international levels. Public health care is amongst the best and most organized in the world (Italy is ranked number 2 in the world for health care provision and Trentino-alto Adige ranks best in Italy according to Demoskopika 2015 National survey). Within our regions healthy life-styles are common (e.g. highest levels of exercise in Italy, out-door activities and natural environment as a key ally in the fight against obesity). We have a long tradition in health-related tourism (winter sports, walking and climbing in the mountains, health spa) based on the alpine environment. EUREGIO has an established scientific research infrastructure with the state of the art tools necessary to fully understand the drivers and possible solutions to age and obesity related disease from farm to gut. Last, but not least, these regions are amongst the main European producers of foods which protect against obesity and the diseases of obesity and old age, foods rich in dietary fibers, plant polyphenols, beneficial fats, fermented foods and dairy products.

This proposal addresses priority themes in Agrifood and Health, priorities identified within current European, National and Regional research plans. It takes a multidisciplinary approach, drawing on scientific expertise in different disciplines (environmental science, public health, psychology of risk perception, dairy science, food science and technology, nutrition, metabolomics, genetics, bioinformatics, gut microbiota, gene ecology, cell biology, biomedicine, epidemiology, clinical nutrition, obesity and gerontology), to tackle the multifaceted challenges of obesity and healthy ageing.

The EUREGIO-EFH project is built around the "one health" concept, and will address how ENVIRONMENT, FOOD and HEALTH are all linked to obesity and healthy ageing.

ENVIRONMENT

The Mediterranean diet forms the basis of healthy eating guidelines in Europe and most of the developed world. Briefly, diets high in vegetables, fruit, whole grain cereals or complex carbohydrate sources rich in fiber, with moderate intake of dairy products (especially fermented dairy products), olive oil, fish/seafood and red wine, and low in red meat, processed foods, sugar and refined carbohydrates appear to be associated with healthy ageing and protective against chronic non-communicable diseases linked to obesity. This dietary description has been built over many decades by examining food intake in epidemiological studies, and determining which foods or dietary patterns are associated with disease risk (Bonaccio et al. 2013). With the realization that human activities have a considerable impact on the natural environment and that our own food security is very much determined by the same natural environment, recent efforts have also been made to measure the effect of various human dietary models on the environment. The double pyramid model proposed by the Barillia Centre for Food and Nutrition (Ruini et al 2015) was one of the first attempts to calculate the environmental impact of the Mediterranean style diet. They suggested that the foods we are recommended to eat most regularly, fruit and vegetables, have the lowest environmental impact, while the foods we are advised to eat rarely, for example sweets or highly processed foods, are those with the highest environmental impact. While there does seem to be some common-sense logic in this proposal, the actual environmental impact of the foods we eat rather than the idealised diets we are recommended to eat is a much more complex question. For example, the environmental impact of animal protein, dairy or meat, is greatly determined by the degree and type of processing, the region of production and its climate, and probably the intensity of farming. Conversely, the environmental impact of fruit and vegetables is low only for fruit and vegetables produced locally and eaten in season. The environmental impact of fresh fruit and vegetables grown intensively and sold out of season on the other side of the world is likely to be considerable. Such considerations have been taken into account by researchers from FEM working with Università Cattolica del Sacro Cuore in Piacenza, who have more recently presented an "hour glass" model of the environmental impact (in terms of green house gas emissions) for the Mediterranean diet and the new Nordic diet, a recent attempt at designing a healthy dietary model in Scandinavia similar in macronutrient and energy composition to the Mediterranean diet but using local Nordic foods (Hillesund et al. 2014; Ulaszewska et al. 2017). Other studies have also emphasised the complexities of calculating the environmental impact of different dietary strategies and recognise the importance of locally produced foods, the "zero kilometer" concept and seasonality (both in terms of environmental impact and nutritional composition) as well as the need to optimize partnership with the local environment which often means incorporating aspects of more traditional production systems into the high intensity modern farming (Donini et al. 2016; Perignon et al. 2017). The "carbon footprint" of our modern diet is now becoming apparent and can be translated into real costs, not only for

the environment and the local economy but also, as discussed below, for population health. This EUREGIO-EFH project will begin the process of estimating the environmental impact of local diets, eating habits and dietary recommendations. It will take into account both the environmental impact of the diets we are recommended to follow, and the foods we actually eat in this Alpine region. Further, we will endeavour to equate these findings to the known impact of these dietary patterns on chronic disease risk, allowing us to estimate health costs associated with low or high adherence to dietary recommendations corrected for the local food supply chain and local consumer food choice. The overall aim will be to translate both the actual and recommended dietary patterns in EUREGIO into quantitative measures of environmental and health impact, providing key decision makers within the three EUREGIO provinces accurate cost-benefit analysis of amiliorating the environmental impact of food production and improving the nutritional quality of the foods consumed. Using a life cycle assessment approach (Heller et al. 2013), we will develop a regional specific life cycle inventory database for food and agriculture, expanding the scope of assessment beyond existing measures of environmental impact (e.g. green house gas emissions) to include ecological biodiversity, microbial biodiversity, nutritional and health related measures by estimating the local economic burden of failing to take on healthy eating guidelines and the health related value of access to locally produced, sustainable food products of high nutritional quality.

FOOD

At its base, the Mediterranean diet is rich in whole plant foods, vegetables, fruit, legumes and whole grain cereals. Bonaccio et al (2013), studying the Moli-Sani cohort in Molise, Italy (about 25,000 people) found that close adherence to the Mediterranean style diet was strongly associated with improved health related quality of life (a valid predictor of mortality). These associations appeared to be independently predicted by the antioxidant (or polyphenol) content of the diet and the fiber content of the diet, suggesting that both polyphenols and fibers played important roles in the observed health associations. Similarly, in one of the largest ever dietary interventions with the Mediterranean diet, the PREDIMED study in Spain, fiber, polyphenol and fruit intakes were all associated with significant (up to 41%) reduced risk of cardiovascular disease (CVD) (Medina-Remón et al. 2011; Tresserra-Rimbau et al. 2014; Buil-Cosiales et al. 2014). Interestingly, both polyphenols and fibers are important modulators of the human gut microbiota, which is now thought to play a key role both in the current epidemic of obesity and in healthy ageing. Indeed, polyphenols and/or fibers are also key bioactive components not only of healthy diets but also of foods and plants shown to protect against chronic diseases such as certain functional foods. For example, we (FEM) have recently shown that two apples per day can mediate a significant shift in the metabolic output of the human gut microbiota and also a clinically significant reduction in total cholesterol (4%) and the arthrogenic vascular cell adhesion protein 1 (VCAM-1), lowering CVD risk in people with slightly elevated cholesterol levels (Koutsos et al. 2016). We have also shown that increasing fruit and vegetable intake in general, either high in flavonoides or low in flavonoides, can reduce CVD risk in an at risk population (McCready et al. 2014), modulate the composition of the gut microbiota (Klinder et al. 2016) and determine the profile of metabolites excreted in urine (Ulaszewska et al. 2016).

A key aspect of the current EUREGIO-EFH project will be to characterise and catalogue both the diversity of food and profile the macro-nutrient and micro-nutrient compositions of diets and local foods within the three EUREGIO provinces, allowing us to identify autochthonous foods rich in polyphenols and fibers with economic and health related potential. From the CHRIS study run by EURAC Institute for Biomedicine in Bolzano, we have an existing dataset characterising the diet of people (n≈10000 individuals

and increasing) living in a rural setting in South Tyrol with detailed information on CVD risk and life-style as well as detailed genetic and metabolomic profiling. This represents an important advance over other Italian population based studies, such as the Moli-Sani study, in that CHRIS will include high resolution genetics and metabolite profiling. At FEM, we have data on dietary intake and biomarkers of CVD risk, gut microbiota profiles and biofluid metabolomics of obese people in Trento and Arco (n=140). This current project will also involve a two centre dietary intervention in obese individuals (WP3) in Bolzano and Trento (n≈120), the ***FASTMOB*** study, providing not only detailed dietary information and CVD risk associations, but also high resolution genetics and also post-genomics data on how the body changes in response to diet/life-style induced weight loss. Together with data from public health sources within the health services of all three provinces, these data will be mined to construct a picture of current EUREGIO dietary intake and associated metabolic disease risk. The aim will be to identify local foods to form the base of a ***EUREGIO dietary pyramid true to the nutrient and energy composition of the Mediterranean style diet but built on local foods of high nutritional quality***. Importantly, these efforts will be benchmarked and co-analysed using multivariate statistical approaches with large European datasets. FEM/C3A is currently a partner in 4 multi-national nutrition biomarker discovery projects, ENPADASI, FOODBALL, HEALTHMARK and CABALA_doet&health, funded through the EUs Joint Programming Initiative, a Healthy Diet for a Healthy Life (http://www.healthydietforhealthylife.eu/). These projects aim to characterise the European nutritional phenotype through multi-omics, multi-variate statistical analysis (http://www.enpadasi.eu/) and to measure the contribution of food constituents to the human metabolome, identifying at once new biomarkers of intake and how nutrients impact on host physiology. By co-analysing the EUREGIO-EFH dietary data with similar datasets from around Europe we will identify key nutritional biomarkers of health and better equip this project to advise on ***local/regional alpine variation of the Mediterranean style diet***. Identifying key food components linked to the health effects of local foods will also allow us to target specific plant species for development as functional foods. Importantly, building on observations and genetic associations found in the CHRIS study and validating such associations using the same level genetic analysis in the ***FASTMOB*** study, we (EURAC-CDM) will generate novel insight into how our genes can predict response to diets and foods rich in bioactive components. This is a first step towards rational personalised nutrition based on genetic make-up, and additionally represents a valuable scientific resource capable of attracting international high level scientific interest and inward research investment (i.e. European level grants). This region of Europe, because of the rich alpine floral biodiversity, has a long and strong tradition of herbal remedies and medicinal plants. EUREGIO-EFH will combine information derived from local dietary assessments and associations with metabolic disease risk.

Dairy products are another characteristic of the Mediterranean diet and most national dietary guidelines recommend moderate intake of low fat or fermented dairy products. Dairy products are important sources of calcium, vitamin D and folate, and have been shown to improve bone health in adolescents, a key stage in bone development which determines later life, especially post-menopausal bone health (Demmer et al. 2016). None the less, there is general assumption that their fat content is associated with increased cardiovascular and possibly cancer risk. However, the evidence for this is not consistent and in fact recent studies are suggesting that not only are dairy products, and especially fermented dairy products, a characteristic of the Mediterranean style diet, but that they may, in moderation, play an active role in the health effects of the Mediterranean diet, especially protection from CVD, metabolic syndrome and obesity (Tapsell 2015). In 2011, the data from the Malmo diet and cancer cohort suggested that overall dairy product consumption was associated with a reduced risk of CVD, with a strong inverse association between fermented milk intake and CVD risk. Those consuming the highest amounts of fermented milk had a 15% reduced incidence of CVD compared to those consuming the lowest

amounts of fermented milk (Sonestdet et al. 2011). There was also a significant sex effect, with cheese consumption in women showing a statistically significant decrease in CVD risk. Other epidemiological studies too have shown an inverse association between dairy intake and hypertension (an important risk factor of CVD) (Talaei et al. 2016) and a recent dose-response meta-analysis of observational studies showed that total dairy intake was inversely associated with the risk of type 2 diabetes. One of the few epidemiological studies to examine diet and chronic disease risk in the Alps has reported that stronger adherence to the Mediterranean diet is associated with lower all-cause CVD and cancer mortality, with consumption of dairy products also consistently associated with lower mortality (Vormund et al 2015). Indeed, de Oliveira Otto et al (2013) in a multiethnic cohort study of 2837 US adults aged 45 to 84 years, found that plasma odd–chain saturated fat pentadecanoic acid (15:0), a biomarker of dairy fat, was actually associated with 19% lower CVD risk and a 26% lower coronary heart disease (CHD) risk. Similarly, in a more recent study, in 3333 adults aged 30 to 75 found that those with higher levels of the dairy fat biomarker plasma 15:0 had a 44% lower risk of diabetes mellitus. Similar results were found for other dairy fat biomarkers heptadecanoic acid (17:0) and the natural ruminant *trans* fat *trans*-palmitoleate (t-16:1n-7) (Yakoob et al. 2016). However, in these studies, although total dairy intake appears to be associated with reduced risk of metabolic disease (e.g. type 2 diabetes, hypertension, CVD), we still do not fully understand which components of dairy products mediate these health effects and dairy products differing in fat, calcium, folate or bioactive peptide profiles may well show different effects. In dietary interventions, cheese intake appears to lower LDL cholesterol compared to either butter or the habitual diet in normo-cholesterolemic individuals (Hjerpsted et al. 2011), while in 12 overweight/obese individuals low-fat dairy products did not have a more favourable impact on CVD biomarkers, and on the contrary, full fat and fermented dairy products were suggested to be more beneficial than low-fat dairy products regarding impact on CVD biomarkers (Nestel et al. 2013). Using a metabolomics approach, Zheng et al. (2015) in a small (n=15 healthy men), short-term, 14 day, cross-over study, found that both milk and cheese consumption decreased urinary choline and trimethylamine-N oxide (TMAO) levels and increased faecal excretion of short chain fatty acids (SCFA) and lipids compared to a control diet. Importantly, TMAO has been suggested as a novel potential biomarker of CVD risk linked to microbiota metabolism of phosphatidylcholine and L-carnitine (Wang et al 2011; Koeth et al, 2013). More recently in 115 moderately hypocholesterolemic individuals, replacement of regular food items rich in fat (e.g. bread spread, cooking oil, cheese, bread and cereals) with products of higher fat quality (replacing saturated fatty acids, SFA, with n-6 polyunsaturated fatty acids, PUFA), serum total (-9%) and LDL –cholesterol (-11%) were significantly reduced after 8 week dietary intervention (Ulven et al. 2016). Importantly this study showed that food quality, in this case the quality of fats in regularly consumed high fat products, can mediate clinically significant improvements in blood cholesterol levels after a relatively short dietary intervention. Such observations suggest that different dairy products, especially those with different profiles of fats may in fact mediate a beneficial impact on human metabolic health. In EUREGIO-EFH, we will characterise the fat profiles of EUREGIO regional dairy products, measure the impact of different production intensity farming systems on dairy product nutritional quality, and examine from existing studies, and the FASTMOB cohort (WP3), the impact of diet on plasma fat profiles (lipidome) in obese subjects upon diet induced weight loss therapy.

HEALTH

Obesity, the diseases of obesity and ageing are related at the biological level. Changes in body composition in old age due to loss of muscle mass, declining subcutaneous fat pads and increasing visceral and ectopic fat depots drive age-related obesity, and the onset of chronic obesity related diseases like type 2 diabetes,

CVD. Unresolved systemic inflammation is central to the patho-aetiology of these diseases. In fact, biological ageing is characterized by chronic low grade systemic inflammation which then leads to cellular damage and metabolic disease. The causes of this un-resolved inflammatory state are not fully understood but are thought to involve redox stress, mitochondrial dysfunction, glycation, lack of immune regulation, hormonal changes, epigenetic modifications, telomere attrition and/or intestinal permeability (Fougère et al. 2016). Similarly, obesity is characterised by chronic low grade systemic inflammation, which is thought to contribute to insulin resistance, type 2 diabetes and CVD (Minihane et al. 2015). Moreover, the inflammatory potential of the diet (e.g. through inflammatory advanced glycation end products) itself has also been suggested to contribute towards obesity, adding another driver of inflammation directly linked to Modern diets (Ruiz-Canela et al. 2015). Our own work (FEM) has shown that high fat diets, by decimating beneficial commensal microbiota, contribute to intestinal permeability, chronic systemic inflammation, metabolic disease and weight gain (Cani et al 2007a). Specifically increased populations of inflammatory macrophages and decreased regulatory T-cell immune dampening during excessive weight gain and in ageing lead to modifications in adipose tissue endocrine and immune function driving both inflammatory processes and metabolic derangement (Martyniak and Masternak et al. 2016). In fact, treating chronic inflammation has become one of the most promising targets for reducing the disease burden in both ageing and obesity.

Unresolved systemic inflammation therefore represents a unifying pathological mechanism linking the ageing process, the onset of metabolic derangement and disease in old age, and obesity, and its related metabolic diseases.

Intriguingly, the human gut microbiota and the metabolites it releases from food has also been closely linked to obesity and health in old age. Ley et al (2006) were the first to show clear differences in the make up of the gut microbiota of obese and lean people, and that this obese microbiota changes to a lean profile upon dietary induced weight loss. Similarly, in old age, frailty and the degree of independent living imprint a clear microbiota signature, one closely linked to dietary composition, markers of inflammation and other health parameters (Claesson et al. 2012). On the other hand, foods and diets rich in fiber, polyphenols and beneficial fats appear to be able to reverse some of these changes within the composition and metabolic activity of the gut microbiota and also mediate improvements in resolution of inflammation and metabolic control (Fava et al. 2006; Marchesi et al. 2016). In laboratory animals, we have shown that certain dietary fibres, prebiotics, can be employed to protect against metabolic endotoxemia, regulate food intake and protect against obesity (Cani et al 2007b; Anastasovska et al. 2012). We found protection from intestinal permeability and subsequent metabolic disease correlated with intestinal bifidobacteria, bacteria long studied for their health promoting attributes (Cani et al. 2007a, b). More recently, other microorganisms have also been shown to play a role, including *Akkermansia muciniphila* (Dao et al. 2016). Similarly, the ability of metabolites produced by the gut microbiota, especially SCFA and bile acids to mediate immune tolerance and control inflammation is now becoming accepted at the mechanistic or cellular level (Park et al., 2014; Fiorucci et al., 2010; Vavassori et al., 2009). Indeed, it appears that certain diets, including the Mediterranean diet, with beneficial fats (MUFA and PUFA), polyphenols and fibers have real potential to impact on inflammatory markers (e.g. CRP) in participants with metabolic disease and in the elderly (Richard et al. 2013; Kolehmainen et al. 2015; Neale et al, 2016; Casas et al. 2016). Recent studies by members of this consortium (FEM and UniBz) have shown that dietary intervention with whole grain cereals, fruit, vegetables or beneficially dietary patterns can all improve markers of metabolic disease and modulate the human gut microbiota towards profiles enriched with health promoting species and activities (Costabile et al 2008; Fava et al, 2013; De Angelis et al. 2015; Connolly et al, 2016; Klinder et al, 2016; De

Filippis et al. 2016). In addition, the physiological role of gut microbiota derived metabolites to control immune function and metabolic disease risk is being studied in two new European projects under the ***JPI-HDHL initiative, HEALTHMARK and CABALA_Diet&Health***, where FEM is a partner and project coordinator respectively.

Similarly, probiotics, safe food-borne microorganisms with the ability to modulate host physiological processes have also been studied for their ability to protect against obesity and the diseases of obesity. At FEM, previous work profiling the composition of local dairy products, including dairy products from low intensity dairy farms in alpine pastures, has delivered a culture collection of some 2000 strains of lactic acid bacteria. We have shown that one of these strains (*L. brevis* FEM 1874 originally isolated from *malga* cheese) produces high levels of the neurotransmitter γ-aminobutyric acid (GABA) and also possesses bile salt hydrolase activity (BSH) enabling it to modify bile acid profiles in mammals. Collaborating with University College Cork in Ireland we have recently shown that ingestion of this strain leads to reduced body weight accretion (Fig. 2a), reduced epididymal adipose tissue (EAT) mass (Fig. 2b) and improved glycaemia (Fig 2c) in high-fat induced obese mice. Indeed, this strain outperformed the diabetic drug metformin in the same experiment. *L. brevis* FEM 1874 produces high levels of the neurotransmitter GABA *in vitro*, in dairy products and within the intestine. Our experiment also showed that this strain has a significant effect on anxiety and depression like symptoms in high fat fed mice. As part of the current project, we will screen the existing LAB culture collection at FEM for similar strains with potential as probiotics.

Figure 2a: Change in body weight of mice fed a low fat diet (LFC), high fat diet (HFC), and then high fat diets supplemented with metformin (MET) and the probiotic strain *Lactobacillus brevis* FEM 1874 isolated from EUREGIO cheese. LFC, MET and FEM 1874 groups all showed significantly lower body weight gain over the 24 week intervention period.

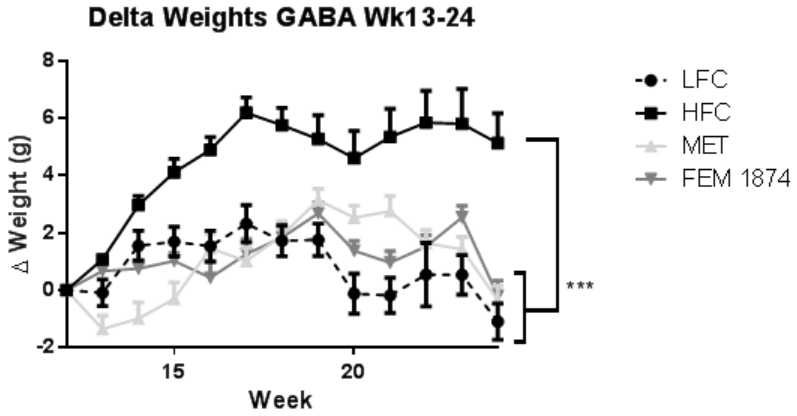


Figure 2b: Change in adipose tissue weight in different body fat deposits, epididymal (EAT), subcutaneous (SAT) and mesenteric (MAT) of mice fed a low fat diet (LFC), high fat diet (HFC), and high fat diets supplemented with metformin (MET) and the probiotic strain *Lactobacillus brevis* FEM 1874 isolated from EUREGIO cheese. LFC, FEM 1874 groups showed significantly lower EAT than mice fed high fat alone.

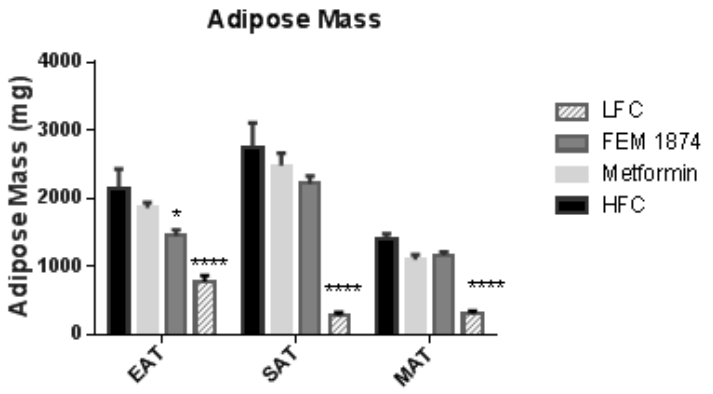
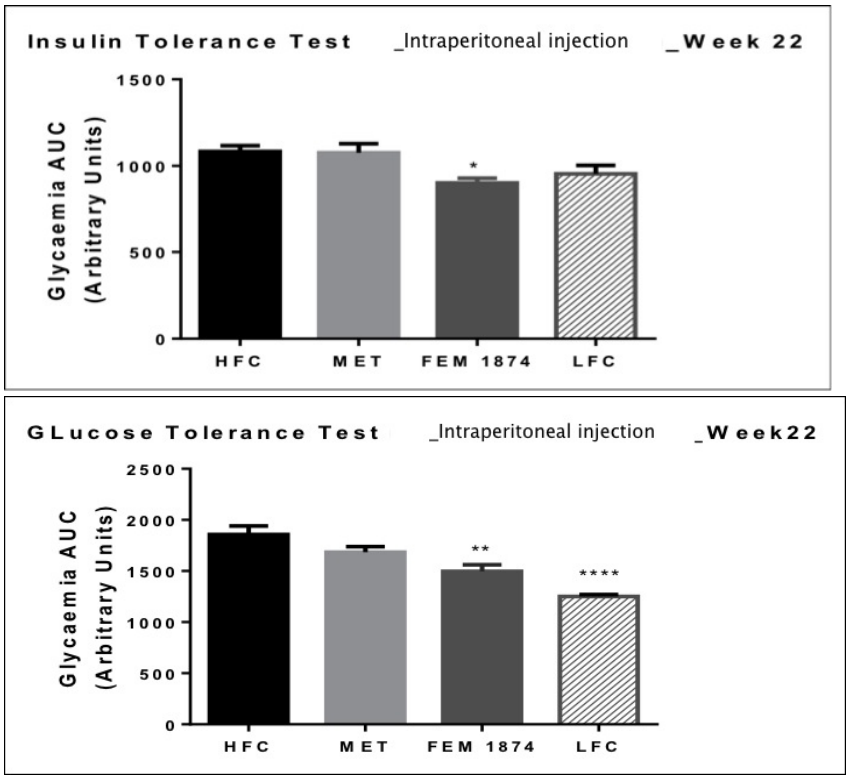


Figure 2c: Glycaemia (area under the curve, AUC, plasma glucose) is improved in *L. brevis* FEM 1874 supplemented animals on a high fat diet compared to mice fed high fat alone (HFC) and high fat plus the diabetes drug metformin (MET) after 22 weeks of feeding upon insulin tolerance test.



Recent evidence points towards controlled periods of fasting being efficacious in reducing body weight and also in helping those who loose weight to maintain this weight loss (Mattson et al., 2016). Human clinical studies have demonstrated that intermediate fasting, as well as prolonged fasting and time-restricted feeding bring along an amelioration of chronic disease symptoms related to overweight and obesity. A clinical study on overweight subjects (n=32) has shown that alternate day fasting is effective for weight loss and protects against CVD, including reduction of circulating leptin and LDL-cholesterol (Bhutani et al., 2010). Similarly, long-term low calorie intake or calorie restriction, is at the cellular and the whole organism

level known to reduce the risk of metabolic disease, chronic systemic inflammation and extend healthy lifespan (Speakman and Mitchell, 2011; Fontana and Partridge, 2015). Calorie restriction, also referred to as dietary restriction, has been shown to induce cellular up-regulation of sirtuitins, including mammalian SIRT1, which provides protection against cellular aging, cognitive decline, and age-related chronic inflammatory diseases (Baur et al., 2012). Certain foods or food components (i.e. polyphenols, aminoacids) might act as sirtuitin activators, thereby carrying out similar effects to a calorie restricted diet at a neuronal and metabolic level (Ma et al., 2015; Brand horst et al., 2015; Johnson et al., 2013, Mitterberger and Zwerschke, 2013). Moreover, it is well accepted that an important beneficial effect of caloric restriction is to reduce insulin-mechanistic target of rapamycin (mTOR) signalling (Fontana and Partridge, 2015). It has been shown that certain food components (i.e. polyphenols) contribute to reduced insulin/mTOR signalling (Mitterberger and Zwerschke, 2013). Indeed, studies in both laboratory animals and in humans have shown that calorie restriction diets or life-long low calorie intake may be a critical feature of diets known to protect against obesity, metabolic disease and enhance healthy aging such as the Mediterranean diet (Baur et al., 2012; Fontana and Partridge, 2015, Pazoki-Toroudi et al., 2016). Diets rich in whole vegetable foods and also certain proteins, such as the Mediterranean diet, might carry out a calorie restricted diet mimicking effect via insulin/mTOR deregulation, and thus protect against cell aging, neuronal dysfunction and obesity-associated inflammation. Intriguingly, recent studies using metabolomics have revealed that many of the molecules associated with calorie restriction diets and their physiological activities derive from combined host:gut microbiota metabolism e.g. ketone bodies, short chain fatty acids, bile acids, small phenolic acids, and metabolites of the tryptophan pathway (Shoaie et al., 2015; Lin et al., 2015). Importantly, many of these metabolites in circulation can be modified by diet:microbe interactions in the gut and therefore specific foods may have the ability to mimic, at least in part, some of the physiological benefits of calorie restriction. As part of the EUREGIO-EFH project, we will conduct a two centred dietary intervention in obese people aiming to reduce body weight by 5 to 10% over 6 months using periods of fasting and fasting mimicking foods. Mechanistically, we aim to trigger the same pathways involved in the calorie restriction effect using microbiota derived metabolites (SCFA, bile acids, ketone bodies, small phenolic acids and certain beneficial fats) combined with periods of reduced energy intake, to stimulate thermogenesis, reduce fat storage, impact on markers of satiety, help resolve chronic systemic low grade inflammation and modify the gut microbiota in composition and metabolite output. Using a multi-disciplinary approach, and taking advantage of start of the art post genomics technologies available to the study partners, we will correlate the metabolic output of the gut microbiota with clinical markers of immune and metabolic function and identify associated patterns or community structures within the gut microbiota. Few studies have so far followed the metabolic and immune consequences of dietary induced weight loss in such detail, and this study, when co-analysed with other data sets is likely to shed new light the physiological processes involved in fasting induced weight loss and associated reduced disease risk and extension of healthy life-years.

In addition, starting from existing studies within EUREGIO, CHRIS, AVAG, MiaCoure and PreBioil, we will mine the dietary information of FASTMOB study to measure current dietary habits within EUREGIO, and associated metabolic disease risk with specific local foods. We will estimate the cost of existing dietary patterns in terms of health-care provision and also the potential benefit, both in economic terms and for the environment, of adhering more closely to the Mediterranean style diet. Further, using information gained on the chemical composition and health associations of specific local foods, we will design a EUREGIO alpine version of the Mediterranean style diet, using local foods, food culture and adding value to the local food chain.

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WORK PACKAGES

WorkPackages (WP, described below, listed in Table 3 and depticted in Figure 1). The work packages will not always operate in a linear fashion, but mainly interact during the entire project (36 months). In parallel to the core Research and Innovation WPs (1-3), WP4 "Project Management" and WP5 "Dissemination and Exploitation" will operate as a horizontal WP during the entire project. In particular, they will ensure that knowledge can be rapidly extracted and presented in ways most appropriate for each target group (dieticians, care givers, health care providers, stakeholders, policy makers and service funders). The complete list of deliverables and the main EUREGIO-EFH scientific/socio-economic outputs output are reported in Table 5 and 6. Their due date completion is also reported in the Gannt chart.

