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## Personalized nutrition in ageing society: redox control of major-age related diseases through the NutRedOx Network (COST Action CA16112)

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### ABSTRACT

A healthy ageing process is important when it is considered that one-third of the population of Europe is already over 50 years old, although there are regional variations. This proportion is likely to increase in the future, and maintenance of vitality at an older age is not only an important measure of the quality of life but also key to participation and productivity. So, the binomial “nutrition and ageing” has different aspects and poses considerable challenges, providing a fertile ground for research and networks. The NutRedOx network will focus on the impact of redox-active compounds in food on healthy ageing, chemoprevention, and redox control in the context of major age-related diseases. The main aim of the NutRedOx network is to gather experts from Europe, and neighbouring countries, and from different disciplines that are involved in the study of biological redox active food components and are relevant to the ageing organism, its health, function, and vulnerability to disease. Together, these experts will form a major and sustainable EU-wide cluster in form of the NutRedOx Centre of Excellence able to address the topic from different perspectives, with the long-term aim to provide a scientific basis for improved nutritional and lifestyle habits, to train the next generation of multidisciplinary researchers in this field, to raise awareness of such habits among the wider population, and also to engage with industry to develop age-adequate foods and medicines.

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Age-related diseases; cellular organelles diagnostic; cellular redox signalling; nutrients-microbiome interactions; redox active secondary metabolites

### Personalized nutrition in ageing society: the challenge

Most European countries have to cope with their increasingly ageing populations. Demographic changes across Europe are associated with many benefits, but also challenges, as the older generation has specific needs to sustain their own, independent lifestyle. Here, the

importance of a healthy ageing process acquires importance when considering that the proportion of people older than 50 years is already greater than one-third across Europe, with several regional variations [1]. This fraction is likely to increase further in the future, and vitality at an older age is not only an important measure of the quality of life, but also key to participation and productivity. Within the context of healthy ageing, nutrition

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plays a fundamental role. It appears, for instance, that people older than 50 years rely more heavily on the intake of vitamins and trace elements and, at the same time, are more sensitive towards malnutrition. Indeed, the older organism seems to lose its ability to synthesise certain substances, and besides insulin, so-called pseudo-vitamins and food bioactives have a more important role with increasing age. Hence the reliance on a balanced, age-tailored diet seems to increase as people age, e.g. from an age of 70 or 80 upwards. Here, adequate life-stage nutrition may become essential for the ageing body to retain and perhaps even to regain certain aspects of health and function [2].

The “redox angle” has been chosen according to the current and still growing evidence that the redox homeostasis governs most cellular processes and is particularly prone to an imbalance in the elderly [3–5]. Reactive oxygen species (ROS) can harm macromolecules such as proteins, DNA, or lipids leading to altered cell functionality or modifications in signalling pathways occur. Several epidemiological surveys showed that some redox food bioactive nutrients play a significant role in the prevention and treatment of illnesses [6–8], and nutritional studies support the notion of a healthy redox active nutrition [9,10], which at the same time also impacts positively on the gut microbiome [11]. Accordingly, the microbiota can activate, inactivate or render bioavailable redox active food metabolites, an issue that is often overlooked, resulting in several myths and demanding attention [12,13]. Food bioactives and the antioxidant response have found their way into popular knowledge, are used and discussed widely and impact significantly on consumer behaviour across Europe [14–16].

This topic is highly relevant today and its significance will be enhanced in the near future. A comprehensive scientific knowledge of the impact of redox physiological and nutritional components on the ageing is urgently needed. Such systematic knowledge can be obtained by a multidisciplinary approach embracing: cell and tissue biology, metabolic conversion studies, genome and epigenome, research, intracellular diagnostics, nutritional and physical sciences, specific biomarkers, age-related microbiome analysis, and animal feeding studies.

Several functional foods, supposedly “healthy diets” and “health products” have recently entered the market to address this issue more or less successfully, including supplementation with vitamins or bioactive phytochemicals [14–16]. However, this topic has not yet been fully and properly studied. The binomial nutrition and ageing has many aspects and poses a lot of challenges which provide a fertile ground for research themes and

networks. Accordingly, the NutRedOx Action is focussed on the impact of redox-active compounds in food on healthy ageing, chemoprevention and redox control in the context of major age-related diseases.

The main aim of the NutRedOx network is to link European experts from different disciplines, who are devoted to biological redox processes induced by redox active food components, which are relevant to the ageing organism (health, function, and vulnerability to disease). These experts form together a major and sustainable EU-wide cluster: the NutRedOx Centre of Excellence, designed to address redox from different perspectives, with the long-term aim to provide a scientific basis to improve nutritional and lifestyle habits, to train the next generation of multidisciplinary researches in this field, to raise awareness of such habits among the wider population, and also to engage with industry to develop age-adequate foods and medicines.

### **Progress beyond the state-of-the-art: the innovation potential of NutRedOx Network**

Many health products have recently entered the market for people older than 50 years, including plant-based or derived phytochemicals designed “antioxidants”. Nutrition, in an ageing society, raises serious scientific and behavioural as well as economic issues, and networks such as NU-AGE [17] and POSITIVE [18] are dealing with various aspects of this complex and facet-rich issue. NU-AGE, for instance, considers the important whole diet intervention in older than 65 years people, and the POSITIVE network was designed to identify interindividual variation in response to consumption of plant food bioactives and determinants involved. NutRedOx recognises the need to bridge the existing gap in knowledge of individual nutritional components and their chemical and biochemical properties on the one side, and their more complex transformations, interactions and effects on whole organisms on the other. Here, science plays to catch up with accelerated demographic changes and a more or less random “shotgun use” use of suspected yet, often also suspect, healthy compounds by the wider public.

The dichotomy between sound knowledge and use, between molecular properties and whole-body impact, applies in particular to redox active compounds and redox regulation in the body. It is already known that cell redox regulation and control change significantly with age and that various age-related diseases are linked to a disturbed cellular redox balance and dysfunction of lysosomes, peroxisomes, mitochondria, and the endoplasmic reticulum. Nutrition and lifestyle affect



the redox state in the body, which potentially results in a wide range of health benefits [19]. Also, redox active components of the daily diet also affect the microbiota [20], which in turn also modifies such redox-active substances, for instance by activation/inactivation or by increasing their bioavailability.

NutRedOx wants to reach from the organism down to the level of individual molecules. Hence, a multidisciplinary network covering all layers from the single molecule and its metabolites to the whole body has a particular relevance and importance.

The NutRedOx Action is a network in the field of molecular nutrition to investigate the most heart-burning issues from the molecule and its metabolites to the gut microbiome, and eventually their impact on the organism, which undoubtedly will affect different diseases. To enable the exchange of expertise across these wide different disciplines and scientific items (e.g. food formulation experts, nutritionists, and chemists), this network will not simply operate via meetings and seminars, but also via a joint infrastructure within its multi-site “NutRedOx Centre of Excellence” and a critical exchange of early career investigators and emerging researchers. As the general theme of NutRedOx by its very nature is of particular interest to inclusiveness target countries (ITCs) and members in North Africa, the Caucasus and the Mediterranean area, it is from the start attracting interested parties and impetus from these countries.

### **Initiation and implementation of the NutRedOx Network: towards a NutRedOx Centre of Excellence**

The first objective of the COST Action CA16112 is to initiate and implement the NutRedOx Network, which includes the execution of the various strategic network-building activities and is based on existing, long-term activities and collaborations in this field, such as the annual “NutRedOx Atelier” for emerging researchers. In the short term, the aim is to bring together members from academia and industry to exchange individual knowledge and expertise. Subsequently, the network has initiated joint research projects via an international, multisite “NutRedOx Centre of Excellence” with mutually accessible methods, techniques, and experienced personnel to conduct joint research and development and to promote staff mobility between the different sites. This approach explicitly includes participants from less research-intensive ITCs. In the medium term, this centre will consolidate and grow to engage interested

members of society, as well as scientists, efficiently in research, training, technology transfer, public outreach, and sustainable fundraising activities.

Accordingly, NutRedOx will create a platform for joint research on age/ageing-relevant topics within an international, multisite and multidisciplinary research environment. It will stimulate considerable mobility of early stage and experienced researchers, e.g. via secondments of Ph.D. students or postdoctoral research fellows, and via specific, designated NutRedOx lectureships for junior faculty members.