Table 3: Work Package (WP) List

WP No.	WP Title	Lead Partner	WP leaders	Start	End
1	Environment, R	EURAC/UIBK/UNIBZ	Gauly	0	36
2	Food, R	FEM/UNITN/LRC	Oberhuber/Mattivi	0	36
3	Health, R	UIBK/ASAA	Grubeck-Loebenstein /Zwerschke/Lucchin	0	36
4	Project management, M	FEM	Battistel	0	36
5	Dissemination & Exploitation, D	GECT /all	Castellani	0	36

R= research & training; M= management and administration of project; D= dissemination and exploitation of results.

WPs represent overarching research themes and project activities. For research themes (WP1, 2 and 3), WP leaders will present on the research area and put individual PhD project activities into perspective of the

wider research area and its implications for the EUREGIO. Reporting will be in the form of a yearly project/WP update and participation in the EUREGIO Environment, Food & Health expert lecture series.

WP Number 1		**Start Month 1 – End Month 36**
WP Title	ENVIRONMENT	
Partners	EURAC/UNIBZ, FEM, LRC	

Objectives:

The overall objective of this WP is to determine which environment we need for our health and sustainable food production systems and to identify novel, innovative strategies to improve the security, economic potential and sustainability of local nutritious foods while safeguarding the quality and economic importance of our natural environment.

Landscape and Environment in the Alps is largely shaped by mountain agriculture. Ongoing changes in terms of mechanization, changes in social structures and globalization lead to specialization in agriculture, followed by an intensification of land use, longer distances from the producer to the costumer and a landscape partially and artificially maintained by subsidies.

The objective of this work package is to characterize and to evaluate two ecologically different land-use types and to assess/quantify their benefits for health and sustainable food production systems. To this end, WP1 will be divided into 2 different tasks:

Task 1.1: Soil biodiversity in farming systems

Optimal food production needs a healthy (soil) ecosystem. Apple orchards will be compared to the current grassland farming in terms of biodiversity (plant diversity, faunistic and microbial biodiversity) and related Ecosystem services, including provisioning ES (i.e. yield), regulating ES (i.e. soil stability) and cultural ES (i.e. aesthetics, tourist economy). The evaluations will mainly be based on existing data collections and databases (see below table 1). Since species and functional diversity of invertebrates and microbiota inhabiting the soil environment are major drivers of (soil) ecosystem functioning due to the many ecosystem processes they contribute to, these data will be newly collected. For each land-use type 5 replicate sites will be chosen, twice a year (spring and autumn) 5 samples per site will be taken. Soil animals will be identified to species (earthworms, millipedes) or family (insect larvae) level and microbiota community composition and structure characterize dusing next generation sequencing (FEM, Donati). To characterise their abiotic environment various soil parameters (linked to soil health) will be analysed: pH, C- and N-content, organic matter content, soil texture. Additionally, the apple fruit associated microbiome will be explored using both culture based and culture independent approaches (FEM, Tuohy). Previous work has identified fruit associated lactic acid microbiota as an important source of potentially valuable microorganisms for biotechnological purposes (Di Cagno et al. Food Microbiology 2013). In the case of fruit, we will equate fruit microbiome biodiversity with that of the plant/soil microbial biodiversity, providing a direct link between ecosystem richness and how it is impacted by farming intensity and microorganisms present on/in EUREGIO food (FEM, Donati, Tuohy)

Parameter/Ecosystem service	Source
Plant and faunistic diversity	EURAC/ALPENV database, UIBK
Plant phenology	LRC databases (LRC, EURAC)
Landscape diversity, quality	EURAC/ALPENV database (Global Change), UIBK
Landscape aesthetics	EURAC/ALPENV database, UIBK
Soil macrofauna diversity	new sampling
Agricultural yield	LRC, EURAC/ALPENV database (Global Change)
Water retention	LTER/MONALISA SWP data
Soil stability	EURAC/ALPENV/UIBK database
Soil physics and chemistry	EURAC/ALPENV database
Economic effects (macroeconomic, business view)	FEM

The collected data will act as a basis for all further analysis on plant food production systems and health in the other Work packages. In particular, close collaboration with public health and economic aspects of WP3 are foreseen linking land use with health risk and costs, both in terms risk (pollution, zoonosis) and benefit (economic value of extensive, population based recreational use of the natural environment).

Main outputs/Deliverables:

Del. 1.1: Comparison of the land-use forms on an environmental perspective (ecosystem status, functions, processes)

Del. 1.2: Comparison of the land-use forms on a social perspective (ES)

Del. 1.3: Comparison of the land-use forms on an economical perspective (macroeconomic, business view)

Del. 1.4: Total synopsis from the perspective of the sustainability of human-nature systems

Task 1.2: Production intensity and dairy food nutritional quality and safety

European dairy cattle sector has undergone profound changes in the last decades motivated by political (the quota system) and economic contexts (the progressive reduction of benefits). Farm number has been decreasing steadily while milk yield per cow and farm size have increased. Farming intensification was adopted as a strategy to increase the economic outcome at the farm level. However, this may also have had negative side effects on animal health, animal welfare, environment and the quality of the resultant food products. Therefore, international negotiations have introduced restrictions and requirements to reduce negative environmental effects of dairy farming, as well as measures to ensure the general well-being of their animals in terms of health, welfare and protection. However, these measures have also affected productivity and profitability of the systems. This, together with the expected price reductions are a challenge that compromise the sustainability of the dairy cattle farms in Europe and especially in the

regions of this project. Therefore, there is an urgent need to estimate the economic (including food product quality) and environmental impacts of traditional (Low-Input) and modern (High-Input) farming systems. In the dairy sector, factors with relevant impact are facilities, nutrition, reproductive performance, genetics and health management. The evaluation of the outcome of such interrelations requires the concurrent integration with many of these different factors and a multidisciplinary approach, which will be employed in this project. The specific objective will be to compare traditional and intensive dairy production systems on the following keywords:

- environment,
- animal health and welfare (incidence of infection, antibiotic use)
- performance,
- economical outcome and
- milk (dairy product) quality (including nutritional quality, nutrient profiling, metabolite profiling , antibiotic residue measurement).

Additionally, based on possible milk quality differences marketing strategies will be developed and the impact on the economic outcome estimated.

Main outputs/Deliverables:

Del 1.5: Identification and recruitment of agriculture partners operating dairy farms at both high intensity and low intensity. Existing relationships between dairy farmers and UNIBZ in Alto Adige, and also between FEM and farmers in Trento will be used to identify dairy herds in valleys and in alpine pastures, and operated at low or high intensity. Permission will be sought to take the necessary environmental, animal associated and food (milk, cheese, yoghurt) related samples (Responsible UNIBZ and FEM). **Month 1.**

Del. 1.6: Environmental assessment of the impact of high and low intensity dairy farming within the EUREGIO region. Employing strengths at UNIBZ, EURAC and FEM in studying the alpine environment, an environmental assessment will be conducted to measure the relative impact of low or high intensity dairy farming in both valley and alpine habitats. Where possible existing data will be mined and used to identify current gaps in the knowledge (responsible UNIBZ). This will be performed in close collaboration with Task 1.1 above. **Month 18.**

Del. 1.7: Measuring the impact of farming intensity on dairy herd health. The impact of farming intensity on herd health, specifically incidence of infection and/or veterinary antibiotic usage will be assessed. **Month 30.**

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Description of Work and Role of Partners

EURAC. The group of Dr. Seeber will provide expertise in soil ecology and soil biodiversity, Dr. Tasser and Dr. Niedrist will provide expertise in biodiversity in farming systems and access to existing datasets and projects.

UIBK: The group of Professor Tappeiner (UIBK) will provide expertise in environment and biodiversity in farming systems and access to existing datasets and projects.

UNIBZ: The group of Professor Gauly will provide expertise in dairy production systems, agriculture and dairy science.

FEM: The group of Dr Rizzoli will provide expertise in environment, zoonosis, climate change and land-use for sustainable human-nature systems and access to existing datasets and projects; the group of Dr Claudio Donati will provide expertise in soil metagenomics; the group of Dr Tuohy will provide microbiology support for characterizing microbiota diversity associated with foods produced under different intensity production systems

The main outputs of this WP will therefore be:

Output 1.1: Evaluation of the land-use forms on an environmental, social and economic perspective (ecosystem status, functions, processes)

Output 1.2: EUREGIO bespoke strategy for adding value, both economic, health-related and social, to land-use forms

Output 1.3: Environmental, food nutritional and animal/human health impact assessment of low intensity compared to high intensity dairy farm production within the EUREGIO region.

Output 1.4: Cost:benefit analysis and improved marketing strategy for dairy production in the EUREGIO region.

Output 1.5: Improved understanding of how production factors, including intensity of farming, animal health, disease incidence, dairy associated microbiota, veterinary antibiotic usage, and type of feeding/location (valley *vs.* alpine pasture) impact on the nutritional quality of dairy foods in EUREGIO.

Early stage researchers involved.

Measuring the impact of biodiversity on agricultural soils will be provided by accessing existing studies and sample sets from the groups of Professor Tappeiner (UIBK) and Dr Seeber (EURAC).

Measurements of food and soil associated microbiomes wil be provided by Dr Claudio Donati and Dr Kieran Tuohy (FEM)

ESR 3: "Measuring the impact of farming production system on the nutritional quality of EUREGIO dairy products and antibiotic resistance transfer". Host: UNIBZ (supervisor Prof. Gauly), FEM (Franciosi), degree awarded by UNIBZ.

WP Number 2		**Start Month 1 – End Month 36**
WP Title	**FOOD**	
Lead Beneficiary (partners)	LRC, FEM, UNITN, UNIBZ, EURAC	

Objective: The objective of this WP is to measure the nutritional quality of EUREGIO foods, investigate the mechanisms by which certain foods or food components may impact on human health and disease risk, and to design new EUREGIO specific foods and diets (fasting mimicking foods/diets) to valorise local agri-food chain. This WP will also provide a state of the art technology platform to investigate at the systems level, the impact of EUREGIO fasting mimicking foods/diet on weight loss maintenance and markers of metabolic disease in the FASTMOB study (WP3).

This WP will by led by LRC, with the collaboration and with the support of FEM, UNITN and UNIBZ. LRC will be responsible for measurements of dietary fibre of the different foods using enzymatic approaches. LRC will also be responsible for communicating on the WP tasks at EUREGIO workshops and coordinating reports (months 18 and 36). Importantly, LRC together with FEM will play a key role in forming a stakeholder board, drawing on their extensive connections with regional food and agriculture industries. All partners will be responsible for writing and reporting the deliverables in both the interim and final reports (months 18 and 36).

Task 2.1: Identify EUREGIO fasting mimicking foods and potential EUREGIO functional foods: We will measure the nutritional profile of local EUREGIO foods with the aim of identifying products useful in the fight against obesity. Specifically we will measure the fibre content, sugar and fat profiles and polyphenol quantity and quality in a range of both ready to eat fresh food products (e.g. fruit, vegetables, milk) and lowly processed products (e.g. pasta, polenta, bread, cheese) (ESR 4, 9 and 12). We (NN Unit at FEM) will collaborate with WP 1.2 (ESR 3) to profile the nutritional composition and microbiota of dairy products derived from production systems of different levels of intensity. This will include isolation, characterization and probiotic screening of EUREGIO lactobacilli and assessment of economic potential, including strain

registration and protection of intellectual property (FEM, UNIBZ, Gauly). A culture collection of EUREGIO lactic acid bacteria, comprising existing strains of lactobacilli at FEM, and new strains isolated in this project, will be mined to identify strains with probiotic potential. High-throughput screening will include GABA production, serotonin production, bile salt hydrolase activity, inhibition of dipeptidyl peptidase-4 (DPP4) and biohydrogenation of fatty acids (production of conjugated linoleic acid, CLA). An important milestone will be the protection of strains housed at FEM, their registration and submission to culture collections and where appropriate intellectual property protection via patent presentation. Strain IP will reside at the partner/region where the strains were isolated (e.g. Trento strains for FEM, South Tyrol strains with UNIBZ) (responsible FEM, ESR 3, 5 and NN Unit staff, FEM).

LRC will be responsible for measurements of dietary fibre of the different foods using enzymatic approaches. FEM will apply MS based analytical approaches to measure both the quantity and chemical composition of polyphenols present in plant based foods of EUREGIO origin. UNITN, using NMR based metabolomics, will provide assistance in profiling fat/lipid composition of selected foods of both dairy and plant origin. FEM will also use a series of in vitro cell based assays to investigate the ability of EUREGIO food derived extracts and medicinal plant extracts to modulate metabolic and inflammatory pathways associated with metabolic disease and healthy ageing and also to influence intestinal barrier function, an important defence mechanisms which appears breached both in obesity/metabolic syndrome and with the onset of age related metabolic/immune decline.

Del. 2.01: Measuring the fibre content of local plant based foods (ESR 4, based at LRC) Month 18

Del. 2.02: Measuring the nutritional profile of selected EUREGIO dairy products (ESR 3, 5, 12, NN Unit staff FEM). Month 30

Del. 2.03: Measuring the polyphenol profile (quantity and quality) of EUREGIO plant based foods (ESR 4, 9 FEM, UNITN). Month 30

Del. 2.04: Compilation of data-base with nutritional profile (quantity of dietary fibre, typical quantity and composition of polyphenols and fats) of EUREGIO healthy foods. This data-base will be hosted by FEM and made open access at the end of the project (responsible FEM, ESR 3, 4, 5, 9, 12).

Del. 2.05: Selection of EUREGIO foods with potential as fasting mimicking foods and development as new food products (responsible FEM, ESR 3, 4, 5, 9, 12).

Task 2.2: Provide a state of the art "omics" level technology platform for measuring metabolites and microbiota, and for processing genotype data for samples collected from WP1 and WP3.

Diet and the foods which make up our diet interact with humans at the whole organism level. This means, that not only are the interactions between the nutrients in our food and the products of our human genome important, but also the nutrient:microbiota interactions between the foods we eat and our resident intestinal microbiota also shape our bodies response to food. In fact, the sum-effect of the foods we eat on human health will depend as much on diet:microbiota interactions in the gut as on diet:human gene interactions. Similarly, it is becoming apparent that small molecules released by the microbiota during digestion of our foods (e.g. small phenolic acids from plant polyphenol metabolism, short chain fatty acids from fibre fermentation, and amino acid metabolism) and also metabolites like bile acids, the result of host:microbiota co-metabolism, play key communication roles in our bodies and regulate physiological processes important both in obesity and healthy ageing e.g. mTOR signalling, energy expenditure/storage, body composition, food intake, inflammation, and immune function, mood/brain function and circadian rhythms. This reality has been encapsulated into the systems level thinking of nutrigenomics which aims to the measure the metabolic and physiological effects of food/nutrients on the whole human organism, microbes and all.

The objective of Task 2.2 will therefore be to provide a high resolution omics platform to study the effect of food, especially EUREGIO functional foods and our bespoke fasting mimicking diet on human metabolism at the whole-organism level to be tested in WP3. Using a trans-omics approach, taking advantage of state of the art infrastructure in metabolomics (FEM, UNITN), and metagenomics (FEM, UNIBz and UNITN), and the experience in genomics data processing and analysis (EURAC), we will provide the ability to profile and identify metabolites in human biofluids (blood, urine, faeces), process genotype data on obese subjects in our FASTMOB intervention study and measure both the composition of metabolic potential of the gut microbiota using sequence based metagenomics. This work will be divided into specific research projects with dedicated ESR and also builds on existing strengths and research interests of partners FEM, UNITN and EURAC. The Nurition and Nutrigenomics team at FEM will also provide support in measuring clinical and biological biomarkers related to inflammation and metabolic regulation for the FASTMOB study.

Del. 2.06: Genotyping of FASTMOB study population (about n = 120) with special reference to polymorphisms in genes known to impact on the risk of metabolic disease and healthy ageing (EURAC-IB, ESR 2)

Del. 2.07: Metabolomics analysis of biofluids collected from the FASTMOB study with special reference to quantification of metabolites thought to be involved in mediating dietary regulation of immune and metabolic features of obesity and chronic age related disease (e.g. bile acids, SCFA, amino acids and small phenolic acids). Responsible FEM/UNITN, ESR 9.

Del. 2.08: Lipidomics: Use of NMR based metabolomics to characterise lipids present in biofluids collected from the FASTMOB study. Responsible UNITN, ESR 12.

Del. 2.09: Metagenomic characterisation of the human gut microbiota and immune/metabolic related biomarker measurement before and after dietary intervention in the FASTMOB study. Responsible FEM (partners UNITN, UNIBZ, ESR 5).

Description of Work and Role of Partners

FEM: Metabolomics Unit, Dr Vrhovsek will lead metabolite (polyphenols, bile acids and amino acids) analysis in EUREGIO foods using MS based metabolomics. Targeted metabolomics of biofluid analysis of FASTMOB study focusing on SCFA, bile acids, amino acids (and derivatives) and small phenolic acids (FEM, Vrhovsek; UNITN, Mattivi). Untargeted biomarker Untargeted biomarker discovery MS based metabolomics to identify biomarkers of fasting mimicking foods and also physiological response to fasting mimicking diets in the FASTMOB study will be performed by the FEM Metabolomics Unit in collaboration with Prof Mattivi and Prof Guella, UNITN; Nutrition and Nutrigenomics Unit, Dr Tuohy, Dr Fava, Dr Franciosi and Dr Rizzetto will provide expertise in dairy microbiology, gut microbiology and metagenomics and functional food analysis.

UNITN: Prof. Guella and Prof. Mattivi, will provide expertise in NMR based lipidomics and MS based food and nutritional metabolomics in collaboration with the Metabolomics Unit FEM. These analyses will be employed to characterise EUREGIO foods and medicinal plants and also investigate the molecular basis of the fasting mimicking diet used in WP3 FASTMOD dietary intervention. Lipid profiles in a selected number of EUREGIO foods and analysis of lipid profiles/lipidomics in FASTMOB biofluids (and subcutaneous adipose tissue biopsies if available or possibly from ex vivo studies of ESR 14, UIBK Profs. Grubeck-Loebenstein and Zwerschke) using NMR lipidomics approach (UNITN, Guella)

LRC: the team of Dr Oberhuber will provide expertise in measuring food macronutrient composition, fibre in particular, and also oversee reporting of WP 2 at the EUREGIO Environment, Food and Health workshops. This team will also play a critical role in forming the Stakeholder Activity, and in particular will be involved in liaising with agri-food industry in South Tyrol (WP5). This key role will involve making contacts to agrifood stakeholders in South Tyrol and to motivate them to join the meetings. Organizational aspects (who organizes which meeting and where) should be defined in during the firs tmeeting of the EUREGIO-EFH Management Committee.

EURAC-IB: the EURAC Institute for Biomedicine will provide expertise in human genomics (Dr. Domingues),

and will process and analyse genotype data in participants recruited onto the FASTMOB study in WP3.

The main outputs of this WP will therefore be:

Output 2.1: Range of EUREGIO food products with detailed nutritional profiling and potential as novel fasting mimicking foods or functional foods.

Output 2.2: State of the art technology platform to serve WP1 and 3

Output 2.3: New mechanistic insight into how fasting mimicking diets/foods may impact on body weight and metabolic health, reducing the disease risks associated with obesity and ageing.

Output 2.4: Novel IP on EUREGIO bioactive foods, food components or therapeutic targets in obesity and healthy ageing.

These outputs will impact on the economic viability of the agri-food and nutraceutical sectors in the EUREGIO region. It will provide a rational, scientifically based, ***marketing strategy based on improved environmental, nutritional and health impact of local EUREGIO food products.*** It will also identify, curate and protect a range of potentially valuable ***functional ingredients (whole plant foods and probiotics)*** which will act as a EUREGIO biological reservoir ***for food and health innovation*** going forward.

Early stage researchers involved

ESR 3: "Measuring the impact of farming production system on the nutritional quality of EUREGIO dairy products.", Host UNIBZ, supervisor Prof Gauly, collaborators, FEM (Tuohy/Franciosi)

ESR 4: "Measuring the nutritional quality of local plant based EUREGIO foods". Host LRC, supervisor Dr Oberhuber, collaborators, FEM (Vrhovsek, Tuohy), UNITN (Mattivi)

ESR 5: "Measuring the impact of EUREGIO foods and fasting mimicking diets (FASTMOB study) on the human gut microbiome". Host FEM, supervisor Tuohy, collaborators UNITN (Mattivi, Segata), APSS, ASAA (FASTMOB study).

ESR 9: "Measuring the metabolic implications of fasting mimicking foods in the obese.". Host FEM, Metabolomics Unit, supervisor Vrhovsek, collaborators UNITN (Mattivi, Guella), APSS (Pedrolli), ASAA (Lucchin)

ESR 12: "NMR-based lipidomics of biofluids (serum and urine) in volunteers undergoing suitable diets". Host UNITN, supervisor Prof Guella, collaborators FEM (Vrhovsek), APSS, ASAA (FASTMOB study)

WP Number 3		**Start Month 1 – End Month 36**
WP Title	**HEALTH**	
Lead Beneficiary (partners)	ASAA Lucchin (APSS, FEM, EURAC, UIBK, UMIT, UNITN, UNIBz)	

Objective:

Model obesity in the local EUREGIO population to predict individuals at risk, design improved dietary interventions with fasting diets based on local EUREGIO foods and propose a regional Alpine version of the Mediterranean style diet, taking into account local food nutritional quality and food culture.

Task 3.1: Obesity in the local population.

The ongoing CHRIS population study (Cooperative Health Research in South Tyrol www.chrisstudy.it) was established in 2011 for the investigation of the molecular basis of common chronic conditions. The study is the result of a successful collaboration between the EURAC Institute for Biomedicine (IB) and the South Tyrolean Health Agency, with more than 10000 individuals already recruited and a total of 13000 expected to be recruited by 2018. A wide range of data is being collected in the study, including clinical assessment based on interviews and questionnaire, medication, BMI, blood and urine tests, family structure, genomic data (~1 million SNPs genotyped and exome sequence data), metabolomics data (targeted and

untargeted), diet and physical activity. A preliminary analysis identifies 15% of obese individuals among the CHRIS participants, and the collection provides a unique opportunity to investigate factors contributing to obesity in the region. Previously, using data from the local population, the EURAC-IB has contributed to the largest ongoing meta-analyses of genome-wide association studies (GWAS) for BMI and related obesity traits (e.g see Locke et al. Nature 2015 518:197-206).

In task 3.1 we will characterise the obese subpopulation in CHRIS and assess the contribution of genetic factors, metabolomics signatures, as well as diet and exercise patterns to obesity. More specifically we will develop models to predict susceptibility to obesity in the local population based on the relevant factors. Of particular interest is to investigate the extremes in the population and to search for potential genetic variants with larger effect size that are unique to, or significant for the region. There is some evidence that yet unidentified genetic factors play a role in severe obesity (Magi et al. PLoS ONE 2013 8:e70735) which will be actively investigated within the CHRIS population. We will also perform familial aggregation analysis to identify families with recurring obesity and explore their unique genetics and diet patterns. The EURAC-IB will make use of the considerable experience in exploring causality using Mendelian randomization methods to determine causal effects for different obesity related factors (metabolic or life style). The models derived to predict obesity will also allow us to identify individuals at high risk that are nevertheless non-obese and healthy, providing a starting point for the discovery of potential protective mechanisms.

The project will contribute to the development of better approaches for stratifying individuals regarding obesity risk according to their genetics and life-style. In general the work will help us bring precision medicine solutions for obesity to the local population, where more effective preventive and therapeutic regimes are assigned to each individual according to their characteristics. As a first step in that direction, Task 3.1 will be closely connected to the FASTMOB intervention study proposed in Task 3.2. More specifically we will investigate the relation between the genotypes of the FASTMOB participants and their response to diet intervention, drawing on the much larger CHRIS dataset for reference. For example, it will be of interest to investigate the outcome in FASTMOB of individuals known to carry a common FTO variant previously strongly associated with obesity in the population and implicated mechanistically in reduced energy expenditure (Claussnitzer et al. N Engl J Med 2015 373:895-907). We will follow with special interest the outcome in Task 3.2 for FASTMOB individuals with obesity related variants that are more unique to the region as they are identified within the CHRIS study.

The relevant findings regarding nutrition, diet and obesity will also be combined with the results from previous regional studies in order to identify local EUREGIO foods associated with lower risk of obesity. Of special interest in this respect are the PreBIOil (https://clinicaltrials.gov/ct2/show/NCT02664428) and the MiaCoure (https://clinicaltrials.gov/ct2/show/NCT02067026) studies.

Del 3.01: Compile different factors (life style and genetic) related to obesity in local population

Del 3.02: Derive model to predict obesity susceptibility in local population

Task 3.02: Dietary intervention in obese people. The second objective of WP3 will be to design, coordinate, and run a dietary intervention in obese persons. The EUREGIO **FAST**ing **M**imicking diets to improve metabolic health in **OB**esity study (***FASTMOB***).

The ***FASTMOB*** study aims to design an effective weight lowering dietary regime based on intermittent fasting/calorie restriction, which improves metabolic health, lowers the risk of CVD and helps obese people maintain their weight loss in the long-term. Recent evidence points towards controlled periods of fasting being efficacious in improving metabolic health, reducing body weight and also in helping those who lose weight to maintain this weight loss. Similarly, long-term low calorie intake or calorie restriction, is at the cellular and the whole organism level known to reduce the risk of metabolic disease, chronic systemic inflammation and extend healthy lifespan. Indeed, studies in both laboratory animals and in humans have shown that calorie restriction diets or life-long low calorie intake may be a critical feature of diets known to protect against obesity, metabolic disease and enhance healthy aging such as the Mediterranean diet. Intriguingly, recent studies using metabolomics have revealed that many of the molecules associated with calorie restriction and their physiological activities derive from combined host:gut microbiota metabolism e.g. ketone bodies, short chain fatty acids, bile acids, small phenolic acids, and metabolites of tryptophan metabolism. Importantly, many of these metabolites in circulation can be modified by diet:microbe interactions in the gut and therefore specific foods may have the ability to mimic, at least in part, some of the physiological benefits of calorie restriction. Here, these "fasting mimicking foods" will be employed during periods of fasting/very low calorie intake, to help patient compliance with the study protocol and also to enhance the metabolic effects of calorie restriction via metabolites shown in animal studies and in the few human studies thus far conducted, to activate metabolic and immune pathways linked to improved metabolic health and the health effects of calorie restriction (e.g. short chain fatty acids, bile acids, small phenolic acids and amimo acids derived from diet:microbe interactions in the gut).

In task 3.2, we will measure the potential of different dietary regimes designed to improve metabolic health in the obese, induce weight loss and help maintain weight loss in the long-term (6 month dietary intervention, 6 month follow-up). Weight loss will be induced using diets with low calorie (LC) intake, traditional reduction of 500 kcal per day), a LC diet plus fasting mimicking foods daily for 6 months, and dietary protocols with intermittent periods of fasting plus fasting mimicking foods. The aim will be to measure the relative impact of standard low calorie intake with and without fasting mimicking foods, and intermittent fasting plus fasting mimicking foods on anthropometric, metabolic, immune and microbiome parameters linked to obesity and the diseases of obesity. **The study primary objective will be improved metabolic health and reduced cardio-metabolic disease risk (HOMA Index, Metabolic Syndrome, dyslipidemia, Framingham 10-year risk score for CHD risk assessment, Pooled Cohort ASCVD Risk Equations) after 6 months of intervention.** Persistence of health effect will be measured at 6 months follow up, during which time the participants will be given general dietary advice according to government guidelines. We will test whether the combination of periodic fasting plus local EURGIO foods which mimic the physiological activities of calorie restriction can improve metabolic health in the obese, and as a secondary objective, prevent body weight re-gain or rebound upon at 6 month follow-up. Selected

EUREGIO foods which have the potential to mimic the metabolic effects of calorie restriction will be chosen as fasting mimicking foods and will be supplied to subjects to be consumed during fasting days or daily throughout the 6 month dietary intervention (diet 2). In a two-centred (Bolzano Hospital and Santa Chiara Trento), randomized, control trial (RCT) in obese participants, we will intervene with the following dietary regimes:

1.) Standard care (dietary/exercise advice) plus a personalised traditional hypocaloric diet (about 15-20% daily calorie restriction or about 500 kcal restriction per day) for 6 months.

2.) Standard care (dietary/exercise advice) plus a personalised traditional hypocaloric diet (about 15-20% daily calorie restriction or about 500 kcal restriction per day), plus selection of EUREGIO fasting mimicking foods provided to participants to be eaten daily for 6 months.

3.) Standard care (dietary/exercise advice) plus very low calorie diet or fasting diet (VLCD) to be followed 2 days/week for 6 months. Participants will be given a selection of EUREGIO fasting mimicking foods to be eaten on fasting days.

4.) Standard care (dietary/exercise advice) plus very low calorie diet or fasting diet (VLCD) to be followed on 5 consecutive days per month for 6 months. Participants will be given a selection of EUREGIO fasting mimicking foods to be eaten on fasting days.