Joint capacities will be set up and shared under the umbrella of the sustainable “NutRedOx Centre of Excellence” to address topics such as (a) redox-active substances and their ability in the human body to maintain/regain biological function (e.g. cardiovascular, Type II diabetes, nervous system, inflammation), (b) redox active nutritional and physiological components and their general impact on cellular signalling and the (epi)genome, (c) redox-active substances and their impact on the gut microbiota, (d) transformation of nutrients in the gut (activation, inactivation, bioavailability), (e) mechanistic studies.

Public Outreach and Technology Transfer measures will accompany and be a major part of the research effort. Specific technology transfer sessions with invited industrial members from the pharmaceutical and food supplement industry during the network meetings will ensure a close involvement of industrial members. The wider public will be engaged as a key stakeholder in each of the network meetings in form of open “Nutrition workshops” (e.g. on age-adequate diets and lifestyle, food supplements) organised by emerging scientists of the network in the simple local language and in town, and advertised via local newspapers and TV/radio. At the local level, each member will strive for a Café Scientifique to engage the wider public in a regular and approachable manner.

### **The added value of NutRedOx Network**

The most important added value of the NutRedOx Network is an exchange across the relevant scientific disciplines, which will result in joint research based on shared knowledge, infrastructure and emerging researchers – and the subsequent engagement of industry and the wider public in form of technology transfer and outreach measures. A joint research infrastructure enables the members to consider different aspects of nutrition, and at different levels of complexity, from the single compound and its chemical (redox) properties via the microbiome in the gut, to cellular

events in the body and the prevention or manifestation of different age-related diseases. The combination of different expertise should also enable the network to unravel and remove some of the myths and mysteries existing in this field of redox active nutritional components, such as the ORAC story, functional and antioxidant foods.

NutRedOx will, for the first time, bring together a significant number of truly multidisciplinary researchers and companies from across Europe, the Mediterranean and Caucasus region to combine their expertise and to build on different layers of biochemical complexity, from the single molecule of a chemist and metabolic transformations in the gut to cell biological signalling events and disease markers in a whole body. Whilst other networks existing in this field, such as NU-AGE [17] and POSITIVE [18] rightly see their strength in applied, whole-diet studies, NutRedOx intends to spice up the field of nutrition via a cocktail of different analytical studies, from the individual molecule via the microbiota and mitochondria all the way to markers of health and disease. Unlike most existing networks, NutRedOx is focussed on redox systems, as those seem to bear particular promise in the context of healthy eating, lifestyle and ageing.

NutRedOx may, therefore, be best described as a vertical scientific approach on the lookout for emerging properties, whilst the existing efforts are more horizontal, rather successfully floating within their particular layers of science and complexity. As such a vertical approach needs to deal with issues of reductionism and emergence, it is obviously considerably more demanding than traditional efforts, yet also promises exciting new insights and ample opportunities for widening individual horizons and expert training. The latter will become a hallmark of the network, starting with its “NutRedOx lectureships” all the way to the public “Nutrition workshops” and the “Café Scientifique”. Indeed, the main actions, beside cooperative research, will include a close cooperation with (local) industry, public outreach and a continuous engagement of additional members from additional countries: A vertical approach obviously lends itself to “add ones” approaches, for instance in the field of physical chemistry, psychology (e.g. of how to change eating habits or even sociology in people older than 50 years (e.g. regional cultures of eating, lifestyle, and cultural acceptance of food).

Hence the COST Action 16112 has welcomed, with open arms, additional players in the field from across disciplines and COST countries, Near Neighbour Countries (NNCs) and international partner countries

(IPCs), joining experts from 38 different countries. A current list of COST Action Management Committee (MC) participants and observers are shown in Table 1. Since no similar cluster exists at this moment, and NutRedOx provides an attractive spectrum of activities, it is anticipated that NutRedOx will become a leading cluster of experts and expertise on nutrition, lifestyle and ageing in Europe and worldwide.

### The NutRedOx working groups

NutRedOx will benefit from previous existing, well-functioning cooperation and network structures, which have been expanded with a new consortium of members from across the European Union and beyond, including ITCs and IPCs. So, the NutRedOx website has been activated and the NutRedOx Centre of Excellence formally created. The various actions have been initiated by as a result of the first network-wide gathering, organised by a local Chapter of the network. This gathering was advertised widely and ultimately has provided the platform for intensive exchanges, network building measures, cooperation, and additional members to join.

Subsequently, NutRedOx will perform its actions under the umbrella of the NutRedOx Centre of Excellence which will harmonise the individual, yet closely interwoven actions of four individual Working Groups (WGs) working towards the objectives defined for the network. Those WGs represent loose clusters of research, temporarily formed to streamline research (often along themes or disciplines), but always be open to change and restructuring. Individual WGs complement each other in science, the management of the scientific process and the various dissemination activities and participation in the WGs are not mutually exclusive. The staff and WG of NutRedOx COST Action CA16112 are shown in Table 2.

### Overall tasks

All WGs (apart from WG1) will engage in research, training, technology transfer, and public outreach. WGs, in turn, will organise the one major network-wide gathering per year. These meetings will be held under the specific theme of the WG organising the meeting and foster the exchange of research, and the planning of further activities. They will provide time for network management and will also feature a public outreach component. Each WG will also hold smaller, WG specific but network-wide open workshop-like meetings (NutRedOx Summer Schools) for junior scientists of the entire network, which will focus primarily on early-stage





**Table 1.** List of COST Action Management Committee (MC) participants and observers.

Country	Name	Position	Institution
Austria	Marko, Doris	MC Member	University of Vienna
Austria	Wagner, Karl-Heinz	MC Member	University of Vienna
Belgium	Jadot, Michel	MC Member	University of Namur
Belgium	Hermans, Nina	MC Member	University of Antwerp
Bosnia-Herzegovina	Grabec, Milkica	MC Member	Faculty of Medicine
Bosnia-Herzegovina	Rudic Grujic, Vesna	MC Member	Public Health Institute
Croatia	Geric, Marko	MC Member	Institute Medical Res. & Occup. Health
Croatia	Garaj Vrhovac, Verica	MC Member	Institute Medical Res. & Occup. Health
Cyprus	Goulas, Vlasios	MC Member	Cyprus University of Technology
Cyprus	Philippou, Elena	MC Member	University of Nicosia
Czech Rep.	Valentová, Katerina	MC Member	Institute of Microbiology, ASCR
Czech Rep.	Landa, Premysl	MC Member	Institute of Experimental Botany, ASCR
Denmark	Davies, Michael	MC Member	University of Copenhagen
Denmark	Poulsen, Henrik	MC Member	Bispebjerg Friederisksberg Hospital
Estonia	Tomberg, Vladimir	MC Member	Digital Technol Institute
Finland	Atalay, Mustafa	MC Member	University of Eastern Finland
Finland	Yang, Baoru	MC Member	University of Turku
France	Cherkaoui-Malki, Mustapha	MC Chair	University of Burgundy
France	Gaucher, Carolina	MC Member	University of Lorraine
France	Elhabiri, Mourad	MC Member	UMR7509 CNRS-Unistra
ŷR Macedonia	Ruskovska, Tatjana	MC Member	Goce Delcev University
ŷR Macedonia	Smilkov, Katarina	MC Member	Goce Delcev University
Germany	Jacob, Claus	MC Member	University of Saarland
Germany	Richling, Elke	MC Member	TU Kaiserslautern
Greece	Kypreos, Kyriakos E.	MC Member	University of Patras Medical School
Greece	Chondrogianni, Niki	MC Member	Institute Biology, Medicinal Chem. & Biotechnol.
Hungary	Radak, Zsolt	MC Member	Semmelweis University
Ireland	O'Brien, Nora	MC Member	University College York
Ireland	Giblin, Linda	MC Member	Teagasc
Israel	Lesmes, Uri	MC Member	Technion – Israel Institute of Technology
Israel	Sasson, Shlomo	MC Member	The Hebrew University
Italy	Ferreri, Carla	MC Member	Consiglio Nazionale delle Ricerche
Italy	Corino, Carlo	MC Member	Università degli Studi di Milano
Latvia	Dambrova, Majda	MC Member	Latvian Institute of Organic Synthesis
Latvia	Skesters, Andrejs	MC Member	Riga Stradins University
Lithuania	Smirnovas, Vytautas	MC Member	Vilnius University Institute of Biotechnology
Lithuania	Kersiene, Milda	MC Member	Kaunas University of Technology
Luxembourg	Diederich, Marc	MC Member	RSLB a.s.b.l.
Malta	McElhatton, Anna	MC Member	University of Malta
Malta	Caruana, Mario	MC Member	University of Malta
Montenegro	Bigovic, Milan	MC Member	Faculty of Natural Sci. and Mathematics
Montenegro	Kosovic, Milica	MC Member	University of Montenegro
Norway	Fladmark, Kari Espolin	MC Member	University of Bergen
Poland	Bartoszek, Agnieszka	MC Vice-Chair	Gdansk University of Technology
Poland	Antosiewicz, Jędrzej	MC Member	Medical University of Gdansk
Portugal	Fernandes, Ana	MC Member	Universidade Lusofona Humanidades e Tecnologias
Portugal	Santos, Claudia	MC Member	Instituto Biologia Experimental e Tecnologica
Romania	Carausu, Elena Mihaela	MC Member	Universitatea Medicina si Farmacie Grigore T. Popa
Romania	Manuc, Daniela	MC Member	UMF Carol Davila
Serbia	Sunderic, Milos	MC Member	Institute for Application of Nuclear Energy
Serbia	Dinic, Svetlana	MC Member	University of Belgrade
Slovakia	Perecko, Tomas	MC Member	Institute Exptl. Pharmacology & Toxicology
Slovenia	Milisav, Irina	MC Member	University of Ljubljana
Slovenia	Ribaric, Samo	MC Member	University of Ljubljana
Spain	Adrover, Maria Gabriela	MC Member	Cluster BIOIB
Spain	Tur, Josep A.	MC Member	University of the Balearic Islands & CIBEROBN
Switzerland	Sykiotis, Gerasimos	MC Member	Lausanne University Hospital
Switzerland	Wiederkehr, Andreas	MC Member	Nestlé Institute of Health Sciences
Turkey	Karasu, Çimen	MC Member	Gazi University
Turkey	Ozben Tomasi, Tomris	MC Member	Medical Faculty Akdeniz University
UK	Tadayyon, Mohammad	MC Member	Pharmidex
UK	Zaibi, Mohamed	MC Member	University of Buckingham
Albania	Mele, Altin	MC Observer	University of Tirana
Algeria	Merzouk, Hafida	MC Observer	University Abou Bekr Belksid of Tlemcen
Armenia	Trchounian, Armen	MC Observer	Yerevan State University
Georgia	Mdzinarashvili, Tamaz	MC Observer	Institute of Medical and Applied Sciences
Morocco	Nasser, Boubker	MC Observer	University Hassan 1 <sup>st</sup>
Ukraine	Cherkas, Andriy	MC Observer	Lviv National Medical University