For the intermittent fasting plus fasting mimicking food diets (diet 3 and 4), subjects will be given a selection of low calorie, high fibre, polyphenol rich EUREGIO foods selected to mimic the physiological response to calorie restriction and help them adhere to the dietary regimes. Subject on diet 2, the traditional low calorie prescribed diet, will be given a selection of low calorie, high fibre, polyphenol rich EUREGIO foods selected to help advance the physiological response to calorie restriction. They will consume these foods daily for the 6 month period. The study will be powered on improved cardio-metabolic risk (homeostatic model assessment (HOMA) insulin resistance and dyslipidemia, CV risk assessment) over 6 months, and subjects will be followed up at 12 months (6 months after the end of dietary intervention), estimated 35 per group and we will recruit for a drop-out rate of 25-30%. Participants will be given standard care (dietary advice) between months 6 and 12. Inclusion criteria will include BMI 30-39.9, age 18-65 and glycaemia up to 1.25. Exclusion criteria will include, pregnancy (or planning pregnancy) or lactation, diabetes, complicated hypertension, high medication, eating disorders/food allergies, previous major bariatric surgery, inflammatory bowel disease, previous history of tumours, mental illness/medication.

Clinical and biological measures will taken during 5 study visits, month 0 (upon recruitment), month 3, month 6 (of dietary intervention) and month 9 and 12 (after 6 months of follow-up). Intermediate sampling points are necessary in order to assess adherence to the protocol or adverse effects of the trial diet. Adherence to the protocol should be also monitored by the patient on a written or electronic format. Clinical measures will include body weight, BMI, waist circumference, % body fat (fat mass index, FMI, and Fat Free Mass Index, FFMI), fasting insulin, glucose, HbA1, blood lipids (TC, LDL, HDL, triglycerides) and

high sensitivity C-reactive protein (hs-CRP), basal metabolic rate (BMR) and respiratory quotient (RQ), physical activity using digital armband or wristband polysensors, and quality of life. These parameters will be measured by the respective hospitals (APSS and ASAA). Other markers, including IFN-γ, IL-6, TNF-alpha, IL-10, LPS, LRCP, Insulin-like growth factor 1 (IGF-1), human growth hormone (HGH) and binding proteins, leptin, adiponectin, irisin, resistin, Plasminogen activator inhibitor-1 (PAI-1), angiotensin II, ghrelin, GLP-1, PYY, dipeptidyl peptidase IV (DPPIV), FGF-19, FGF-15 and FGF-21 will be measured at UIBK (by the group of Professor Grubeck-Loebenstein) from blood samples collected at APSS and ASAA. In a subset of 10 subjects per diet we will perform whole body imaging using DEXA at ASAA Subjects will be requested to keep 4 day dietary records before each study visit (up to month 12) to measure actual food/nutrient intake during both the fasting mimicking and non-fasting mimicking periods (two days habitual diet, two days fasting). We will also ask participants to perform health-related quality-of-life measures allowing the incorporation of the consequences of obesity and related disease on physical and psychological dimensions of quality of life and well-being (e.g. captured by DALYs or QALYs) into final study outcomes (APSS and FEM). This data will specifically feed into task 3.4 (ESR 2 and 3, UMIT) below, and also provide the detailed dietary compositional information needed to facilitate accurate metabolic (pathway) modelling and measurement of the nutritional metabolome before and after dietary intervention (FEM/UNITN, ESR 4, 5, 9, 12).

Other biological measures will include targeted and untargeted metabolomics of blood and urine using LC-MS (UNITN, Mattivi, FEM, Vrhovsek, ESR 9 and 12). Samples will also be taken for metabolomics and microbiota before and after periods of fasting (between month 6 and 12). Metabolomics will be employed to precisely and accurately measure small metabolites associated with the physiological effects of calorie restriction (e.g. SCFA, TRP metabolism, bile acids, small phenolic acids) and more broadly to identify biomarkers of calorie restriction and improved metabolic health through untargeted LC-MS biomarker discovery (FEM Vrhovsek, ESR 9). Lipidomics in biofluids will be carried out using combined NMR and LC-MS based approaches (UNITN, Guella, ESR 12). In addition, faecal samples will be used to measure SCFA, bile acids and excreted cholesterol species (FEM, Vrhovsek), bomb calorimetry will be used to measure faecal energy excretion (FEM/UNITN, Tuohy/Segata, ESR 5) and the gut microbiota will be analysed using both 16S rRNA community profiling and strain and metabolic pathway level metagenomics using deep sequencing of representative samples taken from both responders and non-responders (Fem Tuohy, UNITN, Segata, ESR 5). All participants will be genotyped and then characterised for known genetic predisposition to obesity and the diseases of obesity (EURAC-IB Domingues, ESR 2).

We expect the test intermittent fasting and the intermittent fasting plus fasting mimicking foods to improve cardio-metabolic parameters linked to the metabolic syndrome and type 2 diabetes and to reduce the risk of CVD in this at risk population. We also expect to achieve a 5-10% weight reduction and restore some control of body weight gain over the experimental 6 month intervention period and over 6 months of follow-up. Further, this study will shed new mechanistic understanding on the physiological role fasting plays in regulating body weight and weight maintenance in the long term, it will explore the regulatory role of diet:microbiome interactions in the gut and measure how foods, selected EUREGIO foods, can be harnessed to mimic the physiological health effects of calorie restriction.

The main outcomes therefore will be bespoke EUREGIO dietary regime proven efficacious at tackling obesity using fasting mimicking foods of EUREGIO origin.

Del. 3.03: Dietary intervention in obese subjects with triggering the biological effects of calorie restriction through intermittent fasting and EUREGIO fasting mimicking foods.

Del 3.04: New understanding how diet, through interactions with the gut microbiota, impacts on obesity and the diseases of obesity.

Del 3.05: Clinical data in support of the beneficial health impacts of EUREGIO fasting mimicking foods rich in fiber, polyphenols and beneficial fats.

Del. 3.06: a high-resolution genomic and post-genomic data-sets, with the larger CHRIS study, for comparison with existing multi-omics datasets and mining for novel mechanistic insight ad IP related to diet, microbiome, obesity and healthy ageing.

The impact of this WP will translate into considerable savings at the local level in terms of health care costs of obesity and the diseases of obesity. It will also soften the market for selected new EUREGIO foods, or existing high quality nutritious foods with new health associations, translating into real economic return for both agriculture and the food industry in Trento, South Tyrol and Tyrol.

Task 3.3: *Cell signalling in obesity*: (UIBK, Grubeck-Loebenstein/Zwerschke) Obesity is a major public health problem. Caloric restriction (CR) prevents obesity. It is however unlikely that a big CR movement among the human population will arise and CR interventions are frequently unsuccessful for substantial and persistent weight loss. Thus, there is a need for CR mimetics, agents which mimic beneficial effects of CR without restricting caloric intake (Mitterberger and Zwerschke, 2013. J Gerontol A Biol Sci Med Sci. 2013;68:1356-76.). The adipose tissue phenotype in obesity is characterized by accumulation of dysfunctional and senescent adipose progenitor cells (APCs) (Mitterberger et al., 2014. Exp Gerontol. 56:106-13.) and an increase in size and dysfunctionality of adipocytes associated with detrimental metabolic effects. Health-promoting effects of CR include reduction of adipocyte size and fat mass with associated favourable metabolic effects and beneficial effects on APCs, such as reduced insulin/mTOR signalling, postponement of cellular senescence and reduced adipogenic capacity (Mitterberger et al., 2014. Exp Gerontol. 56:106-13.; Ejaz et al., 2016. EBioMedicine 6:149-61.). PBMCs may reflect metabolic changes taking place in fat tissue, can be easily obtained and provide therefore a useful tool to test the effects of new preventive and therapeutic measures (Bürkle et al. 2015. 151:2-12.). The Zwerschke group has shown that CR mimetics such as resveratrol, a polyphenol commonly found in red wine, slow adipocyte development and accumulation of fat mass in the 3T3-L1 preadipocytes/adipocyte model (Mitterberger and Zwerschke, 2013. J Gerontol A Biol Sci Med Sci. 2013;68:1356-76.). Many of the metabolites linked to CR, and its effect on both obesity and healthy ageing, are metabolites produced by the combined activities of the human genome and gut microbiota, such as short chain fatty acids, ketone

bodies, bile acids, and small phenolic acids (Schroeder and Bäckhed, Nat Med. 2016. 22:1079-89.). The team headed by Professors Grubeck-Loebenstein and Zwerschke at UIBK Institute for Biomedical Aging Research, will investigate the molecular basis of molecules suspected to be involved in the beneficial effects of CR both on obesity and healthy ageing.

The major aim of the research project is to test whether host:microbiota co-metabolites exert similar beneficial effects on metabolic health and prevention of obesity as CR interventions. To this end it should be analysed whether specific host:microbiota co-metabolites (purified and provided by Tuohy group, FEM) mimic CR-like responses on adipose tissue cells (Zwerschke group, UIBK) and peripheral blood mononuclear cells (PBMCs) (Grubeck-Loebenstein, UIBK).

Del. 3.07: Selection of host:microbiota co-metabolites and dietary derived molecules linked to CR

Del. 3.08: Measurement of CR metabolite ability of modulate adipocyte inflammatory and metabolic signalling potential using cell models

Del. 3.09: Measurement of CR metabolite ability of modulate adipocyte and immune cell inflammatory and metabolic signalling potential using cells isolated from human blood.

Del. 3.10: Novel insight into the molecular basis of CR associated healthy ageing and protection against chronic diet/age associated disease.

Task 3.4: Public health & Behaviour This task, led by the Department of Public Health, UMIT, in cooperation with the Department of Psychology and Medical Science, UMIT, will perform a review of of public health nutrition, agri-food, and lifestyle interventions applicable in the EUREGIO provinces. Furthermore, assessment will include the objective interaction of these health related factors and their subjective perception of EUREGIO citizens regarding risk and importance. Outcomes should open a path to understand the economic impact of health related core factors and to plan health promoting interventions.

Del. 3.11: Exploration of core factors of health-related factors, understanding their interactions and their impact on health in EUREGIO.

Del. 3.12: A EUREGIO specific understanding of the risk perception concerning healthy diet and healthy life.

Del. 3.13: EUREGIO specific suggestions for a road-map for reducing the socioeconomic and public health related burden of obesity and diet/age associated chronic disease

Task 3.5: Prototype testing of metabolite profiling via PTR-MS to differentiate participants with metabolic and digestive dysfunction (FEM, UIBK, APSS). Partners UIBK (Mayhew) and FEM (Biasioli) have played a

leading role of applying Volatile Organic Compound (VOC) analysis by PTR-MS to a wide range of food and health related applications. Their recent studies have shown that breath analysis by PTR-MS may have diagnostic potential in hepatic diseases in humans (O'Hara et al., 2016; Morisco et al. 2013) and can be useful in monitoring the diet effect in laboratory animals with fatty liver disease (Aprea et al. 2012). A study on celiac disease has been performed as well (Aprea et al. 2014).

This activity will be included in the work of ESR 5 (FEM Tuohy, UNITN, Segata), and in collaboration with APSS (Pedrolli), ASAA (Lucchin/Pellegrini), and Mayhew (UIBK, who will receive a dedicated budget for Euro30,000 for this activity), together with staff from the Nutrition and Nutrigenomic Unit of FEM, will investigate the potential of PTR-MS to measure human metabolic rates with respect to gut microbiota composition and their fermentative ability. We will explore the potential of PRT-MS to measure metabolic changes (especially ketone body generation) in breath metabolites in lean humans with different microbiota make up and upon microbiota modulation with dietary prebiotics. This acute, pilot scale study (n=10) will combine PTR-MS with traditional clinical breath testing (e.g. methane producer status and hydrogen test for measuring non-digestible carbohydrates) will provide novel tool with increased resolution to differentiate differences in digestion and intestinal metabolism mediated by different microbiota composition and when combined with faecal bomb calorimetry, will provide a new method of measuring gut microbiota fermentation and its contribution to host energy metabolism. Recent studies highlighting an increased potential for "energy harvesting" by the micorbiota of obese individuals, has raised the intriguing possibility that the composition of the gut microbiota may determine the amount of energy a given individual extracts from their diet and thus contribute to weight gain and risk of obesity. However, few recent studies have attempted to accurately measure the energy harvesting potential of the gut microbiota. Using a combination of clinical metabolic calorimetry, bomb calorimetry and faecal microbiota analysis and PTR-MS breath analysis, we will directly measure gut fermentation rates and calculate relative contribution to daily energy intake using specifically designed test meals and subjects of different metabolic risk (e.g. lean v obese individuals). The aim will be to address whether changes in gut microbiota community structure can be reflected in changes in fermentation rate measured by breath analysis, and to calculate, given individual dietary information, the relative contribution to daily energy intake of different gut microbiota community structures (e.g. communities with high or low relative abundance of methanogenic bacteria, keystone species involved in regulating fermentation efficiency and gas management in the gut).

Del. 3.14: Design of PTR-MS based breath test study protocol

Del. 3.15: Ethical approval of additional analysis in participants with different metabolic states and/or digestive dysfunction.

Del. 3.16: Target environment testing of PTR-MS based breath test for identification of metabolic markers defining microbiota fermentation and energy balance.

Description of Work and Role of Partners

ASAA, The Clinical Nutrition Department, Bolzano hospital: A leading centre for Clinical Nutrition in Italy will clinically coordinate (Dr. Lucchin) the FASTMOB study and act as one of the two dietary intervention

centres. Dr Lucchin and Dr Kob, together with their collaborator from the Modena Hospital, Dr Massimo Pelligrini will be responsible for attaining relevant ethic permissions from ASAA, recruiting the FASTMOB cohort in Bolzano, conducting the dietary intervention, distributing test foods/diets, collecting the specified biological samples and conducting clinical measures as described above. In collaboration with Dr Pedrolli, APSS, they will oversee good clinical practice of the study, assess study efficacy and help analyse the data and prepare the study for publication. ASAA will host one early stage researcher and one dietician.

APSS, The Department of Clinical Nutrition and Dietetics, Santa Chiara hospital, Trento: A leading centre for Clinical Nutrition in Italy Dr. Pedrolli will be responsible for attaining relevant ethic permissions from APSS, recruiting the FASTMOB cohort in Trento, conducting the dietary intervention, distributing test foods/diets, collecting the specified biological samples and conducting clinical measures as described above. In collaboration with ASAA Bolzano, Dr Pedrolli will oversee good clinical practice of the study, assess study efficacy and help analyse the data and prepare the study for publication. APSS will host one dietician.

UIBK – Institute for Biological Ageing Research (Professors Grubeck-Loebenstein and Zwerschke) are internationally recognised experts in the field of cell biology, the ageing process, adipose tissue biology, immunology and metabolism. They will provide essential expertise in adipocyte cell biology, unique amongst study partners, and host an ESR to perform cell based studies examining how metabolites derived form the gut microbiota and fasting mimicking EUREGIO foods regulate adipose tissue inflammatory and metabolic (hormonal) output, key processes linked at the biological level to both obesity and ageing**.** Professors Grubeck-Loebenstein and Zwerschke will also be responsible for measuring immune/metabolic parameters from the FASTMOB study and will receive specific budget allocation for this activity and 12 months research assistant/technician (ESR 11). **UIBK - Institute of Breath Research**the group of Professor Mayhew will collaborate with FEM (Tuohy and Biasioli) in developing PTR-MS based analytic methods to study gut microbiota fermentation and energy balance. This work will be carried out by staff of the Nnutrition and Nutrigenomics Unit, FEM, together with ESR 5 and a dedicated budget of Euro30,000 will be provided to UIBK, Professor Mayhew for this task.

UMIT: Professor Siebert and Professor Streicher lead internationally recognised groups expert in public health and the pyschology of risk perception respectively. They will provide identification of health and, therefore diet and metabolic disease related factors of EUREGIO and novel insight into the psychology of how consumers perceive the risk of metabolic disease and relative to life-style change via diet and exercise. They will host ESR1 to work on this project in close collaboration with departments of public health in all three regions of EUREGIO.

EURAC-IB: The Eurac Institute for Biomedicine will collaborate with FEM in analyzing the obese subpopulation in the CHRIS study. The analysis will be performed by ESR2 supervised by Dr Francisco Domingues, Dr. Cristian Pattaro and Dr. Andrew Hicks, with additional support by Dr Kieran Tuohy and Dr.

Francesca Fava at FEM. The EURAC-IB will also perform the genomic analysis and support for the FASTMOB study.

FEM: The Nutrition and Nutrigenomics Unit will collaborate with EURAC-IB in characterising the obesity and CVD risk associations of local foods/diets, through the workshop series, help define a EUREGIO Alpine version of the Mediterranean style diet, provide technical assistance in measuring immune and metabolic parameters for the FASTMOB study, in collaboration with UNITN (Segata) provide microbiota analysis for the FASTMOB study (WP2), and assist Dr Pedroli in running the Trento cohort of the FASTMOB study (about 30 to 40 individuals). They will also design, run and conduct faecal microbiota analysis for obese, lean and participants in the breath analysis experiments with Prof Mayhew. The Metabolomics Unit (Vrhovsek) will provide LC-MS based targeted metabolomics support for the FASTMOB study (WP2, through ESR9). The Computational Biology Department will collaborate with UNITN to provide bioinformatics support for the FASTMOB study. The NN Unit of FEM will provide study support for human studies involving PTR-MS based breath tests at FEM.

Output 3.1: Data mining from existing dietary information within EUREGIO to correlate obesity (BMI) with adherence to specific dietary patterns and identify local foods associated with healthy diet.

Output 3.2: Selection of EUREGIO "fasting mimicking foods" and design of the EUREGIO dietary intervention study protocol.

Output 3.3: Favourable ethics assessment of the FASTMOB dietary intervention in both Trento, Modena and Bolzano Research and Ethics Committees.

Output 3.4: Dietary intervention with EUREGIO fasting mimicking dietary regime.

Output 3.5: Clinical assessment of the efficacy of intermittent fasting and intermittent fasting plus fasting mimicking EUREGIO foods to improve body weight management in the long term and reduce the risk of metabolic disease compared to traditional low calorie diets.

Output 3.6: Scientific evidence in support of EUREGIO fasting mimicking foods to help loose weight and retain weight loss.

Output 3.7: A multi-omics FASTMOB dataset which will be mined for novel mechanistic insight into

obesity, the diseases of obesity and healthy ageing and novel IP.

Output 3.8: Through the workshop series and based in part on results from WP3, we will propose a EUREGIO Alpine version of the Mediterranean style diet, based on the nutritional composition of existing Mediterranean dietary guidelines but using local EUREGIO foods and food culture.

Early Stage Researchers involved.

ESR 1: "Measuring and predicting the interaction of objective factors and their subjective perception: How to promote health and longevity**".**

Host UMIT (Public Health and Psychology and Medical Sciences), Supervisors, Profesors Siebert and Streicher, Apss (Alessandra Schiavuzzi, Pirous Fateh Moghedam and Vittorio Dorigoni, Carlo Pedrolli), ASAA (Dr Lucio Lucchin and Dr Michael Kob), FEM (Tuohy, Fava).

ESR 2: "Characterise the obese subpopulation in the CHRIS study and develop models to predict susceptibility to obesity in the local population". Host, EURAC-IB, Supervisor, Dr. Domingues, collaborators FEM (Tuohy, Fava), EURAC-IB (Hicks, Pattaro).

ESR6: "A two centred dietary intervention with fasting mimicking foods to reduce obesity – EUREGIO obesity cohort study". Host, ASAA, Bolzano hospital, supervisor Lucchin, collaborators APSS (Pedrolli), FEM (Tuohy, Fava, Vrhovsec, Donati), UNITN (Mattivi, Guella, Segata), UIBK (Grubeck-Loebenstein and Zwerschke), EURAC-IB (Domingues, Hicks).

ESR 7: "Dietician to help run FASTMOB cohort in Bolzano". Host, FEM (working location ASAA), supervisor Lucchin, collaborators APSS (Pedrolli).

ESR 8: "Dietician to help run FASTMOB cohort in Trento". Host, FEM (working location APSS), supervisor APSS (Pedrolli), collaborators ASAA (Lucchin).

ESR 10: "Measuring host:microbiota co-metabolite cellular signalling underpinning calorie restriction or fasting mimicking dietary regulation of metabolic health or obesity". Host UIBK, Institute for Biomedical Aging Research, supervisors Grubeck-Loebenstein and Zwerschke, collaborator FEM (Tuohy/Rizzetto).

ESR 11: 12 month research assistant/technician to analyse FASTMOB immune/metabolic parameters. Host UIBK, Institute for Biomedical Aging Research, supervisors Grubeck-Loebenstein and Zwerschke, collaborator FEM (Tuohy/Rizzetto).

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WP Number 4		**Start Month 1 – End Month 36**
WP Title	*Project scientific management and coordination*	
Lead Beneficiary	FEM (scientific coordination)	
Objectives **WP4 Project Management will oversee mainly the scientific coordination and all the related activities.**		
Description of Deliverables		

FEM will host the EUREGIO-EFH project and be responsible for the whole project scientific coordination. A key activity will be to manage relationships with the universities and the other institutions taking part in EUREGIO-EFH and organize the training workshops and scientific research network. These relationships will be regulated by a consortium agreement drawn up with and agreed between the partners once the project has been financed but before the ESR begin their training periods.

Management structures will comprise a **Management Committee** drawn from representative senior management at FEM (Rizzoli, Tuohy and Pironti) and from each EFH partner. It will ultimately be responsible for progress of the project, the preparation of periodical reports and assessemtns, and for project communication. All interactions amongst the partner institutions will be regulated by the consortium agreement which will specify: a) management of the Initiative in its interactions with different institutions; b) obligations and autonomy of the various components of the Initiative; c) modalities and responsibility in the issue of the title by the associated Universities; d) EUREGIO-EFH project funding; e) management of the intellectual property of the discoveries made during the ESR training.

Under the Management Committee, oversight committees will be formed for Research (Research Activity), stakeholders interests (Stakeholder Activity) and training and education (Training Activity). Activity members will be invited from the partner institutions within EUREGIO-EFH.

The **Research Board** will be chaired by leading research scientists proposed by the partner institutions and will be open to all project supervisors/principle investigators involved in the project. The elected chair will report back to the Management Board and communicate on behalf of the Research Board at the EUREGIO-EFH meetings and workshops. The Boards purpose will be to assure not only the highest scientific standards but also to facilitate scientific communication between partner institutions, identify gaps in current scientific skills and expertise, and attempt to fill these research needs both from within the project partner organisations and/or from their wider scientific network. An important aim will be to forge strong, relevant and mutually beneficial collaborations between partner institutions and identify areas of shared interest or opportunities to advance multidisciplinary research within EUREGIO provinces relevant to environment, food and health. An important activity of the Research Board will be to organize the final scientific international congress on “One health – EUREGIO model for environment, food and health: investing in a healthy future” (month 36).

The **Stakeholder Activity** will be jointly chaired by experienced local scientists from each of the three provinces to maximize as far as possible existing collaborative networks between academic, industry and public bodies. The provincial chairs will recruit interested, relevant and energetic partners from the agricultural sector, from the pharmaceutical and nutraceutical industries, industry representative bodies, local public health departments and medical experts. They will also involve local politicians and regional/provincial administrative bodies. The overall aim will be to foster a two-way dialogue, feeding stakeholder interests, needs (especially in terms of training), concerns and collaborations into the EUREGIO-EFH project, and acting as a conduit to transfer new knowledge and scientific discoveries arising from the project to relevant local/regional stakeholders, maximising project dissemination and potential commercialization of the projects research output at the EUREGIO level. The Stakeholder Board will be

responsible for organizing the Consortium Workshops in month 3 (North Tyrol on public health aspects of obesity and healthy ageing in EUREGIO), in month 12 (South Tyrol on the role of nutrition and life-style in obesity and healthy ageing) and in month 24 (Trento, valorisation of EUREGIO food production chain and land-use in the fight against obesity and for healthy ageing). The Board will decide the agenda and participation.

The **Training Activity** will comprise senior academic staff from the partner Universities, a representative from the student/ESR body and a representative from the Stakeholders Board and Management Board. This committee will oversee academic quality and act as an independent advisory body for ESRs. The consortium agreement will stipulate that each ESR will be subject to the rules and regulations of their host institution and also that of the University at which they are registered for the degree of PhD. FEM will allocate the student stipend/salaries for ESR directly to the host institutions at the start of the project according to provisions laid out in the consortium agreement. It will be the responsiability of each host institution to arrange registration of their allocated ESR for professional qualifications/PhD degrees as appropriate. The Training Board will oversee ESR registration, communication of training needs and opportunities. It will organize a series of EUREGIO-EFH training workshops to run in parallel with the EUREGIO-EFH Stakeholder workshops, providing subject specific training and career development strategies for environment, food and health. Importantly, the Training Board will facilitate aspects of ESR training identified as important by the Research Board and the Stakeholder Board to both the ESR student body and to the EUREGIO-EFH University partners. The recruitment and admission of PhD students is done by announcements of competition published in international reviews. Recruitment, appointment and registration of the ESRs at partner Universities will be the responsibility of the host institutions. The Training Board will also oversee transparency of processes for recruiting and admitting candidates making sure the rules and regulations of the host institutions and Universities at which the ESR will be registered for the degree of PhD are compatible. If required, it is the reference body in matters of incompatibility between PhD students and their scientific tutors. Finally, the Training Board will help organize a careers recruitment fair as part of the final international scientific congress (month 36) to assist career development past the life of the current project for the 12 EUREGIO-EFH ESRs, paying particular attention to identifying possible opportunities for career development within the three provinces.

All ESR are offered courses organized by the Training Board and/or their host University. The courses offered will include general research student skills, career development and scientific needs. Subject specific training will be the responsibility of the host institution.

Del. 4.1 Establishment of Research, Stakeholder and Training Boards (month 1).

Del. 4.2 Recruitment, training and report on ends of month 1-17 and 18-35

Del. 4.3 ESR training events (months 3 and 30)

Del. 4.4 Consortium Stakeholder workshops (months 3 [North Tyrol], 12 [South Tyrol] and 24 [Trento].

Del. 4.5: Final EUREGIO-EFH international scientific congress and recruitment fair in Trento, month 36.

WP Number 5		**Start Month 1 – End Month 36**
WP Title	*Dissemination & Exploitation*	
Lead Beneficiary	GECT, (all partners)	

Description of Work and Role of Partners

WP 5, led by GECT, will be responsible for facilitating, maximising and recording project dissemination and exploitation of scientific know-how arising from the project in compliance with the consortium agreement. A major aim will be to energetically engage with the agri-food industry, health sectors and pharmaceutical industries to attract inward investment in EUREGIO environment, food and health research. Starting from existing scientific collaborations of the partner institutions, we will build a large international scientific research network to facilitate EUREGIO involvement in projects funded by the European Commission.

Description of Deliverables

Dissemination to the scientific community, the general public and stakeholder engagement is central to the success for the EUREGIO-EFH. Communication will be divided into internal and external actions. Among priorities of this communication plan is reaching the better dissemination results through innovative, effective and ecological tools, keeping the costs to the minimum. The EUREGIO-EFH partners will benefit from the coordination role of the FEM-CRI Communications Office which operates under the CRI Directorate, whose expertise and experience in communication of scientific data and environment, food and health related news is sound. For internal purposes, this dissemination strategy will provide EUREGIO-EFH members the instruments to keep updated on results obtained by all partners of the different WPs, in order for them to deliver efficient dissemination. Internal communication will be conducted via email, regular teleconferences, and periodic face-to-face meetings centred around the ESR training events (months 3 and 30) and Consortium Stakeholders Workshops around other workshops (months 3, 12, 24 and 36). Shared documents (including administrative project documents, preliminary data reports and publications) will be stored in ownCloud, giving partners access at all times. FEM will set up a EUREGIO-EFH project website with space given to deliver information to both internal and external audiences. External communication is intended to reach out to the civil society, the scientific community and the wider stakeholders. Details about actions to be taken in internal and external communication plan are described in **Table 2: EUREGIO-EFH events**. To guarantee the sustainability of the project over the 36 months covered by the call, great relevance will be given to economic valorisation of the research results

through synergic and integrated actions.

Main Communication and Dissemination tools:

- 1. Scientific community (SC) (All the WPs' and EUREGIO-EFH partners) meetings and workshops: EUREGIO-EFH participants and partners will all be involved in the dissemination of scientific data in appropriate meetings and symposia and through publication of articles in peer reviewed journals. Periodic virtual meetings will help to keep participants updated on the project development. The Research Cluster space on the website will include a private area where consortium members will have priority access to news and to upload and review documents. Consortium Stakeholder workshops (months 3, 12 and 24) are planned, during which partners and stakeholders will contribute to the dissemination of the state-of-art, present new data and generate a position statement to be published locally and internationally as a position statement on the workshop themes decided by the Research, Stakeholder and Management Boards.

Integration into Courses: Seminars, workshops and special courses will be organized by each University partner dedicated to ESR/student training in key subject specific and generic skills, as far as possible drawing on existing provisions within their doctoral training programmes.

Month 36 of the project will see an final international congresss on the One health research theme to aid broad dissemination of the EUREGIO-EFH results, to maximize our exposure to the international scientific community and to focus attention of local, national and international agri-food, pharmaceutical and health related industries on the EUREGIO-EFH results and the scientific infrastructure and capabilities of the EUREGIO partners.

- 2. Civil society (CS): different types of materials for event dissemination will be created in order to provide a coordinated image of the project:

a) EUREGIO-EFH website: the project space on web site will represent one of the main tools to diffuse the public image of EUREGIO-EFH project. The site will allow users to readily collect on-line information about the project and other related issues, which might be of interest to CS. Newsletter will be sent on each update of the website to registered people and stakeholders. The EUREGIO-EFH website will be launched at the start of the project and regularly updated during the three years. It will include all relevant information about the project, links, gateway to the data base etc. Items to be published on the website will be the following: Description of the project including a summary, a standard EUREGIO-EFH consortium presentation and a downloadable leaflet. • Project partnership (with links to partners' web site) • project description • Publications /Analysis, etc./ • Events • Contacts • Relevant Links • Join the EIFAEL Research Network.

b) Mass Media: FEM-CRI Communications Office will ensure the maximum diffusion of EUREGIO-EFH goals and results thanks to their possibility to reach out to general public through

conventional and new media. Regular TV appearances and radio interviews on the main national channels, national newspapers and magazines articles will guarantee a very large coverage for the EUREGIO-EFH project. Dissemination of the results to civil society will be supported also by FEM (http://www.fmach.it/eng/Press/Press-Office) through press releases and by TV interviews ("A come Alpi" with national and European coverage: on ODEON TV circuit in prime time on the national terrestrial digital, to analog and SKY - channel 914). Social media and network: An EUREGIO-EFH project page will be set up on Facebook as well as a Twitter account. Through these popular media, information on the project and all the relevant results and events will be easily and effectively disseminated to civil society and stakeholders.

Level	**Means of Communication**	**Responsible Partner**	**Target groups**
Internal	Virtual meetings	Communication coordinator	RC partners
External	Scientific articles/posters/talks	All RC partners	SC
External	RC website	Communication coordinator	SC/CS
External	TV interviews	Communication coordinator	CS
External	Facebook page – Twitter account	Communication coordinator	CS
External	Newspaper/magazines	Communication coordinator	CS
External	Workshops/Seminars/Meetings	Communication coordinator	CS + Stakeholders
External	RC final conference	Communication coordinator	CS + Stakeholders

Del 5.1: EUREGIO-EFH website and social media sites (FEM, month 3)

Del 5.2: Dissemination through public media (GECT, all, month 36)

Del 5.3: Disseminate scientific results through publications in peer reviewed expert journals (All, month 36)

Table 4: EUREGIO-EFH TRAINING NETWORK, list of post-graduate early stage researcher projects.

ESR	WP	Project title	Lead Host	Supervisor	Collaborators
1	3	Measuring the interaction of objective factors and their subjective perception: How to promote health and longevity	UMIT (PH)	Siebert/ Streicher	APSS, ASAA
2	3	Characterise the obese subpopulation in the CHRIS study and develop models to predict susceptibility to obesity in the local population (including gneotyping for FASTMOB).	EURAC	Domingues	FEM (Fava)
3	1	Measuring the impact of farming production system on the nutritional quality of EUREGIO dairy products.	UNIBZ	Gauly	FEM (Franciosi)
4	2	Measuring the nutritional quality of local plant based EUREGIO foods	LRC	Oberhuber	FEM (Vrhovsek)
5	2	Measuring the impact of EUREGIO foods and fasting mimicking diets (FASTMOB study) on the human gut microbiome.	FEM	Tuohy	UNITN (Segata)
6	3	A two centred dietary intervention with fasting mimicking foods to reduce obesity – EUREGIO obesity cohort study (ESR)	ASAA	Lucchin	APSS, FEM (Fava) UNITN (Mattivi)
7	3	Dietician (early stage career) to help run FASTMOB cohort in Bolzano	ASAA/FEM	Lucchin	APSS, FEM (Fava)
8	3	Dietician (early stage career) to help run FASTMOB cohort in Trento	APSS/FEM	Pedrolli	ASAA FEM (Fava)
9	2	Measuring the metabolic implications of fasting mimicking foods in the obese.	FEM	Vrhovsek	UNITN (Mattivi) APSS, ASAA
10	3	Measuring host:microbiota co-metabolite cellular signalling underpinning calorie restriction or fasting mimicking dietary regulation of metabolic health or obesity	UIBK	Grubeck-Loebenstein Zwerschke	FEM (Rizzetto)
11	3	12 month research assistant/technician to analyse FASTMOB immune/metabolic parameters.	UIBK	Grubeck-Loebenstein	FEM (Fava) APSS, ASAA
12	2	NMR-based lipidomics of biofluids (serum and urine) in volunteers undergoing suitable diets	UNITN	Guella	FEM (Vrhovsek), APSS, ASAA

Fellow *ESR 1*	Host Institution UMIT	Partner Institution(s) APSS, ASAA, FEM	PhD enrolment (Y/N) Yes	Start date *(e.g. Month 6)* *0*	Duration *(e.g. 36 months)* *36*	Deliverables *3.11-3.13*

Project Title and Work Package(s) to which it is related:

Project Title ESR1: Measuring and predicting the interaction of objective factors and their subjective perception: How to promote health and longevity

WP3: Health**Supervisor:** UMIT (Professors Siebert and Streicher Co-investigator Dr. Beate Jahn)

Collaborators: APSS (Carlo Pedrolli, Public Health Department), ASAA (Dr Lucio Lucchin and Dr Michael Kob, Public Health Department), FEM (Tuohy, Fava).

Objectives:

Building on the assumption that specific factors of lifestyle (e.g., exercise) and food (e.g., fresh fruit and vegetables) promote health in general and healthy ageing in particular, this projects pursues the following objectives:

1. To identify core factors and the systemic interactions between core factors (e.g., healthy eaters get involved in sport activities; sports people are aware of healthy nutrition), and estimate their impact on health;
2. To measure the subjective perception and awareness of the EuRegio citizens regarding identified core factors;

(1) In order to reach the first objective, we conduct an intensive review of the relevant current literatures and, more importantly, re-analyse existing datasets of partner organizations with state-of-the-art statistical methods (e.g., causal inference). The datasets should include repeated measurements on behaviour and risk factors (e.g., food consumption, eating behaviour, and/or leisure activities) and health outcomes (e.g., health indices, morbidity) over time from EuRegio citizens. This procedure enables to identify environment, food and behaviour related core factors of health and longevity, and to understand the interactions, interdependencies and causal pathways of these factors.

(2) In order to understand the psychological mechanisms why people do or do not engage in a healthy lifestyle, in a first step we explore the individual, subjective understanding of health relevant factors, the perceived importance and risk of these factors, the attitude towards the factors and according behaviour.

In a second step, including the results of objective (1), we compare individual perceptions of factors with their evidence-based relevance in order to identify potential differences and mismatches.

Expected Results:

Major expected results emerging from this project are:

1. Evidence-based and recommendations for decisions makers, which influencing factors should be changed in order to promote health and longevity among EuRegio citizens.
2. Interdisciplinary insights in the interaction between the core factors of the environment and food regarding health and longevity on the one side, and the individual perception of these factors, the attitude towards them and according behaviour on the other side.

Planned secondment(s): *Host, timing, length and purpose*

One PhD student will be working in this project for three years each. They will be based at UMIT, but will regularly visit partner institutions (preferably including one longer stay of a minimum of six weeks) in order to learn, to network, and to collect and analyse data.

Fellow	**Host Institution**	**Partner Institution(s)**	**PhD enrolment**	**Start date**	**Duration**	**Deliverables**
ESR2	**EURAC IB**	**FEM/ASAA**	**Yes**	***0***	***36***	***2.06, 3.01, 3.02, 3.06***

Project Title: Characterise the obese subpopulation in the CHRIS study and develop models to predict susceptibility to obesity in the local population (including genotyping for FASTMOB).

WP3: Health

Supervisor: EURAC-IB (Domingues)

Collaborators: FEM (Tuohy, Fava).

Objectives:

The ESR will characterize the obesity landscape in the region and will investigate obesity contributing factors based on the data collected within the CHRIS study. Predictive models will also be developed to assess obesity susceptibility based on the relevant genetic, metabolic and life-style factors that have been identified. The work will include a search for rarer genetic variants related to obesity that are more frequent in the local population and that help better characterize obesity in the local population. Potential causal relationships will be explored by Mendelian randomization. The relevant genetic variants and metabolic signatures that are identified within the CHRIS study will be used to explore potential obesity subgroups with common genetics or metabolic signatures and with similar responses to the dietary interventions within the FASTMOB study.

Expected Results:

Identify genetic factors, metabolomics signatures, as well as diet and exercise patterns relevant to obesity in the local population and provide models to predict susceptibility to obesity.

Planned secondment(s): *Host, timing, length and purpose*

The work on the CHRIS data analysis will be performed at the EURAC EURAC-IB in collaboration and under advice from FEM (Tuohy, Mattivi) and ASAA (Lucchin). FASTMOB genotypes and outcomes will be analysed under guidance from the FASTMOB team and EURAC EURAC-IB.

Fellow	**Host Institution**	**Partner Institution(s)**	**PhD enrolment**	**Start date**	**Duration**	**Deliverables** *1.5-1.7, 2.2*
ESR3	**UNIBZ**	FEM,EURAC	**Yes**	***0***	***36***	

Project Title: Measuring the impact of farming production system on the nutritional quality of EUREGIO dairy products.

WP1: Environment

Supervisor: UNIBZ (Prof. Gauly)

Collaborators: FEM (Rizzoli, Franciosi).

Objectives:

European dairy cattle sector has undergone a profound change in the last decades motivated by political (the quota system) and economic contexts (the progressive reduction of benefits). Farm number has been decreasing steadily while milk yield per cow and farm size have increased. A strategy to increase the economic outcome on farm level was the intensification. However, this may also have had negative side effects on animal health, animal welfare, environment and the quality of the products. Therefore international negotiations have introduced restrictions and requirements to reduce negative environmental effects of dairy farming, as well as measures to ensure the general well-being of their animals in terms of health, welfare and protection. However, these measures have also affected productivity and profitability of the systems. This, together with the expected price reductions are a challenge that compromise the sustainability of the dairy cattle farms in Europe and especially in the regions of this project. Therefore it is urgently needed to estimate the economic (including product quality) and environmental effects of traditional (Low-Input) and modern (High-Input) systems. Factors with relevant impact are facilities, nutrition, reproductive performance, genetics and health management. The evaluation of the outcome of such interrelations requires the concurrent integration of so many factors as possible, which will be measured in the project. The specific objective will be to compare traditional and intensive dairy production systems on the following levels:

- environment,
- animal health and welfare,
- performance,
- economical outcome and
- milk (product) quality.

Additionally, based on possible milk quality differences marketing strategies will be developed and the impact on the economical outcome estimated.

1. Microbiological sampling on farms/dairy products operating at different intensity levels. Focus on isolation of lactic acid bacteria and metagenomic 16S based profiling of different samples.
2. Collect data on antibiotic use and residues in milk produced at high and low intensities and also information at international level on antibiotic residues in high intensity produced milk.

Expected Results:

In brief, the result of the project will be a comprehensive dairy farm system analyses (Low- and High-Input), that will be enhanced with environmental, animal welfare and product quality submodels. This will enable to estimate the sustainability of the dairy production systems from the technical, economic, environmental, welfare and quality point of view. Based on potential product differences marketing strategies can be developed and guidelines for practical farming developed.

Planned secondment(s): *Host, timing, length and purpose*

ESR5 will spend periods of training at FEM.

Fellow *ESR4*	Host Institution LRC	Partner Institution(s) FEM, UNIBZ, UNITN	PhD Enrolment Yes (UNIBZ or UNITN)	Start date *(e.g. Month 6)* *0*	Duration *(e.g. 36 months)* *36*	Deliverables *2.1*

Project Title: Measuring the nutritional quality of local plant based EUREGIO foods

WP2: Food

Supervisor: LRC (Oberhuber)

Collaborators: FEM (Vrhovsek, Tuohy), UNITN (Mattivi)

Objectives:

The scope of this work is the characterization of plant-based foods from local production to obtain detailed information on the nutritional quality of EUREGIO foods, with a special focus on new as well as old local plant species.

In particular, this work package pursues the following objectives:

- Deployment of modern analytical methods based on mass spectrometry coupled to separation techniques for the identification and characterization of active compounds relevant for human health, such as polyphenols, anthocyanins, and vitamins
- Determination of the content of primary and secondary metabolites like single sugars and organic acids with ion chromatography
- Determination of the antioxidant capacity and total reductive potential of EUREGIO foods with UV/VIS; determination of the fibre content, including pectins, with enzymatic and gravimetric methods in old and new plant species; measurements of total fat content in fat-rich foods with extraction/gravimetric methods and identification of the fat composition in selected samples with GC-FID; characterization of minerals with ICP-MS.

Expected Results:

The main expected results from this WP are:

- Identification and quantification of bio-active compounds relevant for human health in local plant-based EUREGIO foods
- Characterization of the chemical composition of foods used in this study
- Nutritional information of the foods to evaluate beneficial aspects for human health

Planned secondment(s): *Host, timing, length and purpose*

Laimburg Research Centre will host a PhD student enrolled at a collaborating University during the whole project (36 months). He/She will be working in the Laboratory for Flavour and Metabolites to carry out the analyses described above. They will also spend periods of training at FEM.

Fellow	**Host Institution**	**Partner Institution(s)**	**PhD enrolment**	**Start date**	**Duration**	**Deliverables**
ESR5	**FEM**	APSS, ASAA, UNITN, (Segata)	**Yes (UNITN)**	***0***	***36***	***2.9, 3.04, 3.06, 3.14, 3.15, 3.16***

Project Title: Measuring the impact of EUREGIO foods and fasting mimicking diets (FASTMOB study) on the human gut microbiome.

WP2: Food

Supervisor: FEM (Tuohy)

Collaborators: UNITN (Mattivi, Segata), APSS, ASAA (FASTMOB study).

Objectives: This project will provide the microbiological and metagenomic expertise to assess the impact of the FASTMOB diet on the human gut microbiota and to characterise the microbiota present in EUREGIO foods and collaborate with ESR 16 in measuring the contribution of the human gut microbiota to host energy intake through fermentation. Recognising that the human gut microbiota is both shaped by diet and in turn shapes the biological impact of our diet, we will measure how the FASTMOB diet impacts on the human gut microbiota. Using state of the art next generation sequencing and the bioinformatic expertise at UNITN, FEM and UNIBZ, we will link changes induced by the FASTMOB diet in the composition and activity of the intestinal microbiota with specific physiological biomarkers linked to metabolic and immune health (e.g. antrophometric measures, blood lipids, markers of insulin/glucose metabolism, inflammatory markers. The aim will be to provide cause and effect evidence in support of dietary modulation of the gut microbiota, even to strain level, and improved markers of immune and metabolic health. This student, with the support of the Nutriton and Nutrigneomics unit at FEM, and under the medical supervision of APSS and ASAA will manage subjects recrtuied for breath analysis and microbiome profiling.

In addition, using a combination of next generation sequencing and traditional culture based microbiology,

this studentship will provide novel compositional analysis of the food associated microbiome of EUREGIO foods. The safe food associated microbiota is now recognised as an important determinant of immune education and tolerance, and also has a potential role in chemical modifying the structure and function of other nutrients and macromolecules present in foods. We will determine the load and diversity of the EUREGIO food associated microbiota with the aim of identifying specific local/regional dietary patterns with elevated levels intake of safe microbial passengers capable to improving host immune and metabolic function.

Expected Results:

- High resolution characterisation of the impact of the FASTMOB diet on the composition and metabolic potential of the obese gut microbiota.
- Characterisation of the load and biodiversity of the EUREGIO food associated microbiome and assessment of their contribution to human immune and metabolic health.
- Identification and curation of a selection of EUREGIO food grade microorganisms which can then be stored and screened for biological activities and potential as probiotic food ingredients.
- A young independent scientist expert in food and intestinal microbiology, metagenomics and microbiome analysis.

Planned secondment(s): *Host, timing, length and purpose*

This student will be based at FEM but will spend periods of training at UNITN (up to 6 months in total).

Fellow ***ESR6***	**Host Institution** **ASAA**	**Partner Institution(s)** **FEM, APSS**	**PhD enrolment No.** **Medical doctor**	**Start date** ***0***	**Duration** ***36***	**Deliverables** ***3.03-3.05***

Project Title A two centred dietary intervention with fasting mimicking foods to reduce obesity – EUREGIO obesity cohort study (ESR)

WP3: Health

Supervisor: ASAA, Bolzano hospital (Lucchin)

Collaborators: APSS (Pedrolli), FEM (Tuohy, Fava, Rizzetto, Vrhovsec, Donati), UNITN (Mattivi, Guella, Segata), UNIBZ (Gobbetti), EURAC-IB (Domingues, Hicks)

Objectives:

This ESR, a clinical fellow/medical doctor will be responsible for finalising the study protocol, finalising the ethics assessments (both of which will have been presented and assessed by the Ethics Committees of APSS and ASAA prior to the start of the project). They will oversee recruitment of patients, randomisation, food deliveries, medical/clinical measurements and data storage at both study centres. They will act as study coordinator, visiting both study sites and making sure the study is run according to protocol and that samples and data are stored/measured correctly. They should be based in Bolzano as the main study centre. They will participate in clinical measurement of study outcomes, assessment of clinical significance, data analysis and interpretation, report writing and drafting of the final scientific publications. They will work in under the medical supervision of Dr Lucchin in Bolzano and coordinate with Dr Pedrolli in Trento.

Expected Results:

- Coordination of the FASTMOB cohorts in Bolzano and Trento
- Clinical assessment of the efficacy of the FASTMOB dietary/life-style intervention.
- Scientific assessment, reporting, dissemination and publication of the FASTMOB study results

Planned secondment(s): *Host, timing, length and purpose*

This fellow will spend periods of training at FEM and APSS.

Fellow	**Host Institution**	**Partner Institution(s)**	**Dietician/ research nurse**	**Start date**	**Duration**	**Deliverables**
ESR7	**FEM**	**FEM, APSS**		***6***	***30***	***3.03-3.05***

Project Title: Dietician to help run FASTMOB cohort in Bolzano (24 person months)

WP3: Health **Supervisor:** ASAA (Lucchin), Fem (Tuohy/Fava)

Collaborators: APSS (Pedrolli)

Objectives:

This ESR, a dietician graduate, will be based at FEM and work at ASAA Hospital, Bolzano, and will be responsible for recruitment of Bolzano obese participants, for running the study, food deliveries/allocation, record keeping (including a study report form for each patient/subject). They will also take responsibility for dietary analysis (FFQ and food diaries) both for the FASTMOB study and also for correlating specific local/EUREGIO food intake associated with diets with high adherence to the Mediterranean style diet using existing data from APSS, and in collaboration with other researchers in ASAA, UMIT, EURAC (the CHRIS study) and at FEM (AVAG, MiaCoure, PreBIOIL studies).

Expected Results:

Recruitment and study implementation for the FASTMOB cohort in Bolzano.

Planned secondment(s): *Host, timing, length and purpose*

This ESR will receive periods of training at FEM and APSS.

Fellow	**Host Institution**	**Partner Institution(s)**	**PhD enrolment**	**Start date**	**Duration**	**Deliverables**
ESR8	**FEM**	**APSS, ASAA**	**No (ditician)**	***6***	***30***	***3.03-3.05***

Project Title :Dietician to help run FASTMOB cohort in Trento (24 person months)

WP3: Health

Supervisor: APSS (Pedrolli), FEM (Tuohy/Fava)

Collaborators: ASAA (Lucchin)

Objectives:

This ESR, a dietician graduate, will be based at FEM and work at Santa Chiara, Trento, and will be responsible for recruitment of Trento obese participants, for running the study, food deliveries/allocation, record keeping (including a study report form for each patient/subject). They will also take responsibility for dietary analysis (FFQ and food diaries) both for the FASTMOB study and also for correlating specific local/EUREGIO food intake associated with diets with high adherence to the Mediterranean style diet using existing data from APSS, and in collaboration with other researchers in ASAA, UMIT, EURAC (the CHRIS study) and at FEM (AVAG, MiaCoure, PreBIOIL studies).

Expected Results:

Recruitment and study implementation for the FASTMOB cohort in Trento.

Planned secondment(s): *Host, timing, length and purpose*

This ESR will receive periods of training at FEM and ASAA

Fellow	**Host Institution**	**Partner Institution(s)**	**PhD enrolment**	**Start date**	**Duration**	**Deliverables**
ESR9	**FEM**	**UNITN/ ASAA/APSS**	**Yes (UNITN)**	***0***	***36***	***2.3-2.5, 2.7, 3.04, 3.07-3.10***

Project Title: Measuring the metabolic implications of fasting mimicking foods in the obese.

WP3: Health

Supervisor: FEM (Vrhovsek)

Collaborators: UNITN (Mattivi, Guella), APSS (Pedrolli), ASAA (Lucchin)

Objectives:

The human metabolome, the profile of molecules or chemicals present in human biofluids (blood, urine, faecal water) is a combination of molecules encoded and produced by the human genome, molecules produced via the co-metabolic processes of the human genome and our resident microbiota, and molecules ingested with our food and transformed by host-microbiota co-metabolism. The metabolome is modified by diet and the flux in composition and relative concentrations of these molecules plays a critical role regulating human physiological processes, including those involved in metabolic disease risk and healthy ageing. Using a unique combination of high resolution LC-MS (FEM/UNITN) and NMR (UNITN) based metabolomics, we will characterise the changes induced by the diet on metabolite profiles present in blood, urine and faecal water collected from obese subjects participating in the FASTMOB dietary intervention. Using both targeted (bile acids, short chain fatty acids, amino acids) and untargeted approaches, this studentship will provide both a qualitative and quantitative picture of how the FASTMB diet changes metabolite profiles in obese subjects. Moreover, partners at EURAC will be responsible for genotyping the FASTMOB cohort, allowing us to measure the relative influence of genotype and environmental (diet and microbiota) factors in determining the composition and concentrations of key molecules regulating immune and metabolic processes. This recognised the important interplay between genes and environment in determining obesity risk and metabolic/immune health, and will provide new insight into how diet can be used to modulate disease risk relative to underlying genetic predisposition.

Expected Results:

- Measurement of how the FASTMOB diet can impact on metabolite profiles and concentrations in blood, urine and faecal water of obese subjects.
- New mechanistic insight into how diet shapes key molecular regulators of immune and metabolic function in obese individuals.
- Confirmation of the role of specific EUREGIO food bioactive components in regulating immune and metabolic processes linked to obesity and healthy ageing in humans
- New understanding of how metabolome or metabotype is shaped by genotype in obese individuals.
- A young independent scientist expert in food and human metabolomics, data-analysis, chemometrics and co-analysis of omics level datasets.

Planned secondment(s): *Host, timing, length and purpose*

ESR 13 based at FEM will undertake periods of training at UNITN.

Fellow	**Host Institution**	**Partner Institution(s)**	**PhD enrolment**	**Start date**	**Duration** *Months*	**Deliverables**
ESR10	**UIBK**	FEM	**Yes (UIBK)**	***0***	***36*** (+12 months unpaid submission time)	***3.08, 3.09, 3.10***

Project Title: Measuring host:microbiota co-metabolite cellular signalling underpinning calorie restriction or fasting mimicking dietary regulation of metabolic health or obesity

WP 3: Health

Supervisor: UIBK (Grubeck-Loebenstein, Zwerschke)

Collaborators: FEM (Tuohy/Rizzetto)

Testing host:microbiota co-metabolites as candidates for caloric restriction (CR) mimetics (PhD biology, metabolomics analysis (Rizzetto, FEM), adipose tissue cell biology (Zwerschke group, UIBK) and peripheral blood mononuclear cell biology (Grubeck-Loebenstein group, UIBK).

Background/Objectives:

Obesity is a major public health problem (1). Caloric restriction (CR) prevents obesity. It is however unlikely that a big CR movement among the human population will arise and CR interventions are frequently unsuccessful for substantial and persistent weight loss. Thus, there is a need for CR mimetics, agents which mimic beneficial effects of CR without restricting caloric intake (2). The adipose tissue phenotype in obesity is characterized by accumulation of senescent adipose progenitor cells (APCs) (3) and an increase in size and dysfunctionality of adipocytes associated with detrimental metabolic effects (1). Health-promoting effects of CR include reduction of adipocyte size and fat mass with associated favourable metabolic effects (1) and beneficial effects on APCs, such as reduced insulin/mTOR signalling, postponement of cellular senescence and reduced adipogenic capacity (3, 4). PBMCs may reflect metabolic changes taking place in fat tissue, can be easily obtained and provide therefore a useful tool to test the effects of new preventive and therapeutic measures (6). The Zwerschke group has shown that CR mimetics such as resveratrol, a polyphenol, slow adipocyte development and accumulation of fat mass in the 3T3-L1 preadipocytes/adipocyte model (2). Many of the metabolites linked to CR, and its effect on both obesity and healthy ageing, are metabolites produced by the combined activities of the human genome and gut microbiota, such as short chain fatty acids, ketone bodies, bile acids, and small phenolic acids (5).

The major aim of the research project is to test whether host:microbiota co-metabolites exert similar beneficial effects on metabolic health and prevention of obesity as CR interventions. To this end it should be analysed whether specific host:microbiota co-metabolites (purified and provided by Tuohy group, FEM) mimic CR-like responses on adipose tissue cells (Zwerschke group, UIBK) and peripheral blood mononuclear cells (PBMCs) (Grubeck-Loebenstein, UIBK).

Specific tasks:

1. Measuring impact of host:microbiota co-metabolites on CR signalling pathways (e.g. insulin/mTOR signalling) in mouse 3T3L1 preadipocytes/adipocytes) and human adipose progenitor cells (APCs)/adipocytes (Zwerschke group, UIBK).

2. Testing effects of host:microbiota co-metabolites on proliferation and terminal adipogenic differentiation in mouse 3T3L1 preadipocytes and human APCs (Zwerschke group, UIBK).

3. Testing metabolic effects of host:microbiota co-metabolites on adipocytes (Zwerschke group, UIBK).

4. Testing effects of host:microbiota co-metabolites on CR signalling pathways and immune effector function in PBMCs (Grubeck-Loebenstein, UIBK).

5. Conducting differential metabolomics analysis in preadipocytes, adipocytes and PBMCs in response to host:microbiota co-metabolites, which turned out as promising CR-mimetic candidates in task 1 -5. Cell culture work should be done in UIBK groups (Zwerschke, Grubeck-Loebenstein), subsequent metabolomics analysis in FEM group (Tuohy). This work should link metabolome phenotype to CR phenotype.

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Expected Results:

It is expected that at least some of the host:microbiota co-metabolites tested mimic effects in adipose tissue cells and PBMCs similar to caloric restriction and fasting dietary regimes.

Moreover, the planed experiments should give indications of metabolome phenotypes induced by host:microbiota co-metabolites in adipose tissue cells and PBMCs.

Planned secondment(s): *Host, timing, length and purpose*

One PhD student will be working on the project for four years (36 months paid by EUREGIO-EFH). He/she will have his/her based at the UIBK, but will spend time (a minimum of six weeks each year) at the FEM in order to learn and to help with the planned work in metabolomics.

Fellow ***ESR11***	**Host Institution** **UIBK**	**Partner Institution(s)** FEM	**Research assistant/ technician**	**Start date** ***24***	**Duration** ***Months*** ***12***	**Deliverables** **2.9**

Project Title: 12 month research assistant/technician to analyse FASTMOB immune/metabolic parameters.

WP 3: Health

Supervisor: UIBK (Grubeck-Loebenstein, Zwerschke)

Collaborators: FEM (Tuohy/Rizzetto)

Background/Objectives:

This research assistant/technician will provide laboratory support for the FASTMOB study, performing mainly ELISA based assays to measure human immune, hormonal and metabolic parameters in blood samples collected from the dietary intervention in Bolzano and Trento.

Expected Results:

Measurement of how immune, hormonal and metabolic parameters change upon dietary intervention with different fasting regimes in obese individuals during the FASTMOB study.

Planned secondment(s): *Host, timing, length and purpose*

Fellow	Host Institution	Partner Institution(s)	PhD enrolment	Start date	Duration	Deliverables
ESR12	**UNITN**	**FEM/APSS/ASAA**	**Yes** (UNITN)	***0***	***36***	***2.2, 2.8, 3.04***

Project Title: NMR-based lipidomics of biofluids (serum and urine) in volunteers undergoing suitable diets

WP3: Health

Supervisor: UNITN (Guella)

Collaborators: FEM (Vrhovsek), APSS, ASAA (FASTMOB study)

Objectives:

The greatest advances in lipidomics investigations have relied on two main analytical techniques, nuclear magnetic resonance (NMR) and mass spectrometry (MS), the latter often coupled to a liquid chromatography (LC) system.

As a non-destructive and highly reproducible technique, NMR is often used in lipids analysis for *ab initio* structural elucidation of new lipid species; however, due to its intrinsically quantitative response, it can be used even for reliable quantifications of lipids mixtures obtained by tissues, body fluids and cell cultures. NMR spectroscopy has some advantages over other techniques which include (i) the need for no or minimal sample preparation, (ii) the ability to preserve a sample so that it can be analysed further by other techniques if necessary , (iii) the ability to detect multiple metabolites with a single experiment; hence, there is no need to run specific assays for each metabolite of interest and (iv) the ability to provide highly reproducible results

The main aims of this ESR in the project will be:

- Apply advanced NMR methodologies by carrying out extensive 1D and 2D NMR measurements on lipid extracts obtained from body fluids of volunteers (approximately 200 volunteers undergoing suitable diets x 6 months) at APSS and ASAA. ^{1}H- and ^{31}P- NMR spectra (even ^{13}C- NMR if the available amount of extracts will be sufficient) will be acquired on an high resolution NMR instrument and analysed. ESR13 will work in parallel trough LC-MS and GC-MS measurements on the same samples.