**Table 2.** Staff and Working Groups (WG) of NutRedOx COST Action CA16112.

COST Action Staff	
COST Action Scientific Officer	Inga Dadeshidze
COST Action A Senior Administrator	Gabriela Cristea
Core Group members	
Role	
Chair	Mustapha Cherkaoui-Malki (FR)
Vice-Chair	Agnieszka Bartoszek (PL, ITC)
WG1: Network building and management	
Leader	Claus Jacob (DE)
Co-leader	Patrick Chaimbault (FR)
Co-leader	Mohammad Tadayyon (UK), SME contact
WG2: impact of redox active secondary metabolites on the organism	
Leader	Josep A. Tur (ES)
Co-leader	Elke Richling (DE)
WG3: Impact on and by the microbiome	
Leader	Nina Hermans (BE)
Co-leader	Claudia Santos (PT, ITC)
WG4: Intracellular Diagnostics	
Leader	Marc Diederich (LU, ITC)
Co-leader	Linda Giblin (IR)
GH	
GH Scientific Representative	University Bourgogne Mustapha Cherkaoui Malki (FR)
STSM	
Manager	Mourad Elhabiri (FR)
CoManager	Caroline Gaucher (FR)
Focus Group	
Website manager	Pierre Andreoletti (FR)
Dissemination, Publications	Ana Fernandes (PT, ITC)
Dissemination Contact	Michael J. Davies (DK)
Administrative Manager	Nathalie Bancod (FR)

BE: Belgium; DE: Germany; DK: Denmark; ES: Spain; FR: France; IR: Ireland; ITC: Inclusiveness Target Countries; LU: Luxembourg; PL: Poland; PT: Portugal; SME: Small and medium-sized enterprises; UK: UK; GH: grant holder; STSM: short term scientific mission.

researchers and besides a lively exchange of research will also provide a good time for extensive training. All WGs will interfere with each other and they will have multiple overlaps.