- Apply an NMR-based metabolomics approach to the polar fraction of volunteers biofluids (serum and/or urine samples) at least in some targeted samples where this information is thought to be

relevant. Several biofluid metabolites (aminoacids, glucosides, cholines, intermediates of the tricarboxylic acid cycle, 3-HB (3-Hydroxybutyrate) and TMAO (trimethylamine N-oxide)) can be quantified by ^{1}H-NMR spectroscopy

- Define through NMR spectroscopy the lipid profile of some special foods, developed for this study and proposed in the diet of participants

Expected Results:

^{1}H- and ^{31}P- NMR spectra (even ^{13}C- NMR if the available amount of extracts will be sufficient) will be acquired on an high resolution NMR instrument and analysed. ESR13 will work in parallel trough LC-MS and GC-MS measurements on the same samples. This NMR/MS joined approach is expected not only to afford an accurate and reliable description of the intermediates and the end-products of the metabolism in the volunteers but also to discover useful molecular markers of their disease.

Planned secondment(s): *Host, timing, length and purpose*

One PhD student will be working on the project at UNITN but he/she will spend periods of training an data analysis at FEM .

PROJECT MANAGEMENT

WP4 and 5 will be responsible for the management, dissemination and exploitation of all aspects of the project, ensuring that the different tasks are performed according to the project plan and budget and that the results of the project. A detailed discription of the EUREGIO-EFH management processes (finance, reporting, timings) are presented in the accompaning “consortium agreement”.

FEM will be responsible for WP4 and GECT will lead WP5. Wp4 will provide administrative and reporting guidance to the project partners and be responsible for internal evaluation and risk management. Face to face meetings and teleconferences will be organized in appropriate frequency to secure the continuity of the project. The documentation of meeting results will be the responsibility of the respective chairs of the meetings, archiving and internal distribution will be provided by the Management Committee through the intranet site. Coordinated and appropriate outreach activities will be provided. Templates and work at distance tools (i.e. intranet site, open source teleconference softwares, templates, appropriate management structures and processes) will ensure smooth running of the project.

Dissemination and exploitation has a role in all phases of the project and will be coordinated by GECT in WP5. However, all partners will be expected to play active roles in their respective theaters of operation be they scientific, political, medical or social. Relevant target groups, actors and stakeholders will have to be informed about the the overall results of the project. Specific dissemination efforts will be made for raising awareness of potential exploitation partners in health care and age- and obese-related disease treatment and care. Training elements will be offered first to early researchers and clinicians and patient groups and other selected care providers willing to test the innovative solutions identified within the

project. Included in these WPs will also be inclusion of preliminary and final results in decision making databases and the strategy development for the transfer of the results into other European regions.

A major emphasis will be placed on identifying and exploiting investment opportunities from both public (e.g. EU) and private (e.g. Agri-food industry) at national and international levels. The aim is to attract significant inward financial investment into EUREGIO environmental, food and health research, both during the life-time of this current project and going forward to the medium and long-terms.

EUREGIO-EFH organisational structure

WP4 Management will oversee implementation of the project, structures for recruiting of ESR (transparency and open processes already in place within the EUREGIO Universities and academic partner), allocation of finance to host institutions, establishment of management board, and will establish and report to the boards for research, stakeholders and training. This WP is lead by FEM.

In order to make sure that the project will be properly coordinated and the cooperation between all partners will run as smoothly as possible, an effective management structure will be installed. This structure will be in place for the whole duration of the project (36 months) and consist of:

- Management Committee (MC)

With sub-committees/responsible officiers (Figure 2) for:

  - Research Activities (RA)
  - Stakeholder Activities (SA)
  - Training Activities (TA)

This management structure is designed to:

- ensure that the infrastructure works as an integrated entity;
- maximize the complementarities and synergies between its members;
- guarantee efficient and broad transnational access to the facilities;
- coordinate the partners and stakeholders efforts;
- assess the project progress;
- optimise the knowledge and the use of the infrastructure by the scientific and industrial community.

In particular, FEM will host the EUREGIO-EFH project and be responsible for project administration and management together with the Management Committee, (MC). A Consortium Agreement (CA) will be prepared upon legal advice. The CA will state the objectives of the collaboration within parties and their corresponding expected deliveries. The CA will define the project management structure between the partners including roles and responsibilities, budget allocation, ESR distribution, grant transfer process, access rights to pre-existing know-how and novel knowledge from the project, IPR, exploitation, dissemination activities, publication rights and processes, liabilities, knowledge disclosure and confidentiality.

This agreement comprises:

- A detailed description of the roles of the Management Committee (MC), Research Activity (RA), Stakeholder Activity (SA) and Training Activity (TA), decision-making structures, quality monitoring and procedures.
- Financial distribution to beneficiaries based on activities and type of research performed by the partners. Necessary adjustments of activities and budget might occur after project start; these issues will be discussed and decided by vote within the RC.
- IP related measures: Pre-existing know-how brought by all participants and related rights granted to other participants, participants that shall protect results, conflict management rules, rules applied for joint ownership, access rights to project results and for third-parties.
- Definition of rules and regulation for ESR recruitment and registration for the degree of PhD where appropriate.
- Dissemination matters, rules for managing confidentiality and approving public presentations and publications.

Management Committee (MC) - The administrative management of the project will be performed by FEM. The MC will record project activity and maintain oversight of the overall program to ensure that the project works as an integrated entity and delivers to the work plan agreed. Under the day-to-day management, MC works under the advice of the RA in:

- Organising and coordinating meetings of RA, TA, SA and consortium meetings.
- Coordinating and ensuring administrative information dissemination to partner members.
- Keeping regular contact with the RA, TA, SA and other parties.
- Identifying and reporting to the partners potential problems arising in the project.
- Coordinating practical aspects regarding the exchange of personnel.
- Establishing good operating practice for financial management.
- Producing reports and preparing the annual scientific activity report, implementation plan and financial management report in conjunction with EUREGIO-EFH Partners.
- Checking partner financial statements.
- Distributing project funds and monitoring/reporting project finances
- Management of the intellectual property of the discoveries made during the ESR training.
- Coordinating the networking, dissemination and outreach activities in collaboration with WP5.
- Monitoring scientific progress towards timelines, milestones and deliverables in the project implementation plan and provide update reports to the Research Activity (RA)
- Organizing RA, SA and Ta and annual project meetings and prepare and distribute meeting agendas, working papers, minutes and reports together with the follow-up actions of these meetings in collaboration with WP5.
- Creating a project website with an intranet for the internal documents according to WP5.

Research Broad (RA) will be chaired by leading research scientists proposed by the partner institutions and will be open to all project supervisors/principle investigators involved in the Activity at the EUREGIO-EFH meetings and workshops.

The tasks of the RA are:

- Assuring information flow and implementation of the scientific tasks
- Decision on strategies, contingency plans and dissemination,
- Decision on the strategic objectives and implementation of the project activities
- Establishing quality management- and internal review procedures for technical deliverables and scientific output

- Organise the final EUREGIO-EFH international congress in Trento, month 36 to maximise project and partner international scientific visability, maximise cross-talk and partnering between EUREGIO-EFH academic partners and stakeholders local, national and international levels to foster partnerships to attract inward investment to support EUREGIO environmental, food and health research.

Stakeholder Board (SA) – SA will be jointly chaired by experienced local scientists from each of the three provinces to maximize as far as possible existing collaborative networks between academic, industry and public bodies. The provincial chairs will recruit interested, relevant and energetic partners from the agricultural sector, from the pharmaceutical and nutraceutical industries, industry representative bodies, local public health departments and medical experts.

The task of SB is organizing (with the assistance of the MC) the 3 Consortium Workshops. The Board will decide the agenda and participation.

Training Board (TA) - This committee will oversee academic quality and act as an independent advisory body for ESRs. The Training Board will:

- Advise on ESR registration, communication of training needs and opportunities.
- Assist in specific ESR training and offering courses to improve student skills, career development and scientific needs
- Assist in organizing EUREGIO-EFH training workshops to run in parallel with the EUREGIO-EFH Stakeholder workshops,
- Assure transparency of processes for PhD student recruitment and admission of candidates making sure the rules and regulations of the host institutions and Universities at which the ESR will be registered for the degree of PhD are compatible.
- Help organize a careers recruitment fair as part of the final international scientific congress (month 36) to assist career development past the life of the current project for the 12 EUREGIO-EFH ESRs.

Further details are also given in the WP description.

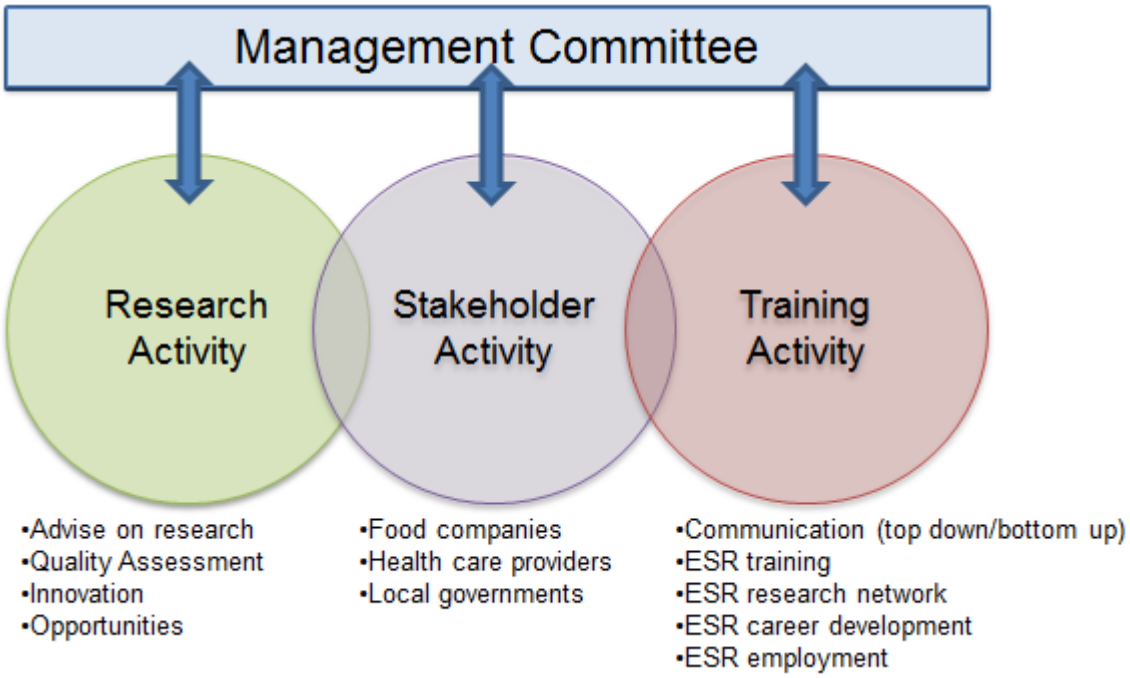


Figure 3. EUREGIO-EFH governance structure

Dissemination activities and results exploitation

EUREGIO-EFH is strongly committed to liaising with the agri-food industry, clinical and health care communities, in academia, pharmaceutical industry and medicine, looking to ensure that our work remains relevant to current demands and challenges, that all possible synergies with other initiatives in the field are exploited, that the developed tools are adopted and that our contribution to the field has a long-lasting, sustainable effect. This will be further developed in WP5 through the dissemination activities and within the Stakholder Board which includes the initial identification and involvement of stakeholders from the food industry and agriculture, health care systems, academic institutes and political leaders harnessed with reducing obesity, the diseases of obesity and fostering healthy ageing.

Such a commitment requires a special effort to be directed towards building solid dissemination, exploitation and knowledge management strategies that support the creation of an environment of mutual trust and understanding beyond the Consortium. For this reason, a number of project objectives and activities in the work plan imply the need for consultation and dissemination activities, the design of exploitation or sustainability scenarios, and the management of the knowledge and intellectual property existing in the Consortium and generated by the project.

Reflecting the above we have structured our work plan so that dissemination and exploitation activities form an integral part of the project. Within the wet-lab packages there are activities and reports to provide consultation and interaction amongst the partners through direct links and with the broader community via specially designed workshops open to participants from beyond the consortium.

Responsabilities and training

One of the major opportunities in this project is to train a group of young researchers (ERS) in the methods whereby scientific findings can be exploited in the cycle of translational research. The appointed staff will be expected to contribute substantially to outreach activities and will be given appropriate training. They

will be encouraged to engage with the other EUREGIO-EFH partners to acquire new transferrable skills and participate in outreach activities. Regularly meeting with the senior sicentists at consortium meetings will provide training support and a yearly review will provide them with opportunities to develop awareness and skills in knowledge transfer.

Strategy for knowledge management

Where available, partners will seek to publish results using open access routes.

The communication activities will be organized as part of WP5 in cooperation with other partners. Further details are also given in the WP description. The communication activities within EUREGIO-EFH will:

- Inform all relevant stakeholders and communities (including the civil society, CS) about the EUREGIO-EFH approach, activities and results
- Contribute to create strategic alliance with stakeholder groups
- Create the basis for a sustainable communication between researchers, users/participants and policy makers/public health authorities

The communication strategy includes communication (i) within the consortium and between the partners, (ii) with the scientific community (iii) but also with the broader public comprising different target groups. In particular, internal communication facilitates an efficient information flow between the partners and the WP activities and ensures maximum transparency and cooperation within the consortium. The CA will define the framework for confidentiality, the coordination and the processes of the communication.

Planned publications will be announced to the Management Committee that distributes the information to the WP leaders for their review and approval. This process ensures transparency of the activities that co-authorships are fair and in accordance with respective contributions. This will also be done with projects results that have potential for exploitation. Any documents or information produced for publication to the public must be presented to the Research Committee for review and approval to ensure coherency of the communication. The internal communication will be coordinated via a protected area of the project webpage. Via this instrument all project partners will have access to relevant documents, and can use this platform to exchange information.

For the external communication with the scientific community, we will employ effective methods for communication of the findings of EUREGIO-EFH to a wider scientific audience: (1) the project portal, (2) open meetings with invited speakers from outside the consortium, (3) participation to scientific conferences and (4) publications using the open-access model:

(1) The EUREGIO-EFH project portal - developed from the first days of the project will provide the scientific community with complete information about the project's background, goals and progress (WPs). All public deliverables will be easily accessible through this web site. However, in order to move beyond a static project site, we envision an active with Facebook and Twitter links, documenting the ongoing concerns within the project, reaching out to the scientific world.

(2) We have designed specific meetings to take place over the course of the project (Table 2 and WP5). These meetings will inform the community of our work, but will also provide us with an opportunity to consult and obtain feedback at every stage of work: from inception and experiment design, to modelling and on to the validation studies and post-project planning.

(3) We will ensure we engage maximally with the scientific community by attending several major conferences in diet-related disease, ageing- and obese-related topics and medicine, further interacting with key stakeholders in the community. Publications in high-impact journals will be pursued throughout the project. All scientific partners are prolific in publication and regularly present work at major national and international meetings.

(4) Publications – while we will seek publication of our results in prestigious journals, in order to maximise the impact of our research publications we will publish using the open-access model wherever possible.

Knowledge management and knowledge brokering

The knowledge management agenda of EUREGIO-EFH aims to facilitate knowledge transfer both internally among partners and to the external community, while also guiding new knowledge generation according to detected 'gaps'. 'Internal' knowledge management activities have the ultimate objective of making the best use of knowledge and expertise existing in the consortium for undertaking the project itself. The need for this focus stems from the interdisciplinary nature of the consortium (from nutrition to ecology to medicine) and the specificity of the field addressed. To deal with this in practice, knowledge 'offers' and 'demands' will be detected as early as possible and managed so that know-how is rapidly transmitted between consortium members as and when needed. For this purpose, training meetings will be utilized to provide a common arena for the exchange of ideas, on top of which collaboration can be developed. We will perform continuous surveillance of training needs in the consortium around specific issues, and the organisation of workshops and events that dynamically fulfil these needs. Specific attention will be paid to appropriate handling of intellectual properties rights (IPR) issues (if any arise) so that this does not hamper project development.

Internal knowledge-management and training will thus be designed to bring about: a) mutual knowledge sharing of partner's expertise, fostering better understanding and productive interactions amongst partners from different disciplines (typically needed more at an early stage of the project), and b) sharing knowledge on specific technologies/concepts/issues that may be needed by other partners for them to carry out their work within the project. Special attention will be paid to promote the training of students and younger researchers in the consortium. We envision a series of exchange visits among the 12 early stage researchers amongst the partners to learn new technologies and conduct cross-disciplinary research. 'External' knowledge management, in contrast, will deal with the transmission of knowledge generated by the project to the outside world.

For both internal and external knowledge management undertakings, the EUREGIO-EFH project portal will be a key enabler. It will serve as one of the main platforms that gives visibility to the project's activities, it will give access to our results, and it will gather feedback from prospective users about their knowledge 'gaps'. Tracking user access and downloads, and enabling of feedback channels, will be important in these respects. It will also incorporate a private area to support internal exchange of training materials and tools to support knowledge transfer among partners. Finally, it will be a major route by which we publicise the progress of the project and keep track of events and training workshops, thereby raising awareness among prospective users and making the impact of the project in the community as high as possible.

Table 5 Deliverables List

Scientific Deliverables						
Deliverable Number16	**Deliverable Title**	**WP No.**	**Lead Beneficiary Short Name**	**Type**	**Dissemination Level19**	**Due Date (Month)**
1.1	Comparison of the land-use forms on an environmental perspective (ecosystem status, functions, processes)	1	EURAC	Research (R)	All	30
1.2	Comparison of the land-use forms on a social perspective (ES)	1	EURAC	R	All	36
1.3	Comparison of the land-use forms on an economical perspective (macroeconomic, business view)	1	EURAC	R	All	36
1.4	Total synopsis from the perspective of the sustainability of human-nature systems	1	EURAC	R	All	30
1.5	Identification and recruitment of agriculture partners operating dairy farms at both high intensity and low intensity.	1	UNIBZ	R	All	6
1.6	Environmental assessment of the impact of high and low intensity dairy farming within the EUREGIO region.	1	UNIBZ	R	All	36

1.7	Measuring the impact of farming intensity on dairy herd health.	1	UNIBZ	R	All	30
2.1	Measuring the fibre content of local plant based foods	2	LRC	R	All	18
2.2	Measuring the nutritional profile of selected EUREGIO dairy products	2	UNIBZ FEM UNITN	R	All	30
2.3	Measuring the polyphenol profile (quantity and quality) of EUREGIO plant based foods	2	FEM UNITN	R	All	30
2.4	Compilation of data-base with nutritional profile (quantity of dietary fibre, typical quantity and composition of polyphenols and fats) of EUREGIO healthy foods. This data-base will be hosted by FEM and made open access at the end of the project	2	FEM	R	All	36
2.5	Selection of EUREGIO foods with potential as fasting mimicking foods and development as new food products	2	FEM	R	All	30
2.6	Genotyping of FASTMOB study	2	EURAC-IB	R	All	36

	population (n = 120) with special reference to polymorphisms in genes known to impact on the risk of metabolic disease and healthy ageing					
2.7	Metabolomics analysis of biofluids collected from the FASTMOB study with special reference to quantification of metabolites thought to be involved in mediating dietary regulation of immune and metabolic features of obesity and chronic age related disease (e.g. bile acids, SCFA, amino acids and small phenolic acids).	2	UNITN FEM	R	All	36
2.8	Lipidomics: Use of NMR based metabolomics to characterise lipids present in biofluids collected from the FASTMOB study.	2	UNITN	R	All	36
2.9	Metagenomic characterisation of the human gut microbiota and immune/metabolic related biomarker measurement before and after dietary intervention in the FASTMOB study. Responsible FEM	2	FEM UNITN UIBK	R	All	36

3.01	Compile different factors (life style and genetic) related to obesity in local population	3	EURAC-IB	R	All	30
3.02	Derive model to predict obesity susceptibility in local population.	3	EURAC-IB	R	All	36
3.03	Dietary intervention in obese subjects with triggering the biological effects of calorie restriction through intermittent fasting and EUREGIO fasting mimicking foods.	3	ASAA/APSS	R	All	24
3.04	New understanding how diet, through interactions with the gut microbiota, impacts on obesity and the diseases of obesity.	3	FEM	R	All	36
3.05	Clinical data in support of the beneficial health impacts of EUREGIO fasting mimicking foods rich in fiber, polyphenols and beneficial fats.	3	ASAA APSS	R	All	30
3.06	A high-resolution, genomic and post-genomic data-sets, with the larger CHRIS study, for comparison with existing multi-omics datasets and mining for novel mechanistic insight	3	UNITN EURAC-IB FEM	R	All	36

	ad IP related to diet, microbiome, obesity and healthy ageing.					
3.07	Selection of host:microbiota co-metabolites and dietary derived molecules linked to CR	3	FEM	R	All	3
3.08	Measurement of CR metabolite ability of modulate adipocyte inflammatory and metabolic signalling potential using cell models	3	UIBK	R	All	30
3.09	Measurement of CR metabolite ability of modulate adipocyte and immune cell inflammatory and metabolic signalling potential using cells isolated from human blood.	3	FEM	R	All	30
3.10	Novel insight into the molecular basis of CR associated healthy ageing and protection against chronic diet/age associated disease.	3	UIBK	R	All	30
3.11	Exploration of core factors of health-related factors, understanding their interactions and their impact on health in EUREGIO..	3	UMIT	R	All	24
3.12	A EUREGIO specific understanding of the risk perception	3	UMIT	R	All	36

	concerning healthy diet and healthy life.					
3.13	EUREGIO specific suggestions for a road-map for reducing the socioeconomic and public health related burden of obesity and diet/age associated chronic disease	3	UMIT			
3.14	Design of PTR-MS based breath test study protocol	3	FEM UIBK	R	All	24
3.15	Ethical approval of additional analysis in participants with different metabolic states and/or digestive dysfunction.	3	FEM	R	All	6
3.16	Target environment testing of PTR-MS based breath test for identification of metabolic markers defining metabolic and digestive disorders and breath volatile metabolites related to metabolic flexability.	3	FEM	R	All	36
Management, Training, Recruitment and Dissemination Deliverables						
Deliverable Number	**Deliverable Title**	**WP No.**	**Lead Beneficiary Short Name**	**Type**	**Dissemination Level**	**Due Month**
4.1	Establishment of Research, Stakeholder and Training Boards	4	FEM	Management (M)	All	1

4.2	Recruitment, training and report on ends of month 1-17 and 18-35	4	FEM	M	Consortium and regional governments	35
4.3	ESR training events (months 3 and 30)	4	FEM	Training (T)	All	30
4.4	Consortium Stakeholder workshops (months 3 [North Tyrol], 12 [South Tyrol] and 24 [Trento].	4	FEM	T	Consortium Stakeholders	24
4.5	Final EUREGIO-EFH international scientific congress and recruitment fair in Trento	4	FEM	Dissemination (D) & Training	All	36
5.1	EUREGIO-EFH website and social media sites (FEM, month 3)	5	FEM	D	All	3
5.2	Dissemination through public media	5	All	D	All	36
5.3	Disseminate scientific results through publications in peer reviewed expert journals	5	All	D	All	36

Table 6 Main EUREGIO-EFH Scientific/Socio-economic Outputs

Number	Title	Month	WP	Partner
1.1	Evaluation of the land-use forms on an environmental, social and economic perspective (ecosystem status, functions, processes)	30	1	EURAC/UIBK/FEM
1.2	EUREGIO bespoke strategy for adding value, both economic, health-related and social, to land-use forms	36	1	EURAC/UIBK/FEM
1.3	Environmental, food nutritional and animal/human health impact assessment of low intensity compared to high intensity dairy farm production within the EUREGIO region.	30	1	EURAC/UIBK/FEM
1.4	Cost:benefit analysis and improved marketing strategy for dairy production in the EUREGIO region.	36	1	UNIBZ/UIBK/FEM
1.5	Improved understanding of risks associated with antibiotic resistance transfer in animal production systems.	36	1	UNIBZ/UIBK/FEM
2.1	Range of EUREGIO food products with detailed nutritional profiling and potential as novel fasting mimicking foods or functional foods.	36	2	LRC/FEM
2.2	State of the art technology platform to serve WP1 and 3	6	2	UNITN
2.3	New mechanistic insight into how fasting mimicking diets/foods may impact on body weight and metabolic health, reducing the disease risks associated with obesity and ageing.	36	2	UIBK ASAA APSS
2.4	Novel IP on EUREGIO bioactive foods, food components or therapeutic targets in obesity and healthy ageing.	36	2	All
3.1	Data mining from existing dietary information within EUREGIO to correlate obesity (BMI) with adherence to specific dietary patterns	36	3	EURAC-IB /FEM

	and identify local foods associated with healthy diet.			
3.2	Selection of EUREGIO "fasting mimicking foods" and design of the EUREGIO dietary intervention study protocol.	1	3	FEM ASAA APSS
3.3	Favourable ethics assessment of the EUREGIO dietary intervention in both Trento, Modena and Bolzano Research and Ethics Committees.	1	3	FEM ASAA APSS
3.4	Dietary intervention with EUREGIO fasting mimicking dietary regime.	30	3	ASAA APSS, FEM
3.5	Clinical assessment of the efficacy of intermittent fasting and intermittent fasting plus fasting mimicking EUREGIO foods to improve body weight management in the long term and reduce the risk of metabolic disease compared to traditional low calorie diets.	30	3	ASAA APSS FEM UIBK
3.6	Scientific evidence in support of EUREGIO fasting mimicking foods to help loose weight and retain weight loss.	30	3	ASAA APSS FEM, UIBK
3.7	A multi-omics FASTMOB dataset which will be mined for novel mechanistic insight into obesity, the diseases of obesity and healthy ageing and novel IP.	36	3	FEM UNITN EURAC-IB UNIBZ
3.8	Through the workshop series and based in part on results from WP3, we will propose a EUREGIO Alpine version of the Mediterranean style diet, based on the nutritional composition of existing Mediterranean dietary guidelines but using local EUREGIO foods and food culture.	36	3	ASAA APSS FEM LRC UIBK UIBZ

Table 7: PROJECT BUDGET

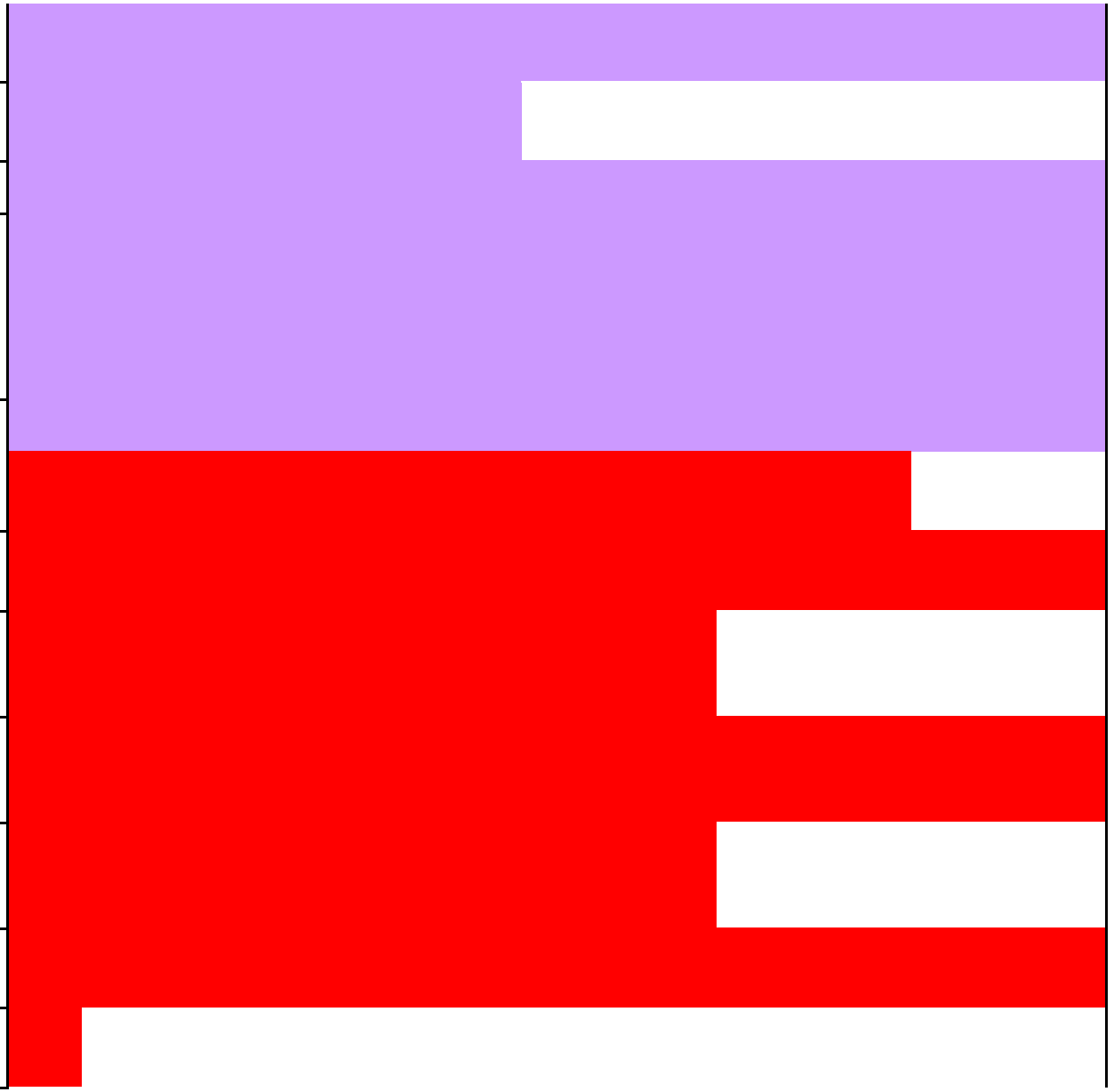
ESR	Project title	PI	Host	Year 1	Year 2	Year 3	Totals /activity
1	Measuring and predicting the interaction of objective factors and their subjective perception: How to promote health and longevity	Siebert/Streicher	**UMIT**	30000	30000	30000	
	Consumables ESR1: Computing (UMIT)			5000	5000	3000	103000
10	Measuring host:microbiota co-metabolite cellular signalling underpinning calorie restriction or fasting mimicking dietary regulation of metabolic health or obesity	Grubeck-Loebenstein	**UIBK**	38000	38000	38000	114000
	Consumables & other costs, PhD plus FASTMOB lab analyses			5000	5000	81000	91000
10	Research assistant /technician 12 months FASTMOB lab analyses	Grubeck-Loebenstein	**UIBK**		20000	12000	32000
WP1	Consumables for UIBK contribution to WP1	Tappeiner	**UIBK**	10000	10000	10000	30000
WP3	Consumables for breath analysis experiments	Mayhew	**UIBK**	10000	10000	10000	30000
North Tyrol							**400000**

2	Characterise the obese subpopulation in the CHRIS study and develop models to predict susceptibility to obesity in the local population (including genotyping for FASTMOB).	Domingues	**EURAC**	26662	26662	26662	
	Consumables & other costs including FASTMOB genetics			3300	3300	3400	89986
3	Measuring the impact of farming production system on the nutritional quality of EUREGIO dairy products.	Gauly	**UNIBZ**	26662	26662	26662	
	Consumables & other costs			3300	3300	3400	89986
4	Measuring the nutritional quality of local plant based EUREGIO foods	Oberhuber	**LRC**	26662	26662	26662	
	Consumables & other costs including testing FASTMOB foods			3300	3300	4000	90586
6	A two centred dietary intervention with fasting mimicking foods to reduce obesity – EUREGIO obesity cohort study (ESR)	Prof. Lucchin	**ASAA**	30000	30000	30000	90000
	Consumables & other costs including ethics, clinical measures & foods			15000	14442	10000	39442
South Tyrol							**400000**

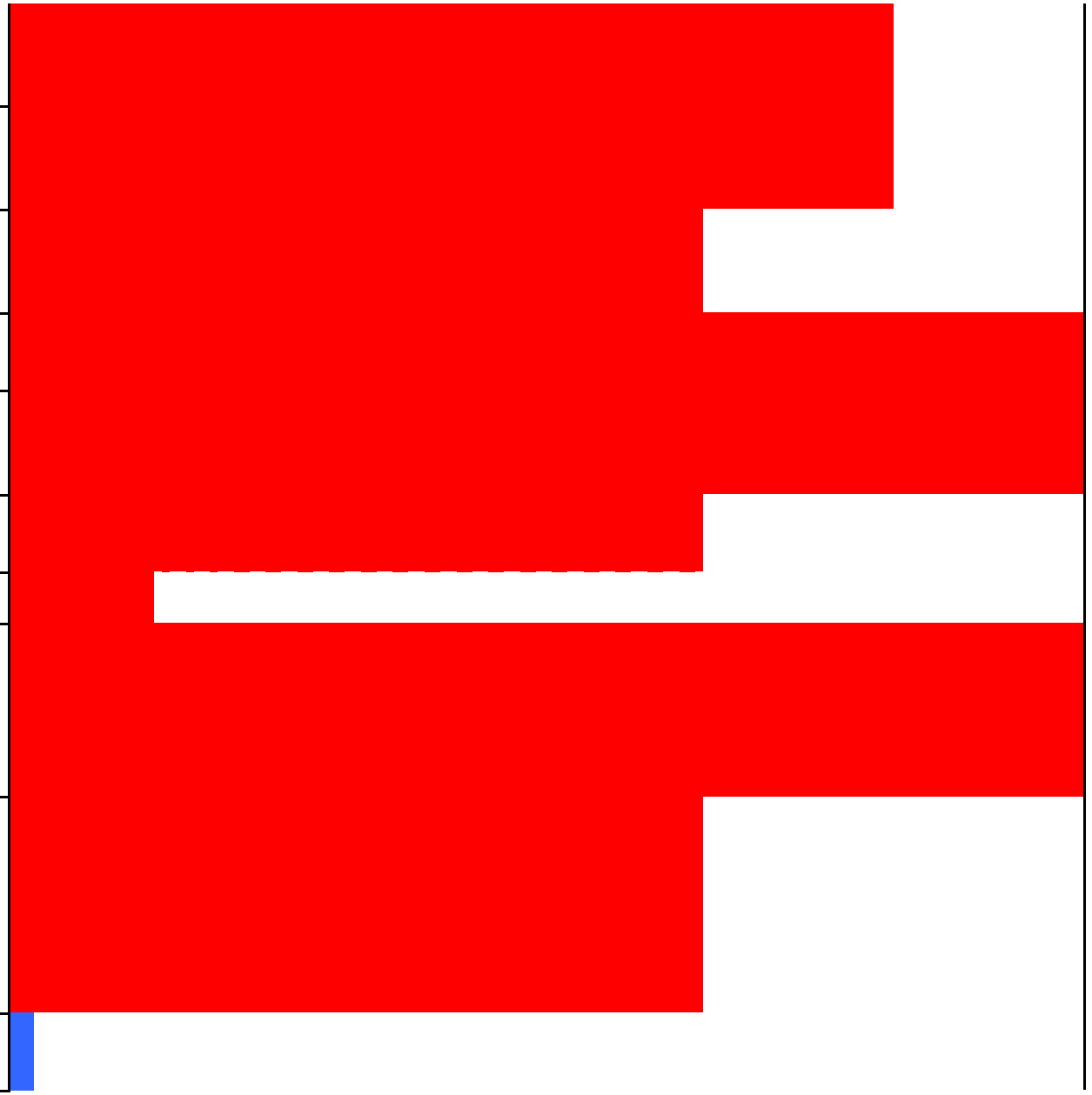
9	Measuring the metabolic implications of fasting mimicking foods in the obese.	Vrhovsek	**FEM**	26662	26662	26662	
	Consumables & metabolomics analysis of FASTMOB foods & biofluids			3300	3300	3400	89986
7	Dietician (early stage career 24 month) to help run FASTMOB cohort in Bolzano	Tuohy	**FEM**	9000	36000	9000	54000
WP3	Consumables FASTMOB Trento: Food, ethics, clinical measures (APSS)	Tuohy/Pedrolli	**FEM**	10114	8928	3000	22042
8	Dietician (early stage career 24 month) to help run FASTMOB cohort in Trento	Pedrolli	**APSS**	9000	36000	9000	54000
12	NMR-based lipidomics of biofluids (serum and urine) in volunteers undergoing suitable diets	Guella	**UNITN**	26662	26662	26662	
	Consumables & other costs			3300	3300	3400	89986
5	Measuring the impact of EUREGIO foods and fasting mimicking diets (FASTMOB study) on the human gut microbiome.	Tuohy	**FEM**	26662	26662	26662	
	Consumables & other costs including FASTMOB microbiota sequencing			3300	3300	3400	89986
Trento							**400000**

GANTT deliverables and timings		
Deliverable, title, partners	**Month**	1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36
1.01 Comparison of the land-use forms on an environmental perspective (ecosystem status, functions, processes), EURAC/UIBK/FEM	30	
1.02 Comparison of the land-use forms on a social perspective (ES), EURAC/UIBK/FEM	36	
1.03 Comparison of the land-use forms on an economical perspective (macroeconomic, business view), EURAC/UIBK/FEM	36	
1.04 Total synopsis from the perspective of the sustainability of human-nature systems, EURAC	30	
1.05 Identification and recruitment of agriculture partners operating dairy farms at both high intensity and low intensity. UNIBZ	6	
1.06, Environmental assessment of the impact of high and low intensity dairy farming within the EUREGIO region. UNIBZ	36	
1.07 Measuring the impact of farming intensity on dairy herd health. UNIBZ	30	
2.01, Measuring the fibre content of local plant based foods , LRC	18	
2.02, Measuring the nutritional profile of selected EUREGIO dairy products. UNIBZ/FEM/UNITN	30	
2.03, Measuring the polyphenol profile (quantity and quality) of EUREGIO plant based foods. FEM/UNITN	30	

2.04, Compilation of data-base with nutritional profile of EUREGIO healthy foods. FEM	36
2.05, Selection of EUREGIO foods with potential as fasting mimicking foods and development as new food products , FEM	30
2.06, Genotyping of FASTMOB study EURAC-IB	36
2.07, Metabolomics analysis of biofluids collected from the FASTMOB. UNITN, FEM	36
2.08, Lipidomics: Use of NMR based metabolomics to characterise lipids present in biofluids collected from the FASTMOB study. UNITN	36
2.09, Metagenomics for FASTMOB study. FEM/UNITN/UIBK	36
3.01, Compile different factors (life style and genetic) related to obesity in local population EURAC-IB	30
3.02, Derive model to predict obesity susceptibility in local population. EURAC-IB	36
3.03, Dietary intervention in obese subjects with triggering the biological effects of calorie restriction through intermittent fasting and EUREGIO fasting mimicking foods. ASAA/APSS	24
3.04, New understanding how diet, through interactions with the gut microbiota, impacts on obesity and the diseases of obesity. FEM	36
3.05, Clinical data in support of the beneficial health impacts of EUREGIO fasting mimicking foods rich in fiber, polyphenols and beneficial fats. ASAA/APSS	30
3.06, A high-resolution, genomic and post-genomic data-sets for correlation analyses. UNITN/ EURAC-IB /FEM	36
3.07, Selection of host:microbiota co-metabolites and dietary derived molecules linked to CR, FEM	3



3.08, Measurement of CR metabolite ability of modulate adipocyte inflammatory and metabolic signalling potential using cell models, UIBK	30
3.09, Measurement of CR metabolite ability of modulate adipocyte and immune cell inflammatory and metabolic signalling potential using cells isolated from human blood., FEM	30
3.11, Exploration of core factors of health-related factors, understanding their interactions and their impact on health in EUREGIO. UMIT	24
3.12, A EUREGIO specific understanding of the risk perception concerning healthy diet and healthy life. UMIT	36
3.13, EUREGIO specific suggestions for a road-map for reducing the socioeconomic and public health related burden of obesity and diet/age associated chronic disease. UMIT	36
3.14, Design of PTR-MS based breath test study protocol. FEM/UIBK	24
3.15, Ethical approval for breath tasts with PRT-MS. FEM	6
3.16, Target environment testing of PTR-MS based breath test . FEM	36
3.11, Exploration of core factors of health-related factors, understanding their interactions and their impact on health in EUREGIO. UMIT	24
4.01, Establishment of Research, Stakeholder and Training Boards, FEM	1



4.02, Recruitment, training and financial status report on ends of month 1-17 and 18-35, FEM	35	
4.03, ESR training events (months 3 and 30), FEM	30	
4.04, Consortium Stakeholder workshops (months 3 [North Tyrol], 12 [South Tyrol] and 24 [Trento]. FEM	24	
4.05, Final EUREGIO-EFH international scientific congress and recruitment fair in Trento. FEM	36	
5.01, EUREGIO-EFH website and social media sites (FEM, month 3), FEM	3	
5.02, Dissemination through public media , All	36	
5.03, Disseminate scientific results through publications in peer reviewed expert journals , All	36	

Table 8: Participting Organisations

Beneficiary Legal Name:	**Fondazione Edmund Mach**
General Description	**Department of Food Quality and Nutrition** *Head of Department, Dr Kieran Tuohy* The activities in the field of research and innovation aimed at the qualitative, technological and nutritional enhancement of agri-food products are carried out by this Department, in order to improve the food quality and respond to the needs of the consumer. The research activities are carried out using new study methods, based on advanced technological platforms and infrastructures (metabolomics, stable isotopes, sensory panels, innovation incubators), and by adopting an integrated approach of a multidisciplinary nature. Innovative technical platforms and a systematic approach make it possible to carry out studies of fundamental significance, generate new study methods and obtain improved knowledge of agri-food products. The Department aims to support product and processing innovation based on knowledge of the food and agriculture sector. It promotes the use of research in the fields of biological sciences, consumer science, metabolomics and traceability as tools for innovative production. Provides a human nutritional research nucleus for the emerging strategic area of nutrigenomics. It carries out research, both in the laboratory and at the pilot project and company levels, providing scientific support for the creation of products and processes with added value, based on knowledge, ideas and innovation. **Chief scientific office** (ADR) - Management of the scientific, research and technological operations of CRI. The Research and Innovation Centre (FEM-CRI) is led by Annapaola Rizzoli. She

	is responsible for the strategic development of the excellence of the scientists, facilities and technological resources. She helps to set the research and scientific priorities so that they line up with the overall mission and goals of the FEM. **Applied ecology, Annapaola Rizzoli.** **Research unit (AE)** - Investigating the effects of global changes and biodiversity loss on Alpine species, and related eco-systemic interactions The mission of the Applied ecology unity is to generate knowledge on the effects of global changes and biodiversity loss on Alpine species, and related eco-systemic interactions, including host-pathogens dynamics. These objectives are pursued with a multi-disciplinary approach that combines molecular epidemiology and genomics, mathematical modelling and statistics, animal and behavioural ecology, and the use of bigdata managed through innovative IT platforms. In addition, innovative technologies, such as wireless sensor networks, or machine-learning algorithms, are used to study the relationships between individual animal behavior, including animal movement, and abiotic and biotic variables The development of interdisciplinary research activities within the unit permits to implement large-scale projects covering several research topics in collaboration with the main International agencies (Programme Horizon 2020, WHO, OIE, ECDC, CDC, ESA, NASA). These research activities are essential to deeply understand the complexity of the Alpine ecosystem where the effect of global change are particular evident, favouring, for instance, the re-emergence of endemic diseases, due to varied abiotic and biotic conditions, or the introduction of new invasive alien pathogens. This would increase the risk and economic damage to public health and to the local animal husbandry affecting the health and quality of agro-food and dairy products as well as for the welfare of the resident population and tourists. The main research lines developed within the unit are the following: ***-Eco-health***. In this line of research, we study the consequences of global changes on the spread of medical and veterinary infections focusing on the dynamics of the interaction between pathogens, vectors and reservoir hosts.

	For this purpose, we develop predictive mathematical models to quantify the risk of vector- and rodent-borne infections for agro-forestry workers, employees of the livestock sectors, as well as for living populations. ***-Conservation and Movement Ecology.*** In this line of research, the study of individual animal behaviour, and movement in particular, is used to disentangle the proximate response and resilience of ecosystems to climate and landuse change. By means of innovative methodologies and approaches (biologging, mathematical modelling and data sharing of big data), we propose mitigation and develop predictive models at the local, regional and continental scale, and identify mitigation and conservation solutions to improve and promote human-wildlife co-existence in the high human-density European (and Alpine in particular), landscape. ***- Spatial Ecology.*** This research line deals with the spatial characterization of the landscape at local, regional and global scales from an orographic and bioclimatic point of view, with applications in the following fields: i) animal epidemiology, ii) biodiversity, agricultural suitability, estimate of the spatial spread of alien species under climatic changes. We are making use of throughput spatial analysis techniques supported by an advanced hardware platform and by the development of open source software for geostatistical analysis. **Nutrition and Nutrigenomics (NN) Unit,** *Kieran Tuohy* The NN mission is to measure how food and diet modulates host health and protects against chronic disease through microbial interactions. We have a special interest in fermented foods (especially fermented dairy products), whole plant foods, their bioactive fractions (fibres, prebiotics and polyphenols) and probiotics. We examine how microorganisms impact on food nutritional composition and also, how diet shapes and regulates the gut microbiome. Both of these microbial food interactions impact on host health, and we conduct studies in human volunteers and model systems to test these health promoting activities, with a view towards demonstrating clear cause and effect between

	food intake and host physiology. We also aim to provide novel mechanistic insight into how functional foods work. We are particularly interested in how microorganism, either by changing the nutrient profile of foods or by changing the metabolic output of the gut microbiota can impact on host immune function, metabolism and brain function. We collaborate closely with the Metabolomics and the Computational Biology groups at FEM, to provide combined high resolution metabolite and microbiome profiling which together with multivariate statistical analysis helps us to describe these diet:microbe interactions in foods, in humans, in our model gut and in animals. Human health is closely intertwined with plant and animal health through our food. Animal health, and foods which promote production animal health, determine animal derived food safety (e.g. incidence of zoonosis) and nutritional profile (e.g. fatty acid composition). Similarly, plants produce a range of complex molecules which contribute to plant self-defence and which promote human health when present in our foods (e.g. flavonoids and carotenoids). The One-health approach holds that feed and production systems which maximise farm animal and crop plant health will also improve the nutritional profile of our food products. We apply the "one-health" concept to our research, aiming to contribute to healthy diets, healthy lives and healthy ecosystems at regional, national and international levels. Group members participatin in the project include Dr. Elena Franciosi, Dr Francesca Fava, Dr Matthias Scholz and Dr Lisa Rizzetto. **Metabolomics Unit** *Urska Vrhovsek* Research unit (ME) - new methods of study and knowledge about nutritionally and sensorially significant compounds. The metabolomics unit (ME) is designed to mediate progress in science through development of new analytical methods and provision of measurement services applicable to plants, human, animal, cell models. The activities include both profiling (analyses of all measurable analytes to identify differences) and targeted analyses (quantification of a chosen set of analytes).

	ME generates new methods of study and knowledge about nutritionally and sensorially significant compounds, even participating in nutritional intervention studies, tracing the path of natural bioactive compounds inside the human body. Such information has the ultimate goal of improving the understanding of the impact of diet on human health and the production of higher value-added foods. It pursues the study of the molecular mechanisms that underlie the biosynthesis of secondary compounds in plants, knowledge of which is essential to progress in the field of biotechnology applied to plants and micro-organisms and breeding programs. The new knowledge is incorporated in the design and development of modules on platforms combinatorial biosynthesis of natural products that can have a significant interest and a substantial demand from the pharmaceutical industry (pesticides, nutraceuticals) and food (additives, supplements). The unit also pursues a significant research activity aimed at the development of products of the vine and wine sector in order to improve their quality by responding to the needs of producers and consumers, creating added value. **Sensory Quality,** *Franco Biasioli* Research unit (QS) - The unit combines skills and objectives of the Sensory Quality Group and of the Volatile Compound Facility. *Mission* Understanding the mechanisms underlying the perceived quality of food and the physiological and psychological factors that influence perception, preference development and consumer behaviour. Supporting food choices associated with health and wellness. Maintaining and developing a sensory / instrumental / statistic facility to support innovation in the agroindustry. *Research lines and main methodologies* Sensory analysis. Innovative methods for the multidisciplinary investigation of sensory quality and consumer choice. In addition to its fundamental relevance, the research activity supports innovation in agroindustry, in particular at local

	level. *Instrumental analysis.* Novel, non-invasive, rapid, on-line techniques for product characterization and process monitoring in the agri-food sector or in other fields of interest to FEM. Of particular relevance the technology for rapid and highly sensitive monitoring of volatile compounds based on direct injection mass spectrometry. *Statistic analysis.* Software development and implementation of innovative statistical approaches for the analysis of sensory (descriptive and hedonic) and instrumental data and their correlation to identify the drivers of sensory quality and set descriptive and predictive models. **Computational biology,** *Claudio Donati* Research Unit (BC) - Integrates the most advanced computational techniques, as bioinformatics, computational modelling, computational biochemistry and genomics, and systems biology. The Computational Biology Unit is the reference point of the Research and Innovation Centre (CRI) for the analysis and statistical modeling of data, with an emphasis on "omic" technologies. This mission is pursued by conjugating an original research activity in method development with the collaboration with the other groups of CRI. The main research themes are: genomics, in particular of plants, metagenomics, metabolomics, transcriptomics, statistical modeling and data integration. In addition, the Computational Biology Unit manages the High Performance Computing infrastructure of CRI and guarantees the storage and traceability of data generated by high throughput technologies. *Fulvio Mattivi* (Professor at the University of Trento-Fondazione Edmund Mach joint research centre, ***C3A*** or Centre for Africulture, Food and Enviornment (***CAFE***) as of Febuary 1st, 2017).

Role and Commitment of key persons (including supervisors)	• Kieran Tuohy will have overall responsibility for implementation, management and dissemination of the project, oversight of nutrition, biomedical assay (immune and metabolic) measurements and microbiology analysis of FASTMOB study. • Fulvio Mattivi – LC-MS based metabolomics, food quanity, nutrition, food industry network • Annapaola Rizzoli – environment, ecology, zoonosis, antibiotic resistance transfer in the environment, project management oversight • Urska Vrhovsek – LC-MS and GC-MS based metabolomics and targeted analysis of human biofluids and foods composition. • Franco Biasioli – will asdvise on profiling of volatiles in food and breath using PTR-MS based approache • Francesca Fava – nutritional, metabolic, immune bioassays and data management for FASTMOB study, in vitro cell assays for food bioactive components. • Elena Fransciosi – dairy microbiology, measurement of bioactives in dairy products, dairy production • Claudio Donati – computational biology, metagenomics and microbial comparative genomics • Matthias Scholz – high resolution microbiot adeep sequencing, comparative genomics, multi-variate, multi-omics data analysis • Lisa Rizzetto – immune and metabolic bioassays, ELISA, bioactivity of microbial metabolites in human cells ex vivo.
Key Research Facilities, Infrastructure and Equipment	FEM has extensive research facilities and research groups including genomics, computational biology and statistics, food chemistry and biology agro-ecosystems and crops. A set of technology platforms support research, such as sequencing, metabolomics, high-performance computing. The metabolomics platform is equipped with the state of the art instruments for GC/MS and LC/MS
Previous Involvement in	CRI has hosted 5 Marie Curie grantees (FPVII, COFUND and 1 PhD as a benificiary of an FP7-ITN project (PIMMS). Since 2009, FEM/CRI's Doctoral

Research and Training Programmes	Research School (FIRS>T) offers training and funds to doctoral candidates. The programs offer yearly around 200 hours of training activities dedicated to young researchers. The FIRS>T training programme includes training in both soft skills and specific disciplines. In addition, FEM is involved in a number of EU funded projects under the JPI-Healthy Diet for a Healthy Life sheme, ENPADASI and FOODBALL. They are also a partner in the project HEALTHMARK and are coordinating the project CABALA_Diet&Health recently funded JPI-HDHL project on biomarkers in health and nutrition. These projects deal with different aspects of diet (and food) interaction with the human body at the systems level using post-genomics technologies. They will serve EUREGIO-EFH as a valuable data source for cross-comparisons and data-mining but will also give this current project a direct international line into on-going, high visibility Euroean projects, maximising EUREGIO-EFHs ability to reach a wide, inter-sector (academia and food infustry) audience at the highest international levels.
Current Involvement in Research and Training Programmes	CRI manages/has managed 40 FP5, 6, 7/H2020 projects and 15 national projects; it is involved in 3 Marie Curie networks (1 as ITN coordinator, 1 as ITN partner, 1 as associated partner) and 1 Erasmus Mundus network. FIRST doctoral community counts 30 PhD candidates of 15 nationalities, affiliated to international Universities and 11 PhD funded by other entities
Relevant Publications and/or Research / Innovation Product	1. Staudacher HM, Lomer MCE, Farquharson FM, Louis P, **Fava F, Franciosi E, Scholz M, Tuohy KM,** Lindsay JO, Irving PM, Whelan K. Diet Low in FODMAPs Reduces Symptoms in Patients with Irritable Bowel Syndrome and Probiotic Restores Bifidobacterium Species: a Randomized Controlled Trial. **Gastroenterology. 2017** Jun 15. pii: S0016-5085(17)35744-X. doi: 10.1053/j.gastro.2017.06.010. [Epub ahead of print] 2. Hill CJ, Lynch DB, Murphy K, **Ulaszewska M,** Jeffery IB, O'Shea CA, Watkins C, Dempsey E, **Mattivi F,Touhy K,** Ross RP, Ryan CA, O' Toole PW, Stanton C. Evolution of gut microbiota composition from birth to 24 weeks in the INFANTMET Cohort. **Microbiome. 2017** Jan 17;5(1):4.doi: 10.1186/s40168-016-0213-y. 3. Basso N, Soricelli E, Castagneto-Gissey L, Casella G, **Albanese D, Fava F, Donati C, Tuohy K,** Angelini G, La Neve F, Severino A, Kamvissi-Lorenz V, Birkenfeld AL, Bornstein S, Manco M, Mingrone G. Insulin Resistance, Microbiota, and Fat Distribution Changes by a New Model of Vertical

	Sleeve Gastrectomy in Obese Rats**. Diabetes.** 2016 Oct;65(10):2990-3001. 4. **Ulaszewska MM,** Trost K, Stanstrup J, **Tuohy KM,** Franceschi P, Chong F-F, M, George T, Minihane, A.M.; Lovegrove, J.A.; **Mattivi, F.** (2016). Urinary metabolomic profiling to identify biomarkers of a flavonoid-rich and flavonoid-poor fruits and vegetables diet in adults: the FLAVURS trial. METABOLOMICS, 12 (32). doi: 10.1007/s11306-015-0935-z handle: http://hdl.handle.net/10449/27017. 5. Baldacchino F, Bussola F, Arnoldi D, Marcantonio M, Montarsi F, Capelli G, Rosà R, **Rizzoli A**. An integrated pest control strategy against the Asian tiger mosquito in northern Italy: a case study. **Pest Manag Sci. 2017** Jan;73(1):87-93.

Beneficiary Legal Name: ASAA	
General Description	Current staff at the Combined Unit of Dietetics and Clinical Nutrition (UDNC) Bolzano hospital includes three full time one 75% medical specialists in Clinical nutrition and 20 dieticians.
Role and Commitment of key persons (including supervisors)	The unit has a Day-Hospital, indirect calorimetry and telemetry, bioimpedentiometry, multi-sensors for monitoring physical activity and energy expenditure, AGE-reader, oximeters, dynamometers, antropometri.
Previous Involvement in Research and Training Programmes	Coordinating centre for detecting the prevalence of protein-energy malnutrition in Italy, guidelines for obesity, also in English, the study of the metabolic effects of whey protein (in press)
Relevant Publications and/or Research / Innovation Product	1. Lucchin L,Schrei M.Does diet still retain a value in gastrointestinal pathology? In Grossi E, pace F:Human Nutrition from the gastroenterologist's perspective. Springer eds Switzerland 2016:67-78 2. Lucchin L.Overview of the Management of Obese Participants.In: Sbraccia P,Nisoli E, Vettor R. Clinical Management of Overweight

	and Obesity. Springer Switzerland 2016:3-12 3. Lucchin L et al. Manifesto delle criticità in nutrizione clinica e preventiva. Le prime 10 sfide italiane (2015-2018). Recenti Progressi in Medicina 2015, supplemento al volume 106,6:1-31 4. Poli A,Marangoni F,Avogaro A,Barba G,Bellentani S,Bucci M,Cambieri R,Catapano AL,Costanzo L,Cricelli C,De Gaetano G,Di Castelnuovo A,Faggiano P,Fattirol F,Fontana L,Forlani G,Frattini S,Giacco R,La Vecchia C,Lazzaretto L,Loffredo L,Lucchin L,Marelli G,Marrocco W,Minisola S,Musicco M,Novo S,Nozzoli C,Pelucchi C,Perri L,Pieralli F,Rizzoni D,Sterzi R,Vettor R,Violi F,Visioli F.Moderate alcohol use and health:A consensus document.Nutrition,Metabolism and Cardiovascular Diseases 2013;23(6):487-504 5. Cereda E,Lucchin L,Pedrolli C,D'Amicis A,Gentile MG,Battistini NC,Fusco MA,Palmo A, and Muscaritoli M on behalf of the PIMAI group.Nutritional care routines in Italy:results from the PIMAI (Project:Iatrogenic MAlnutrition in Italy) study.European Journal of Clinical Nutrition 2010;64:894-898

Beneficiary Legal Name: Centro di Sperimentazione Laimburg	
General Description	Founded in 1975, Centro di Sperimentazione Laimburg (LRC) has established itself over the last forty years as an international reference point in agriculture. Its research activities today focus on: fruit growing and viticulture, pest management and disease prevention, mountain agriculture, cultivation of vegetables and berries, enology and fermentation techniques as well as fruit and vegetable processing. The laboratories are an important part of Centro di Sperimentazione Laimburg: the Agricultural Chemistry Laboratories perform chemical analyses of soil, plants and fodder as well as residues; the Laboratory for Flavour and Metabolites examines the components of plants and foodstuffs that determine the quality of food; the Wine Laboratory carries out chemical-physical and microbiological analyses of grape must, wine, fruit juices and distillates; disease diagnosis is tackled at the Virology Laboratory; the Molecular Biology Laboratory explores the functions of plant genes and enables targeted breeding of new varieties using modern methodology.
Role and Commitment of key persons (including	The following persons will be leading and supervising the work at Centro di Sperimentazione Laimburg:

supervisors)	• Michael Oberhuber, Ph.D. Director and Scientific responsible for the project • Peter Robatscher, Ph.D. Head of the Laboratory for Flavour and Metabolites
Key Research Facilities, Infrastructure and Equipment	Centro di Sperimentazione Laimburg is equipped with laboratories for chemical, microbiological and molecular biology analyses. The main laboratory involved in this project is the Laboratory for Flavour and Metabolites, which will also host the PhD student (ESR6). The Laboratory for Flavour and Metabolites is a state-of-the-art equipped laboratory for chemical analysis. It conducts research on the characterization of food products and plant material by applying analytical tools, mainly focused on the identification and quantification of known and unknown metabolites in various matrices derived from agricultural products. The lab equipment includes two triple quadrupol mass spectrometers coupled to HPLC and GC, respectively, for the quantitative determination of primary and secondary metabolites in food products and plant materials as well as a PTR-MS instrument for the fingerprinting of aroma profiles and. In addition, a High Resolution Mass Spectrometer (HRMS) Platform, consisting of a LC-Q-TOF and a GC-TOF, is available for the identification of unknown non-volatile and volatile compounds in agricultural matrices. In recent years, many analytical methods have been established, mainly during the implementation of externally funded projects, and can now be applied for further projects. HPLC-based methods used for the quantification of polyphenols, anthocyanins and vitamins have been validated and applied for the quantification of these components in food. Three different methods for measuring the total antioxidant capacity are implemented and can be used for this project. Additional instrumentation is present for analyzing single sugars and single acids as well as volatile compounds to determine the aroma profile of foods.

Previous Involvement in Research and Training Programmes	Centro di Sperimentazione Laimburg has been involved in numerous externally funded projects, for example: • MONALISA – Monitoring key environmental parameters in the alpine environment involving science, technology and application: financed by the Autonomous Province of Bolzano • POMOSANO – Health benefit and nutritional value of old and modern apple varieties and their juices: financed by the ERDF (European Regional Development Fund) • OriginAlp - Analysis of the origin and quality of regional Alpine agricultural products: financed by Interreg IV Italia – Austria • BioPhyTirol – Chlorophyll catabolites as biomarkers for early detection of microbes in local crops: financed by Interreg IV Italia – Austria Training programmes: So far, three bachelor and five master theses as well as one PhD thesis were completed in the laboratory for flavour and metabolites.
Current Involvement in Research and Training Programmes	At the moment, Centro di Sperimentazione Laimburg is involved in the following research projects (selection): • Technology Park for Food Sciences: financed by the Autonomous Province of Bolzano • Technology Park for Environmental Sciences: financed by the Autonomous Province of Bolzano • Vitisana - Dissecting genetic traits in resistant grapevines: interregional project network financed by the Euregio Science Fund Current training programmes: At the moment, a Master student from the University Innsbruck carries out a Master's thesis at the Laboratory for Flavour and Metabolites. Additionally, a PhD student from UniBz is supported in collaboration with

	Eco-Research (lab at Bolzano) during his work to study the isotopic characterization of agricultural products by means of strontium isotopic ratio. A PhD student will start his/her work this year in a recently approved project financed by the European Regional Development Fund (ERDF).
Relevant Publications and/or Research / Innovation Product	Chlorophyll Catabolites in Senescent Leaves of the Plum Tree (Prunus domestica). Erhart, Theresia; Mittelberger, Cecilia; Vergeiner, Clemens; Scherzer, Gerhard; Holzner, Barbara; Robatscher, Peter, Oberhuber, Michael; Kräutler, Bernhard. (2016) Chemistry & Biodiversity (13), 1441–1453. Near-infrared reflection spectroscopy and partial least squares regression to predict α-farnesene and conjugated trienol content in apples during storage. Eisenstecken, Daniela; Stürz, Stefan; Robatscher, Peter; Huck, C. W.; Zanella, Angelo; Oberhuber, Michael (2016). Postharvest Biology and Technology (117), 49–56. Mead fermentation monitoring by proton transfer reaction mass spectrometry and medium infrared probe. Cuenca, Martha; Ciesa, Flavio; Romano, Andrea; Robatscher, Peter; Scampicchio, Matteo; Biasoli, Franco (2016) European Food Research and Technology (242), 1755–1762. Multi-method Approach to Trace the Geographical Origin of Alpine Milk: a Case Study of Tyrol Region. Matteo Scampicchio, Daniela Eisenstecken, Lorenzo De Benedictis, Calogero Capici, Davide Ballabio, Tanja Mimmo, Peter Robatscher, Luis Kerschbaumer, Michael Oberhuber, Annemarie Kaser, Christian W. Huck, Stefano Cesco (2016). Food Anal. Methods, 9 (5), 1162 – 1273.

	Chemodiversity in the fingerprint analysis of Volatile Organic Compounds (VOCs) of 35 old and 7 modern apple cultivars determined by Proton-Transfer-Reaction Mass Spectrometry (PTR-MS) in two different seasons. Ciesa, Flavio; Höller, Irene; Guerra, Walter; Berger, Jennifer; Dalla Via, Josef; Oberhuber, Michael (2015) Chemistry & Biodiversity S. 800–812.

Beneficiary Legal Name: University of Trento-Department of Physics-Bioorganic Chemistry Lab	
General Description	The fundamental focus of the research activities carried on in this Laboratory is to understand and solve problems laying at the interface between chemistry, biology or physics. In particular 3 main topics are covered: 1. Natural products chemistry 2. Bioorganic methodologies in environmental chemistry; 3. Lipidomics in cells biology
Role and Commitment of key persons (including supervisors)	*Graziano Guella, professor of Organic Chemistry University of Trento, Department of Physics, Bioorganic Chemistry Lab, 30%* *Fulvio Mattivi* (Professor at the University of Trento-Fondazione Edmund Mach joint research centre, ***C3A*** or Centre for Africulture, Food and Enviornment (***CAFE***) as of Febuary 1st, 2017). The main research activity of Fulvio Mattivi concerned food chemistry, investigating the different classes of polyphenols under the analytical, technological and nutritional point of view. More recently, he moved his research interests towards plant biochemistry and human nutrition, and

	he is now coordinating biochemical studies in the fields of plant, animal and human metabolomics. He completed in 2009 the establishment at FEM of a state-of-the-art MS-based laboratory of metabolomics.
Key Research Facilities, **Infrastructure and** **Equipment**	***Key Research Facilities*** *MALDI-TOF-TOF mass spectrometer.* • *High resolution NMR spectrometer operating at 400 MHz (^{1}H) with inverse and broadband tunable probes equipped with a Pulse Field Gradient unit* • *High resolution Fusion-Orbitrap mass spectrometer with ESI and nanoESI ion sources coupled to UPLC and nano LC systems* • *Triple qadrupole mass spectrometer with ESI and APCI ion sources coupled to LC system.* • *Ion-trap mass spectrometer with ESI and APCI ion sources coupled to LC system.* • *Coupled Gas chromatograph-Mass spectrometer with EI and CI ion source and FID detection.* **Infrastructure** *The Bioorganic Chemistry Lab belongs to the Physics Department of the University of Trento The Lab is a wide infrastructure wherein researchers can carry out all the necessary experimental operations and measurements required in the project* ***Equipment*** *The Lab has all the necessary equipment for* • *samples extraction and preparation* • *sample purification, analysis and isolation* • *bioorganic compounds identification also through ab initio structure elucidation*
Previous Involvement in **Research and Training**	• Research Unit in the National Project PRIN2008-10 "*Structural and dynamical Aspects of the pheromone-receptor interaction in the" model "ciliate Euplotes"* (Coordinator: prof P. Luporini) • Research Unit in the 2010-2013 EULAKES scientific project (*HPLC-*

Programmes	*MS-UV analysis of pigments in lake-sediment cores*), financed by the European Union - from 2010 to 2013 - throughout *Central Europe Programme (Local Coordinator M. Tolotti, FEM)* • Lecturer at the PhD School of Metabolomics San Michele July 2011 • Membership in , International Doctoral School of Biomolecular Sciences-UNITN • Membership of the Executive Committee of the International Doctoral School of Biomolecular Sciences-UNITN • Supervisor of the following PhD theses on the topic a. Callone Emanuela, (17th cycle) *Structures, ecological role and phylogenetic significance of protistan secondary metabolism,* PhD Dissertation Defense 23 December 2004, University of Pisa Doctoral School in "Evolutionary Biology" b. Sandron Tommaso (23th cycle) *Investigation of biological membranes by NMR and ESI-MS Methodologies,* PhD Dissertation Defense 19 December 2010, University of Trento, Doctoral School in in "Physics" c. Yang Yu (26th cycle) *Lipidomics Investigations in Cell Biology,* PhD Dissertation Defense 24 June 2014, University of Trento , International Doctoral School in Biomolecular Sciences • Advisor of the following PhD theses on the topic a. Dong Yonghui (26th cycle) *Mass Spectrometry Imaging: Looking Fruits at Molecular Level,* PhD Dissertation Defense 24 June 2014, University of Trento, International Doctoral School in Biomolecular Sciences b. Gasperotti Mattia (26th cycle) *Fruit Polyphenols and their Fate in the Mammalian System after Ingestion*, PhD Dissertation Defense 24 June 2014, University of Trento , International Doctoral School in Biomolecular Sciences
Current Involvement in **Research and Training**	• Research Unit in the national project PRIN 2011-2016: *Structural and functional effects produced by molecules involved in the chemical defense mechanisms of invertebrates* (Coordinator : prof Ballarin, UNIPD)

Programmes	• Research Unit coordinating the local project 2015-17 *Industrial-scale production of oil enriched in omega-3 fatty from processing waste of local trouts" funded by CARITRO- Trento* • PhD supervision of the PhD project granted by CIBIO-UNITN "*Expanding the field of cell proteomics and lipidomics through development of Advanced Mass Spectrometric and NMR methodologies*". • Membership in PhD School of Biomolecular Sciences-UNITN • Supervisor of the following PhD theses on the topic a. Ferrazza Ruggero (29th cycle), *Development of Advanced Mass Spectrometric and NMR methodologies for cell lipidomics*, International Doctoral School in Biomolecular Sciences-UNITN, granted by CIBIO project (2014-2017)
Relevant Publications **and/or Research /** **Innovation Product**	1. Yang Yu, Matej Skočaj, Mateja Erdani Kreft, Nataša Resnik, Peter Veranič, Pietro Franceschi, Kristina Sepčić, Graziano Guella, *Comparative lipidomic study of urothelial cancer models: association with urothelial cancer cell invasiveness*, *MOLECULAR BIOSYSTEMS, **2016**, 12, 3266-3279,* DOI: 10.1039/c6mb00477f 2. Ferrazza R.; Griffin, J.L.; Guella G., Franceschi P., *IsotopicLabelling: an R package for the analysis of MS isotopic patterns of labelled analytes*, **2016**, BIOINFORMATICS, IN PRESS, doi:10.1093/bioinformatics/btw588 3. Anesi, A.; Guella, G. *Fast liquid chromatography/Mass Spectrometry methodology for membrane lipid profiling through hydrophilic interaction liquid chromatography* **2016**, JOURNAL OF CHROMATOGRAPHY A, 1384 44-52, DOI: 10.1016/j.chroma.2015.01.035 4. Novak, M.; Sepcic, K.; Krasevec, N.; Krizaj, I.; Macek, P.; Anderluh, G.; Guella, G; Mancini, I. *Targeted Lipid Analysis of Haemolytic Mycelial Extracts of Aspergillus niger, **2014,*** MOLECULES Volume: 19 Issue: 7 Pages: 9051-9069; DOI: 10.3390/molecules19079051 5. Yu, Y.; Vidalino, L.; Anesi, A.; Macchi, P.; Guella, G., *A lipidomics investigation of the induced hypoxia stress on HeLa cells by using MS and NMR techniques*, **2014**, MOLECULAR BIOSYSTEMS Volume: 10 Issue: 4 Pages: 878-890; DOI: 10.1039/c3mb70540d

Beneficiary Legal Name:University of Trento, CIBIO

General Description	The University of Trento (UniTN) is a medium size University in Italy, ranked among the best Italian Universities and among the first 200 institutions according to the THE - Times Higher Education Rankings 2015-2016. The Centre for Integrative Biology (CIBIO), founded in 2007, is a cutting-edge and top-ranked academic biomedicine institute within UniTN, organised as a hybrid research centre/university department. The Centre has recently grown to 30 Research Laboratories headed by successful, independent and international Principal Investigators. CIBIO is successful in grant attraction, capitalising a projects portfolio of almost 16 Million Euro in 3 years, and publishing articles in peer reviewed journals with an average impact factor of 7.8, with prestigious records on Nature, Cell, Neuron.
Role and Commitment ofkey persons (including supervisors)	Nicola Segata will be involved in ESR training and bioinforamtic support for ESR 9 and will contribute to microbiome characterisation of the FASTMOB study.
Key Research Facilities, Infrastructure and Equipment	UNITN provides a high level of research services through Core Facilities operated by highly skilled staff scientists. Biomedical research projects are supported with the required level of technological sophistication, including facilities for High-Throughput/High Content Screening (Tecan Evo 200, PerkinElmer EnSpire-Alpha Screen, PerkinElmer Operetta HCS, BioTekEL406 Microplate washer-dispenser, xCELLigence System Roche, Li-Cor Odyssey), Next Generation Sequencing (Illumina HiSeq 2000 and MiSeq, Ion Torrent Personal Genome Machine - PGMTM, Ion Chef and Ion OneTouch system, PerkinElmer NGS express automation, Bioruptor, Caliper LabChip GX, Bio-Rad C1000 cycler, CFX Connect real time, Pippin Prep gel), Microarray (Agilent G2505C High-Resolution Microarray Scanner, Bio-Rad CFX96 real-time, Bio-Rad CFX384 real time, Corbett RotorGene 6000 real-time, Agilent Bioanalyzer), Cell Analysis and Separation Cell Technology (FACS Canto A, FACS Aria II, DEP-Array, Tali® Image Cytometer, Gentle MACS™ Dissociator), Advanced Imaging (Leica TCS SP5 II confocal microscope, MZ16 Fluorescence stereomicroscope. Zeiss AXIOVERT OBSERVER Z1 with Apotome and CellObserver modules, Axio Imager M2 microscope. Nikon ECLIPSE 90., IMIC Digital Microscope System Andor Ultra 897), Mass Spectrometry (ThermoFisher Fusion MS, Bruker MALDITOF/TOF-MS), Model

	Organisms (hosting Mus musculus, Danio rerio, Xenopus laevis, Notobranchius furzeri), Protein Science and Bioinformatics.
Previous Involvement in Research and Training Programmes	UniTN has an extensive experience with the management of EU projects, being awarded with 119 FP7 projects and 39 H2020 projects. CIBIO at UNITN has a good track in hosting Marie Curie fellows under FP7 and H2020, within both postdoctoral and re-integration programmes (7 Incoming and 2 Outgoing fellows, 5 Marie Curie CIG, 3 IF), developing adequate research infrastructures, training and administrative capacities for effective implementation of this kind of fellowships.
Current Involvement in Research and Training Programmes	Highlights of major CIBIO results in research funding are: 2 ERC Grants; 40% of DuLRCecco Telethon Institute (DTI) Assistant researchers are represented at CIBIO; CIBIO is the most awarded Institute in Italy from the prestigious Armenise-Harvard Foundation; 20% of CIBIO projects are awarded by EC; 50% of success rate on 2015 applications to 6 H2020 MSCA-IF-2015; 45% of grants from prestigious national and international foundations. CIBIO's staff is composed for around the 70% of its FTEs by postdoctoral and doctoral fellows. A number of measures are taken to ensure continuous training allowing also incoming and visiting researchers to benefit of training programmes.
Relevant Publications and/or Research / Innovation Product	*Max. 5* • Donati, C., et al., and Segata, N. 2016. Uncovering oral Neisseria tropism and persistence using metagenomic sequencing. Nature Microbiology 1, Article number: 16070 • Zolfo, M. et al, and Segata, N. 2016 MetaMLST: multi-locus strain-level bacterial typing from metagenomic samples. Nucleic Acids Research, gkw837 • Scholz, M., et al, and Segata, N. 2016. Strain-level microbial epidemiology and population genomics from shotgun metagenomics. Nature methods • Truong,DT, et al, and Segata, N. MetaPhlAn2 for enhanced metagenomic taxonomic profiling. Nature methods 12 (10), 902-903

	• Segata, N. et al, 2014. PhyloPhlAn is a new method for improved phylogenetic and taxonomic placement of microbes. Nature communications 4

Beneficiary Legal Name: Accademia Europea di Bolzano	
General Description	The Institute for Biomedicine at the European Academy of Bozen-Bolzano (EURAC IB) is a dedicated research institute focused on biomedical research. The Eurac IB includes four research groups: Cardiovascular Health; Neuromedicine; Biomedical Informatics; Biostatistics & Epidemiology. The core scientific research and activities rely on results from population-based studies and clinical data collections set up by the Institute and within collaborations. The results from the Biostatistical, Bioinformatic and epidemiological analysis inform follow-up projects to investigate disease mechanisms. Eurac IB holds expertise in genetic epidemiology study design, genetic data analysis, including genome-wide association studies (GWAS) and large meta-analysis, along with candidate gene approaches, family data analysis, bioinformatic candidate prioritization and pathway analysis, DNA sequencing and iPS cell generation and reprogramming to various cell types. The EURAC-IB is involved in identifying predisposition genes for the most common chronic conditions, especially in cardiovascular, neurological and metabolic disorders along with biomarkers for healthy ageing. This is achieved through the Cooperative Health Research in South Tyrol (CHRIS) study, one of the largest European single centre longitudinal population-based studies on the genetics of common diseases, currently with more than 10000 enrolled participants. Scientists at EURAC-IB are involved in many ongoing genome-wide association studies (GWAS) and subsequent meta-analyses, and have leading roles in some of them. Development of statistical and bioinformatic tools is another central activity, which is key for adequate processing and analysis of diverse datasets. EURAC-IB scientists are also able to follow up on promising genetic discoveries with functional

	studies, creating patient specific cell models via iPS cell reprogramming, and characterizing them through multiple laboratory technologies, including advanced imaging and electrophysiological characterisation.
Role and Commitment ofkey persons (including supervisors)	The following researchers will be leading and supervising the work at the EURAC IB: • Cristian Pattaro, Ph.D. (5% full-time) Biostatistics & Epidemiology group leader • Andrew Hicks, Ph.D. (5% full-time) Deputy Scientific Director, Neuromedicine group leader • Francisco Domingues, Dr.rer.nat. (5% full-time) Biomedical informatics group leader
Key Research Facilities, Infrastructure and Equipment	The EURAC-IB manages the ongoing CHRIS population study. The CHRIS study center at the Silandro Hospital is staffed with nurses and study assistants, and is equipped for performing a health assessment of participants based on interview/questionnaires, ECG and blood pressure measurements and blood collection. The study center enrols up to 10 participants a day. The EURAC-IB also manages biobanks at the Merano and Bolzano Hospitals that are equipped to store blood, plasma, serum, DNA and urine samples. The Bolzano biobank is also provided with automated liquid handlers for collection, processing and preservation of the biosamples. The EURAC-IB laboratory in Bolzano has a dedicated cell culture facility equipped for iPS cell work. The laboratory also includes an imaging and electrophysiology suite, with a Leica SP8 confocal microscope, and a Nikon Ti-U microscope with recording equipment from Axon instruments and fast photometric capabilities. The laboratory also includes Envision and Victor X3 plate readers from Perkin Elmer, and an Oxygraph 2K high resolution respirometer from Oroboros for measurement of mitochondrial metabolism. The Mass Spectrometry facility is equipped with a Shimadzu Nexera X2 UPLC connected to a Sciex Qtrap 6500 mass spectrometer and an Eksigent MicroLC200 connected to Sciex Tripletof 5600+ mass spectrometer, which allows for both sensitive and comprehensive metabolic profiling of the cell models. The laboratory is also furnished for

	real-time PCR capabilities with the Biorad CFX96, and equipped with a Sanger DNA sequencer as well as an Illumina MiSeq high-throughput sequencer adequate for micrombiome profiling. The EURAC-IB is provided with dedicated calculation servers (144 cores) and a data storage system (150TB) to fulfill the data processing needs.
Previous Involvement in Research and Training Programmes	Previous population study: • The MICROS Study (2002-2003 was a genetic study of population microisolates in South Tyrol with 1259 participants. • Participated in the European special populations research network Consortium (EUROSPAN) in 2006-2010. Nine researchers completed their PhD at the EURAC IB since 2007.
Current Involvement in Research and Training Programmes	Current activities involving our population and clinical studies • CHRIS is a population-based study with a longitudinal lookout to investigate the genetic and molecular basis of age-related common chronic conditions and their interaction with life style and environment. Started in 2011, with more than 10000 participants currently enrolled. • Cristian Pattaro is leading the CKDGen consortium in the investigation of the genetic basis of chronic kidney disease. • We participate in the GIANT consortium (The Genetic Investigation of ANthropometric Traits Consortium), an international research collaboration to identify genetic loci that modulate human body size and shape, including height and obesity. • We also participate in many working groups within the Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE) Consortium, a research network for genome-wide association studies meta-analyses among large population-based cohort studies. • We have implemented a clinical study in collaboration with the Bolzano and Trento hospitals to identify genetic variants associated with appropriate therapy in 286 participants implanted with implantable cardioverter defibrillator.

	• We are working closely with Bolzano hospital and Clinicians in Cagliara on the genetics of Parkinson's disease. There are currently eight PhD students working at the EURAC-IB and enrolled in doctoral programs at different universities. Four of these students participate on a joint doctoral program (BIDOC) between the EURAC IB and the Medical University of Innsbruck.
Relevant Publications and/or Research / Innovation Product	*Max. 5* 1. Pattaro et al. Genetic associations at 53 loci highlight cell types and biological pathways relevant for kidney function. Nat Commun. 2016 7:10023. doi:10.1038/ncomms10023. 2. Shungin, D. et al. New genetic loci link adipose and insulin biology to body fat distribution. Nature. 2015 518:187-196. doi:10.1038/nature14132. 3. Locke, A. E. et al. Genetic studies of body mass index yield new insights for obesity biology. Nature. 2015 518:197-206. doi:10.1038/nature14177. 4. Vimaleswaran, K. S. et al. Causal relationship between obesity and vitamin D status: bi-directional Mendelian randomization analysis of multiple cohorts. PLoS Medicine. 2013 10:e1001383. doi:10.1371/journal.pmed.1001383. 5. Yang, J. et al. FTO genotype is associated with phenotypic variability of body mass index. Nature. 2012 490:267-272. doi:10.1038/nature11401.

Beneficiary Legal Name: Free University of Bolzano (UNIBZ)	
General Description	**The Faculty of Science and Technology (FaST)**
Role and Commitment of key persons (including supervisors)	The following scientific stuff will be involved in the research, training and supervision (the foreseen extent of involvement in % of full-time employment) 1. Matthias Gauly, Prof. Dr. Dr., Full-Professor (5) 2. and collaborators

Key Research Facilities, Infrastructure and Equipment	The Free University of Bolzano (UNIBZ) was founded in 1997 as a multilingual, internationally oriented institution. The Faculty of Science and Technology (FaST) was established in 2007 and since then it has grown rapidly, recruiting highly qualified scientific staff from Italy and abroad, expanding the teaching offer to the Masters and PhD levels, developing a range of local, national and international scientific collaborations, and enlarging its research facilities. The UNIBZ has about 3200 students, 240 staff and 21 international frame agreements. At the FaST a wide range of scientific expertise in the agricultural and environmental sciences, also encompassing aspects related to the energy production, are available. In the last national evaluation of the quality of the research (VQR), the area of agriculture of the FaST ranked at the second place among all the Italian universities and research centers active in agricultural research. At the FaST, complex problems, such as the sustainable use of resources in food and energy production, as well as the management of the mountain environment, are tackled by an interdisciplinary approach. Excellent field and laboratory equipment is available. The FaST has been running a number of PhD programmes including "Mountain Environment and Agriculture and in "Sustainable Energy and Technology" and "Food Engineering and Biotechnology".
Previous Involvement in Research and Training Programmes	1. DFG, SFB 299 (2006-2008). Nutzung funktionaler Merkmale in der Kreuzungszucht von Schafen und Rindern für extensive Verfahren der Grünlandnutzung. 2. DFG (AB 30/8-1) (2007-2010). Einflüsse von Nicht-Stärke-Polysacchariden des Futters auf die Auswirkungen von experimentellen *Ascaridia galli* und *Heterakis gallinarum* Infektionen beim Haushuhn (*Gallus gallus domesticus*). 3. Funktionelle Genomanalyse im tierischen Organismus (FUGATO) (2007-2011). Identification of genetic causes of a pre-disposition for economically important factor-bound diseases of feet and legs in cattle, swine and sheep. 4. Programm des Bundesministeriums für Verbraucherschutz, Ernährung und Landwirtschaft zur Innovationsförderung (2009-2012). Entwicklung eines schnellen und sicheren Diagnostikums zur Trächtigkeitsfeststellung beim Rind (33.9-42502-05-10A014).

	5. Programm des Bundesministeriums für Verbraucherschutz, Ernährung und Landwirtschaft zur Innovationsförderung (2009-2012). Untersuchungen zu den Möglichkeiten der Integration von Verhaltensmerkmalen in Zuchtprogrammen beim Schwein (28-1-35.026-08). 6. KLIFF Forschungsverbund „Klimafolgenforschung – Szenarien für die Klimaanpassung des Niedersächsischen Ministeriums für Wissenschaft und Kultur (2008-2013). Konsequenzen und Anpassungen für die niedersächsische Milch- und Rinderproduktion durch Klimaänderungen auf regionaler Skala (Speaker). 7. Bundesministerium für Bildung und Forschung (BMBF) über den Projektträger Jülich – Forschungszentrum Jülich GmbH (PTJ) (2010-2014). Excellenzcluster. Phänomics – Ein systembiologischer Ansatz zur Genotyp-Phänotyp Abbildung im Kontext von Leistung, Gesundheit und WohLRCefinden bei Nutztieren. Project 2.4: Verhaltensmerkmale beim Rind and 4.3: Merkmalsassoziation der Biomarker. 8. Europäischer Fond für regionale Entwicklung (EFRE-Projekt) (2011 – 2013). Pathologie, Ethologie und Ökonomie beim Einsatz eines automatischen Huf- und Klauenreinigers für Pferde und Milchkühe. 9. Bundesministerium für Wirtschaft (BMWi), ZIM – Kooperationsprojekte (2011 – 2014). Entwicklung eines neuartigen ELISA-Tests für den Nachweis und die Differenzierung von Antikörpern gegen endoparasitäre Nematoden bei Legehennen. 10. Bundesministerium für Bildung und Forschung (BMBF) über den Projektträger Jülich - Forschungszentrum Jülich GmbH (PTJ) (2010 - 2015). Verbundprojekt NaLaMa-nT: Nachhaltiges Landmanagement im Norddeutschen Tiefland unter sich ändernden ökologischen, ökonomischen und gesellschaftlichen Rahmenbedingungen. Project: Analyse und Modellierung von Produktionsverfahren bei Rind und Schwein zur optimierten Anpassung an wechselnde Umweltbedingungen.
Current Involvement in Research and Training Programmes	1. Niedersächsisches Ministerium für Wissenschaft und Kultur (2013 - 2018). Forschungsverbund „Verfahrensanalyse Milch: Produktion von Milch in Weide- oder Stallhaltung (ZN 2864) 2. Free University of Bolzano (2015 – 2017): Investigations on the efficiency and safety of anthelmintics in goats of South Tyrol. 3. BLE - Förderung von Innovationen zur Verbesserung der Haltung von landwirtschaftlichen Nutztieren (2015 – 2017): Einfluss verschiedener Abferkel- und Aufzuchtsysteme auf Tierwohl, Tiergesundheit und Wirtschaftlichkeit in der Schweinehaltung - ein interdisziplinärer Ansatz. 4. Province of South Tyrol (2016 – 2020): Aktionsplan zur

	Weiterentwicklung der Berglandwirtschaft.
Relevant Publications **and/or Research /** **Innovation Product**	1. Lambertz C., Sanker C., **Gauly M**., 2014. Climatic effects on milk production traits and somatic cell score in lactating Holstein-Friesian cows in different housing systems. Journal of Dairy Science, 97, 319-329. 2. Geburt K., Piechotta M., König v. Borstel U., **Gauly M**., 2015. Influence of testosterone on the docility of German Simmental and Charolais heifers during behavior tests. Physiology and Behavior, 141, 164–171. 3. Meyer-Hamme S., Lambertz C., **Gauly M.,** 2016. Does group size have an impact on welfare indicators in fattening pigs? Animal (10), 142-149 4. Ammer S., Lambert C., **Gauly M.,** 2016. Is reticular temperature a useful indicator of heat stress in dairy cattle? Journal of Dairy Science, in press, http://dx.doi.org/10.3168/jds.2016-11282

Beneficiary Legal Name: University for Health Sciences, Medical Informatics and Technology (UMIT) Eduard Wallnöfer-Zentrum 1, 6060 Hall i.T., Austria	
General Description	UMIT is a young and vivid modern health and life sciences university with is strong focus on applied research and health policy decision advice. UMT has specialized in new vocational fields and research areas and thus in the prevailing challenges in the health care system. With its focus areas of psychology, public health, health sciences, health technology assessment, nutritional sciences, nursing science biomedical informatics / health informatics / technology, business management in the health system, , complemented by the university training courses in the areas of physiotherapy, health prevention as well as crisis and disaster management, UMIT offers academic education and advanced training of high quality in the fields that have turned out to be of increasing importance in the modern health care system.
Role and Commitment of	**Social and Personality Psychology**

key persons (including supervisors)	Prof. Dr. Bernhard Streicher Head of Department of Psychology and Medical Sciences Head of Social and Personality Psychology Working Group Prof. Dr. Uwe Siebert Professor of Public Health and Health Technology Assessment (UMIT) Adjunct Professor of Health Policy and Management (Harvard University) Chair, Dept. of Public Health, Health Services Research and Health Technology Assessment Senior Scientists: Stephan Pidner (risk perception, risk behavior, and psychological intervention programs) Beate Jahn (health economics and decision-analytic modelling) Felicitas Kühne (causal/epidemiological inference and health promotion) Raffaella Gothe (biostatistics, epidemiology and causalinference) Annette Conrads-Frank (cost-effectiveness of obesity and nutrition) Petra Schnell-Inderst (public health technology assessment, EUnetHTA, ethical/legal/social implications, biomarker assessment
Key Research Facilities, Infrastructure and Equipment	**1) Social and Personality Psychology** Prof. Dr. Bernhard Streicher **Short Description:** In our research group at the RiskLab at UMIT (www.umit.at/risk) we explore

	the psychological mechanisms of risk perception, assessment, and behavior. For example, we aim to understand how people struggle to be actively engaged in planning for their future, and their life as elderly people and according age-related risks in particular. While people fear age-related health issues, these risks are perceived as unavoidable. Therefore, risk prevention for future risks like age-related health problems should go beyond presenting facts and, for example, include appropriate risk communication and preexperiencing future outcomes. Considering our experience and research focus we are confident that we can substantially contribute to the proposed EUREGIO project on food and health. **Areas of Participation:** We are interested in contributing to research projects, to which the psychological mechanisms of perception, behavior and communication under risk and uncertainty are relevant. This interest can span from lab-experiments on specific effects to risk government or risk communication to the general public. Furthermore, we can contribute lectures both to the proposed expert lecture series and the innovation training network. **2) Public Health** Prof. Dr. Uwe Siebert **Area of Competence:** Quantitative and interdisciplinary comprehensive short- and long-term assessment of public health nutrition, agrifood, and lifestyle interventions in Europe and its countries and regions. The analyses should include a comprehensive assessment of combined individual and system-based strategies for nutrition, educational and lifestyle interventions considering ageing and changing socioeconomic factors in different regions. Outcomes should include short- and long-term effects on health and economic burden of disease. The project also fits in very well with the new Department focus on health services and outcomes research in the region of Tyrol. A particular focus together with psychologists and risk communicators could be the topic

	of risk preferences for the development and assessment of meaningful preventive and therapeutic measures, including the aspects of "individualized prevention" and "patient-shared medical decision making". In this context, Prof. Siebert could connect with the Society of Medical Decision Making (www.smdm.org), where he served as President Elect and currently established a platform to bring physicians, psychologists, epidemiologists, decision modelers and policy and health technology decision makers together to better inform health-related strategies. The team of the Institute for Public Health has a broad and comprehensive competence and publication track record in the causal assessment of benefits, risks, cost-effectiveness, as well as ethical, legal and social implications of such interventions as well as ageing and its effect on diabetes, cardiovascular disease, cancer and other chronic diseases including inflammation-related disorders. They have developed mathematical models to evaluate the short- and long-term effects combining data from clinical trials and observational studies using individual-level and aggregated data with meta-analysis and decision analysis with adjustment for (baseline and time-dependent) confounding in observational data. We also have applied such models to evaluate the burden of disease, budget impact and cost-effectiveness of such strategies and factors like age, overweight, biomarkers, and disease history on the related savings by preventing future disease and complications. The inclusion of health-related quality-of-life measures allows for incorporating the consequences of obesity and related disease on physical and psychological dimensions of quality of life and well being (e.g. captured by DALYs or QALYs). The team has collaborated with many national and international partners in this field including collaboration with WHO in the project "Comparative Quantification of Health Risks" / "Avoidable Burden of Disease". **Areas of Participation:** The team would be mainly interested in participating in a research cluster with the topics and methods described above, closely collaborating with partners from Psychology / UMIT , in Tyrol (Campus Tirol Partners), and internationally. In addition, they would provide lectures or participate in a PhD program with specific methodological topics listed above.

Previous Involvement in Research and Training Programmes	*Detail any relevant EU, national or international research and training projects in which the partner has previously participated* Prof. Siebert and Prof. Streicher have both supervised many PhD students in the past. Relevant programs of Prof. Streicher: 2014 - 2015 Unbiased decision making of experts. Wissenschaftsförderung der Sparkassen-Finanzgruppe e.V. [Advancement of Science by the Federation of Saving Banks] 2014 Risk and Driving Savety Training. Allgemeiner Deutscher AutomobilcLRC (ADAC e.V.) [General German AutomobilecLRC]. 2014 Evaluation Risk Savvy Training for Young Drivers. Allgemeiner Deutscher AutomobilcLRC (ADAC e.V.) [General German AutomobilecLRC]. 2013 - 2014 Psychology of Risks of Young Drivers. Allgemeiner Deutscher AutomobilcLRC (ADAC e.V.) [General German AutomobilecLRC]. 2013 - 2014 Training in Risk Competence. LMU Funds for Transfer of Knowledge. 2013 Risk Perception and Decision Making among Veterinarians and Farmers. Deutscher Verband für Leistungs- und Qualitätsprüfungen e.V. (DLQ) [German Associaton for Performance and Quality Testing]. 2012 Training in Risk Competence. Department of Psychology, LMU. 2011 - 2016 Risk Perception and Decision Making under Risk and Uncertainty. Munich RE. 2009 HTADS - Program on Health Technology Assessment & Decision Sciences (Continuing Education Program)

	2012-2017 ERAWEB ERASMUS–WESTERN BALKANS (Academic mobility program) Ongoing Society for Medical Decision Making (SMDM) (Core Course Director, Mentor, Education Committee Member, President-Elect since 2016)
Current Involvement in Research and Training Programmes	*Detail any relevant EU, national or international research and training projects in which the partner is currently participating* Prof. Streicher: 2016 - 2017 Rituals and Risk. Tyrolean Science Foundation (TWF). 2017 - 2018 Risk Literacy. Tyrolean Science Foundation (TWF). 2017 - 2018 Prevention in sports. Significance of the coach at the example of doping- and injury prevention. Tyrolean Science Foundation (TWF). 2016 - 2019 IOCw: Doping Prevention Monitoring Program (DPMP) – development, implementation and assessment of a surveillance tool to monitor doping prevention activities and its impacts on micro- and macro level factors of doping behavior. International Olympic Committee (IOC) Anti-Doping Research Fund. 2015 - 2018 EU H2020-Project: EUthyroid – Towards the Elimination of Iodine Deficiency and Preventable Thyroid-related Diseases in Europe, Work Package 5: Health Economy, Health Technology Asessment and Health Policy 2015 - 2018 EU H2020 MDMS-Right – Providing tha Right Care to the Right Patient with MyeloDysplastic Syndrome at the Right Time, Work Package 3: HRQoL Issues in Elderly Participants with Anaemia. 2015 - 2018 Female cancer prediction using cervical omics to individualise

	screening and prevention (FORECEE) 2014 - 2018 Decision Support for Health Policy and Planning: Methods, Models and Technologies based on existing health care data (DEXHELPP) 2017 – 2022 HBM4EU European Human Biomonitoring Initiative (EC)
Relevant Publications **and/or Research /** **Innovation Product**	*Max. 5* Raue, M., Lermer, E. & **Streicher, B.** (Eds.) (in press). Psychological aspects of risk and risk analysis: Theory, models, and applications.New York, NY: Springer. Lermer, E., **Streicher, B.**, Sachs, R. Raue, M. & Frey, D. (2016). Thinking concretely increases the perceived likelihood of risks: The effect of construal level on risk estimation. Risk Analysis, 36(3), 623-637. doi 10.1111/risa.12445 Lermer, E., **Streicher, B.**, Sachs, R., Raue, M., & Frey, D. (2015). The effect of construal level on risk-taking. *European Journal of Social Psychology*, *45*(1), 99-109. **Siebert U**, Alagoz O, Bayoumi AM, Jahn B, Owens DK, Cohen DJ, Kuntz KM. State-Transition Modeling: A Report of the ISPOR-SMDM Modeling Good Research Practices Task Force -3. Medical Decision Making 2012;32(5):690-700. Jahn B, Rochau U, Kurzthaler C, Paulden M, Kluibenschädl M, Arvandi M, Kühne F, Goehler A, Krahn M, **Siebert U**. Lessons learned from a cross-model validation between a discrete event simulation model and a cohort state-transition model for personalized breast cancer treatment. Medical Decision Making 2016;36(3):375-90.

Beneficiary Legal Name: Accademia Europea di Bolzano	
General Description	The Institute for Alpine Environment was founded in 1995 to perform problem-oriented research on the conflicting priorities of ecology and economy. Located in the heart of the Alps, the Institute offers the ideal conditions for user-oriented research of mountain areas. The major tasks are focused within the pulsing field of conflict between man and nature, namely mountain farming and mountain forests, nature and landscape as well as environmental precaution, all of which belong to the topic "sustainable development in mountain regions". Thereby, all research projects are based on a multidisciplinary approach: landscape ecological and ecosystem research is always combined with socio-economic and social aspects. The institute for Alpine Environment has a strong focus on biodiversity research and ecosystem services analyses. Scientists of the Institute are currently involved in many international projects and therefore have an extensive network of international experts.
Role and Commitment ofkey persons (including supervisors)	The following researchers will be leading and supervising the work at the EURAC "Alpine Environment": • Julia Seeber, Ph.D. (7% part-time) Soil group leader • Michael Steinwandter, MSc. (5% full-time) Soil invertebrate taxonomy • Erich Tasser, PD (5% full-time) Ecosystem services, ecosystem and landscape ecology
Key Research Facilities, Infrastructure and Equipment	The Institute for Alpine Environment has a fully-functional soil laboratory for studying soil invertebrate biodiversity (including a heat-extraction apparatus, high resolution light microscopes) and their abiotic environment (muffle furnace, pH-Meter, drying facilities, ball mills). The Institute is involved in various national and international LTER activities (ILTER, LTER Italia, GNOMO, etc.) and is therefore embedded in an

	international network of experts on biodiversity and ecosystem research. Furthermore, the Institute has access to many databases dealing with (soil) biodiversity, management and land-use types, and ecosystem services: • Soil invertebrate diversity (SoilDiv, data from Erwin Meyer, an expert on alpine invertebrates at the University of Innsbruck, from all three regions) • Mapping the Alps (almost 200 sustainability indicators at municipal level for the whole Alpine region) • AlmAtlas (agricultural indicators for the ArgeAlp region at municipality level) • AlpES (32 ES indicators and 150 sustainability indicators at municipal level for the whole Alpine Space) • Plant diversity database (12000 releveés for the whole Alps) • Landscape database (trajectories of land-use, land cover and land structure for the last 150 years for all three regions)
Previous Involvement in Research and Training Programmes	The Institute for Alpine Environment has a strong connection to the University of Innsbruck and has continuously been involved in the supervision of PhDs. Eleven PhDs have finished their thesis at the Institute since 2007. The Institute has also been involved in the EU SOCRATES programme.
Current Involvement in Research and Training Programmes	There are currently ten PhD students working at the Institute for Alpine Environment and enrolled in doctoral programs at the University of Innsbruck.
Relevant Publications and/or Research / Innovation Product	*Max. 5* **1.** Egarter Vigl L, Schirpke U, Tasser E, Tappeiner U, 2016. Linking long-term landscape dynamics to the multiple interactions among ecosystem services in the European Alps. Landscape Ecology 31, 1903-1918. 2. Fontana V, Radtke A, Walde J, Tasser E, Wilhalm T, Zerbe S, Tappeiner U, 2014. What plant traits tell us: Consequences of land-use change of a traditional agro-forest system on biodiversity and ecosystem service provision. Agriculture, Ecosystems & Environment 186, 44-53. 3. Rüdisser J, Tasser E, Peham T, Meyer E, Tappeiner U, 2015. The dark

	side of biodiversity: Spatial application of the biological soil quality indicator. Ecological Indicators 53, 240-246. 4. Rief A, Arthofer W, Steiner F, Schlick-Steiner B, Seeber J, 2015. You are not what you eat: massive parallel sequencing reveals different microbiomes in diet and gut of larval Dilophus febrilis (Diptera: Bibionidae). Genomic Resources Notes Accepted 1 June 2015 – 31 July 2015. Molecular Ecology Resources, 15: 1510–1512. 5. Kitz F, Steinwandter M, Traugott M, Seeber J, 2015. Increased decomposer diversity accelerates and potentially stabilises litter decomposition. Soil Biology and Biochemistry 83, 138-141.

Beneficiary Legal Name: Universität Innsbruck - Institute for Biomedical Aging Research (IBA)	
General Description	The University of Innsbruck (UIBK) was founded in 1669 and is the biggest and most important institution for research and higher education in westerly Austria. Today it comprises almost 27.000 students and more than 4.000 staff and faculty members. With its long-lasting educational tradition and scientific history, the UIBK provides perfect contemporary conditions for strong research and teaching. International rankings confirm the University's leading role in basic research. In this productive environment 15 faculties provide a broad range of programs in almost all fields of studies. In order to promote international exchange in research and teaching, the University collaborates with numerous international institutions in research and higher education. In September 2012, the ***Institute for Biomedical Aging Research (IBA)***, founded by the Austrian Academy of Sciences in 1992, was assigned to the Faculty of Biology of the UIBK as a distinguished Research Unit for human biogerontology. Researchers at the IBA study aging processes at the cellular and molecular level. The goal is to apprehend the etiology of age-related impairments and diseases and to define distinct measures to postpone/prevent disorders to improve the quality of life of individuals at advancing age. The institute houses 5 research groups, two of which are represented in the present programme: the Immunology group and the ***Cell Metabolism and Differentiation Research Group (CMDR).*** The goal of the Immunology group is to reach a better understanding of age-related changes occurring in the immune system in order to find new ways to prevent loss of immune function within age and to ensure healthy aging. CMDR works on adipose tissues ageing and obesity. The main goal is to better understand ageing of adipose stem cells and adipocytes. Moreover, CMDR studies mechanics underlying caloric restriction, an intervention which prevents obesity and extends health and maximum life span of a wide variety of species, and aims to develop

	caloric restriction mimetics.
Role and Commitment of key persons (including supervisors)	*Beatrix Grubeck-Loebenstein is the head of the Institute for Biomedical Aging Research at the UIBK. Werner Zwerschke is the head of the Cell Metabolism and Differentiation Research Group. Beatrix Grubeck-Loebenstein and Werner Zwerschke will be co-supervising one PhD student and will also organize the planned cooperation with the FEM.*
Key Research Facilities, Infrastructure and Equipment	Equipment available at the Institute for Biomedical Aging Research: confocal microscope (Bio-Rad), Cell Voyager (Visitron), phosphoimager, densitometer for gel analysis, PCR thermocyclers, including Real time LightCycler (Roche), protein purifier (ÄKTA, Amersham) ELISA Readers, luminometer (Anthos Lucy-1), microfuges, FACScan (Calibur, Becton Dickinson), ultracentrifuges, light and fluorescence microscopes, cell disrupter, spectrofluorimeter and spectrophotometer (Beckman), tissue culture hoods and CO2 incubators, Revco freezers and liquid nitrogen storage facilities, beta- and gamma- counters, warm and cold rooms. Standard equipment for molecular biological work. All the assays needed for the performance of the proposed project are well established.
Previous Involvement in Research and Training Programmes	*Beatrix Grubeck-Loebenstein and Werner Zwerschke have both supervised many PhD students in the past.*
Current Involvement in Research and Training Programmes	*Presently Werner Zwerschke supervises several graduate students in his lab. Beatrix Grubeck-Loebenstein is a faculty member of the "HOROS-programme" funded by the Austrian Science Fund (FWF), in which she cooperates with colleagues from the Medical University of Innsbruck. There are presently 3 PhD students participating in this programme in her lab and another one, who is funded by the "DOC programme" of the Austrian Academy of Sciences (ÖAW).*
Relevant Publications and/or Research /	1. MacLean PS, Higgins JA, Giles ED, Sherk VD, Jackman MR. The role for adipose tissue in weight regain after weight loss. Obesity Reviews.

Innovation Product	2015;16:Supplement1:45-54. 2. Mitterberger M.C., Zwerschke W. Mechanisms of resveratrol induced inhibition of clonal expansion and terminal adipogenic differentiation in 3T3-L1 preadipocytes. J Gerontol A Biol Sci Med Sci. 2013;68:1356-76. 3. Mitterberger MC, Mattesich M, Zwerschke W. Bariatric surgery and diet-induced long-term caloric restriction protect subcutaneous adipose-derived stromal/progenitor cells and prolong their life span in formerly obese humans. Exp Gerontol. 2014;56:106-13. 4. Ejaz, A., Mitterberger, M.C., Lu, Z., Mattesich, M., Zwierzina, M.E., Hörl, S., Kaiser, A., Viertler, H.P., Rostek., U., Meryk A, Khalid, S., Pierer, G., Bast Jr, R.C., Zwerschke W. Weight Loss Upregulates the Small GTPase DIRAS3 in Human White Adipose Progenitor Cells, Which Negatively Regulates Adipogenesis and Activates Autophagy via Akt–mTOR Inhibition. EBioMedicine 2016;6:149-61. 5. Schroeder BO, Bäckhed F. Signals from the gut microbiota to distant organs in physiology and disease. Nat Med. 2016;22:1079-89. 6. Bürkle A. et al. MARK-AGE biomarkers of ageing. Mech Ageing Dev 2015;151:2-12.

Beneficiary Legal Name: Universität Innsbruck – Institute of Ecology	
General Description	The Institute of Ecology was founded in 2006 by merging most ecological sections of the Institutes of Botany and Zoology & Limnology. Since then, additional chairs in Ecosystem and Landscape Ecology, Molecular Ecology and Alpine Freshwater Ecology have contributed to our interdisciplinarity and commitment to high quality. The main research focus lies on the study of interactions among biota, between biota and their physicochemical environment, and between biota and society. Being both, basic and applied, it covers a wide range of organizational levels and time scales: from molecular to landscape and from seconds to millennia. Given the strategic geographical position of the University in the Alps, our research is centered on the Alpine space which offers a large diversity of ecosystems, as well as scientific and real-world challenges. Our students acquire skills in this broad range of expertise through an attractive curriculum that offers a blend of theoretical and practical courses on Ecology, Biodiversity and

	Evolution. The Institute's research is organized in three research units according to strategic themes: Ecosystem Research and Landscape Ecology, Alpine Freshwater Ecology, Animal and Molecular Ecology. The Research Group Ecosystem and Landscape Ecology, headed by Ulrike Tappeiner integrates relevant ecological disciplines and methods (soil and vegetation science, hydrology, micrometeorology, remote sensing, spatial statistics, ecological and geo-statistical modelling) to analyse ecosystem functions and services across spatial and temporal scales. Beneath systematic survey and monitoring of fundamental data, experiments and modelling of global change impacts on biodiversity, catchment yield, natural hazards risk and land-use/land-cover are conducted. Furthermore, the high profile research is embedded in a broader context as a result of a wide range of national and international collaborations with leading research groups in Europe and USA.
Role and Commitment of key persons (including supervisors)	*Ulrike Tappeiner is the Dean of the Faculty of Biology and Head of the Research Group: Ecosystem Research and Landscape Ecology. She will supervising one PhD student (hosted by EURAC) together with Dr. Seeber (EURAC) and Dr. Rizzolli (FEM).* *Dr. Johannes Rüdisser will be involved in geo-spatial analysis and modelling with a special focus on biodiversity and land-use management.*
Key Research Facilities, Infrastructure and Equipment	Equipment available at the Institute of Ecology for this project: Soil physics and soil fauna lab with standard equipment, Comprehensive database on biodiversity in farm systems. All the assays needed for the performance of the proposed project are well established.
Previous Involvement in Research and Training Programmes	*A range of EU research projects (FP2- Integralp, FP4-Ecomont, FP5-Carbomont, Era-Net Vital, Alpine Space-DIAMOND, Alpine Space-AlpES), and numerous international and national projects have provided studies on biodiversity and ecosystems services, various aspects of biogeochemical cycles (C, N, H_2O), potential risks (incl. surface runoff, avalanches, erosion), in managed und natural mountain ecosystems, up-scaling form plant to habitat and landscape, sustainability indicators, interactions between socio-economy and ecology and*

	related landscape processes. *Ulrike Tappeiner was a member of several international Training Programmes (EU-Socrates, EU Leonardo, EU-Lifelong Learning) and supervised many PhD students in the past. Moreover, she collaborates strongly with EURAC and has many experiences in co-supervising PhD students hosted by EURAC.*
Current Involvement in Research and Training Programmes	*Presently Ulrike Tappeiner is principal investigator (PI) in several national and international projects: P) of the Austrian part: Landschaft im Visier (Autonomous Province of Bolzano/Bozen South Tyrol, Abteilung Bildungsförderung, Universität und Forschung), PI: Viel-Falter Top Citizen Science (Austrian Agency for International Cooperation in Education and Research), PI: ESS - Experiencing Ecosystem Services (FWF), PI of the Austrian part: AlpES - Alpine Ecosystem Services – mapping, maintenance and management (European Regional Development Fund (ERDF, EU), PI of the Austrian part: ClimAgro: Valorization of agriculture for the water supply in context with climate change (Autonomous Province of Bozen-Südtirol), Co-ordination of the HRSM – cooperation project KLIMAGRO: In-Wertsetzung der Landwirtschaft für die Nutz- und Trinkwasserbereitstellung unter Berücksichtigung des Globalen Wandels. (Austrian Federal Ministry of Science, Research and Economy)* *Currently Tappeiner supervises 6 PhD students (4 of them together with Erich Tasser from EURAC)*
Relevant Publications and/or Research / Innovation Product	1. Locatelli B, Lavorel S, Sloan S, Tappeiner U, Geneletti D (forthcoming): Archetypes of trajectories of ecosystem services in mountains. Frontiers in Ecology and the Environment 2. Tasser E, Leitinger G, Schirpke U, Tappeiner U (2017): Climate Change vs Land-Use Change - which affects the landscape more? Land Use Policy, 60, 60-72, http://dx.doi.org/10.1016/j.landusepol.2016.10.019 3. Egarter Vigl L, Schirpke U, Tasser E, Tappeiner U (2016) Linking long-term landscape dynamics to the multiple interactions among ecosystem services in the European Alps. Landscape Ecology, 31/9, 1903–1918, DOI 10.1007/s10980-016-0389-3 4. Rüdisser J, Tasser E, Peham T, Meyer E, Tappeiner U (2015): The dark side of biodiversity: spatial application of the Biological Soil Quality Indicator (BSQ) in South Tyrol, Italy. Ecological Indicators 53, 240-246

	5. Kirchner M, Schmidt J, Kindermann G, Kulmer V, Mitter H, Prettenthaler F, Rüdisser J, Schauppenlehner T, Schönhart M, Strauss F, Tappeiner U, Tasser E, Schmid E (2015): Assessing trade offs and synergies of ecosystem services and economic impacts in Austrian agriculture under climate change and policy change. Ecological Economics 109:161-174

Beneficiary Legal Name: Universität Innsbruck - The Breath Research Institute	
General Description	The Institute for ***Breath Research, University of Innsbruck***, is an internationally oriented interdisciplinary research centre focusing on the detection of trace volatile organic compounds in exhaled breath, saliva, urine or sweat or emitted by skin for applications in non-invasive clinical screening and diagnosis and drug monitoring. Research includes in vitro investigations of volatiles released by bacteria or cell lines, urban search and rescue operations of entrapped persons after earthquakes and other major disasters based on compounds released through breath and urine, and monitoring anaesthetics in breath during and after surgery. The institute provides an interface between pure sciences, medical sciences and industry.
Role and Commitment of key persons (including supervisors)	*Chris Mayhew will collaborating with the Nutrition and Nutrigenomics Unit at FEM and Professor Segata from UniTN, will be involved in applying PTR-MS based breath analysis to measure the contribution of the human gut microbiota to whole body energy metabolism.*
Key Research Facilities, Infrastructure and Equipment	The Institute of Breath Research has a major research facility in Dornbirn, Vorarlberg, Austria, but also has offices and laboratories in Innsbruck for access to clinical research programmes with the Medical University of Innsbruck. The Institute currently consists of 6 members of staff, 1 Early Stage Researcher, 2 PhD students and up to 5 Masters students/year. Instrumentation includes PTR-ToF-MS systems, IMS, and various GC-MS.
Previous Involvement	*Chris Mayhew successfully led a Marie Curie FP7-PEOPLE-2011-Initial Training*

in Research and Training Programmes	*Network: Proton Ionization Molecular Mass Spectrometry (PIMMS) 1st June 2012 – 31st May 2016. PIMMS was a multidisciplinary and intersectoral analytical chemistry programme which trained 15 Early Stage Researchers within a collaborative academic and commercial research network involving 12 beneficiary and 6 partner organisations (3 industrial, 5 governmental research institutes, 6 universities, 2 hospitals, and 2 communication consultancy companies).*
Current Involvement in Research and Training Programmes	Chris Mayhew is currently leading a MARIE SKŁODOWSKA-CURIE ACTIONS H2020 Innovative Training Network: Ion-Molecule Processes for Analytical Chemical Technologies (IMPACT) 1st January 2016-31st December 2019, involving the training of 10 Early Stage Researchers, within an integrated partnership of commercial, governmental and academic organisations.
Relevant Publications and/or Research / Innovation Product	1. O'Hara ME, Fernández Del Río R, Holt A, Pemberton P, Shah T, Whitehouse T, Mayhew CA. Limonene in exhaled breath is elevated in hepatic encephalopathy. J Breath Res. 2016 Nov 21;10(4):046010 2. Fernández Del Río R, O'Hara ME, Holt A, Pemberton P, Shah T, Whitehouse T, Mayhew CA. Volatile Biomarkers in Breath Associated With Liver Cirrhosis - Comparisons of Pre- and Post-liver Transplant Breath Samples. EBioMedicine. 2015 Jul 26;2(9):1243-50. doi: 10.1016/j.ebiom.2015.07.027. 3. O'Hara M, Mayhew CA. A preliminary comparison of volatile organic compounds in the headspace of cultures of Staphylococcus aureus grown in nutrient, dextrose and brain heart bovine broths measured using a proton transfer reaction mass spectrometer. J Breath Res. 2009 Jun;3(2):027001. doi: 10.1088/1752-7155/3/2/027001. 4. O'Hara ME, Clutton-Brock TH, Green S, Mayhew CA. Endogenous volatile organic compounds in breath and blood of healthy volunteers: examining breathanalysis as a surrogate for blood measurements. J Breath Res. 2009 Jun;3(2):027005. doi: 10.1088/1752-7155/3/2/027005. 5. Fernández Del Río R, O'Hara ME, Pemberton P, Whitehouse T, Mayhew CA. Elimination characteristics of post-operative isoflurane levels in alveolar exhaled breath via PTR-MSanalysis. J Breath Res. 2016 Oct 12;10(4):046006.

Beneficiary Legal Name:	SDNC-TN
General Description	Servizio di dietetica e Nutrizione Clinica – Ospedale S. Chiara Trento (herein, APSS)
Role and Commitment of key persons (including supervisors)	Dr Carlo Pedrolli, Dietetics and Clinical Nutrition Service, Santa Chiara hospital, Trento and responsible for the operating Unit "Semplice Ristorazione Collettiva and Artificial Nutrition (estimated 10% time)
Key Research Facilities, Infrastructure and Equipment	The Dietetic and clinical Nutrition Service, Santa Chiara, Trento comprises 11 employees, medical specialists (Dr. Carlo Pedrolli and Dr. Antonio Costa) and dieticians, and administrative staff. Its mission is the management of nutrition at the Hospital S. Chiara, from collective catering for both employees and patients to special diets, artificial nutrition (enteral and parenteral) necessary for optimal patient care within all operating units of the hospital. It provides counseling at the Center Eating Disorders, through teaching activities at the faculty of sciences nursing of the University of Trento, Faculty of dental Hygiene of the University of Verona. It is also responsible for selection of purchasing specifications for all prescription nutritional products acquired by APSS.
Previous Involvement in Research and Training Programmes	Numerous studies on the validation and implementation of nutritional screening "tools", and a radnomised control trial dietary intervention study in collaboration with FEM measuring the impact of the food ingredient wheat bran aleurone, on metabolic risk and the gut microbiota in obese people.
Current Involvement in Research and Training Programmes	Research on the clinical efficacy of artificial nutrition.

Relevant Publications and/or Research / Innovation Product	1. Cereda E, Pedrolli C, Klersy C, Bonardi C, Quarleri L, Cappello S, Turri A, Rondanelli M, Caccialanza R. (2016) Nutritional status in older persons according to healthcare setting: A systematic review and meta-analysis of prevalence data using MNA®. Clin Nutr. Apr 6. pii: S0261-5614(16)00099-6. doi: 10.1016/j.clnu.2016.03.008. [Epub ahead of print] 2. Ticinesi A, Meschi T, Lauretani F, Felis G, Franchi F, Pedrolli C, Barichella M, Benati G, Di Nuzzo S, Ceda GP, Maggio M. (2016) Nutrition and Inflammation in Older Individuals: Focus on Vitamin D, n-3 Polyunsaturated Fatty Acids and Whey Proteins. Nutrients. Mar 29;8(4):186. doi: 10.3390/nu8040186. Review. 3. Pedrolli C, Sacchi MC, Togni M, Cereda E. (2015) A case of hyperemesis in bulimia nervosa Int J Eat Disord. May;48(4):446-8. doi: 10.1002/eat.22315. Epub 2014 Jun 5. 4. Cereda E, Klersy C, Pedrolli C, Cameletti B, Bonardi C, Quarleri L, Cappello S, Bonoldi A, Bonadeo E, Caccialanza R. (2015) The Geriatric Nutritional Risk Index predicts hospital length of stay and in-hospital weight loss in elderly participants. Clin Nutr. 2015 Feb;34(1):74-8. doi: 10.1016/j.clnu.2014.01.017. Epub 2014 Jan 29. 5. Cereda E, Costa A, Caccialanza R, Pedrolli C. (2013) A malfunctioning nasogastric feeding tube. Nutr Hosp. 2013 Jan-Feb;28(1):229-31. doi: 10.3305/nh.2013.28.1.6259.