### **WG1: network building and management**

WG1 deals with the more administrative tasks of NutRedOx, which are crucial for the success of the network. Besides the coordinator, this WG initially involves all members enrolled in the network. WG1 has been developed during the first NutRedOx meeting (Strasbourg, September 27–28 2017), when it has been also constituted as the Management Committee (MC) of the Action. WG1 organises the communication across the network, including the NutRedOx website. It links the individual, well-defined actions of the project, with the more flexible realisation of the NutRedOx Centre of Excellence. For instance, it coordinates the various meetings, seminars, and workshops. WG1 accompanies technology transfer and interactions with companies where necessary. It also takes an active role in the various public outreach measures. Furthermore, this WG monitors progress and engage with journals to commission reviews, a Special Issue or book project. WG1 also represents the trouble-shooter unit in charge of identifying, addressing, and ultimately resolving any issues or

conflicts in an effective, democratic, open and amenable manner. In essence, WG1 is staffed by the NutRedOx Core Group involving other volunteers from the Management Committee (MC).

### **WG2: the impact of nutrition, lifestyle and redox active secondary metabolites on the organism**

This WG considers the impact of redox active food and individual food microcomponents, especially polyphenols, oxysterols, and various organic sulphur compounds (including recently discovered inorganic  $S_x^{2-}$  polysulphide species) selected from different sources across Europe, as well as, newly designed functional foods, on healthy, ageing animals and humans, as well as on humans or animals suffering from age-linked diseases, such as diabetes, neurodegenerative disorders or inflammation-related diseases. The focus of this WG resides firmly on a better understanding of individual molecules and their impact on the organisms, bearing in mind that compounds never act alone yet that whole-diet approaches also cannot access the kind of information on the molecular level, which is relevant for nutritional intervention or supplementation.

As part of the top-down approach, in the first step, biomarkers are defined and considered as indicators of changing health, including markers indicative of the



preservation or regaining of health/disease states, the retardation of degeneration and the maintenance or recovery of certain (functional) capacities. Such markers may be based on morphology or function, but also on an adequate blood or tissue analysis, or may be related to nutrigenomic events. The relationship between dietary intake, lifestyle and sociodemographic determinants on one-side and plasma levels of specific biomarkers (bioactive lipids, proteins, redox state) on the other will be also assessed. Chemists form an integral part of this WG as they will provide chemically pure compounds for studies, either by isolation or total synthesis and perform the analysis of biomarkers and other modified biomolecules, such as proteins or enzymes, for instance by employing mass spectrometric analytical methods.

### **WG3: impact on and by the microbiome**

Whilst the direct impact of such food and its components on the organism is of prime importance, a particular focus will also reside on effects on the structure (composition) and function (physiology) of the organism's microbiome. The latter changes in ageing organisms, yet are still able to be modulated by nutrition and nutritional components, a fact that is often underestimated. Indeed, nutrition and the microbiome control each other, i.e. the diet can change the microbiome, which in turn metabolises individual components of the diet. This interplay impacts significantly on the health of the host, especially in ageing or aged organisms, as recently highlighted by a series of key publications [11,21–25]. Whilst WP2 will consider the impact of redox active nutritional components on the body's biomarkers, WP3 will monitor the changes of the composition and function of the corresponding microbiome. Additional links arise, of course, from the metabolic action of the microbiome, which will affect the food components. Hence isolated microbiomes will be cultured and used to metabolise redox active food components, in parallel with similar metabolic studies in liver homogenates, in order to identify putative metabolites from the parent nutritional components.

### **WG4: intracellular diagnostics**

Whilst WG2 will focus on changes on the organism as a whole and WG3 will consider the impact on the microbiome, WG4 will investigate changes at the cellular level. Such cellular events are often indicative of changes to the whole organism, and in many ways bridge the gap – *in vivo* and also in our understanding – between the individual compound on one side and

its complex interactions with the organism on the other. A diverse array of cell-based analytical techniques will be assembled to investigate how individual substances, either alone or in combination, act on cells or interact with relevant cellular constituents, including the genome and epigenome. The topics of WG4 bring in another barrage of bioanalytical techniques, which include emerging proteomic and nutrigenomic methods, the latest molecular cell and fluorescent based staining and imaging techniques as well as Live Cell Imaging and chaemogenetic screening to obtain a more global assessment of events. This WG will also investigate redox-related nutri-epigenetic events.

## **Conclusions**

The NutRedOx Network is a platform for joint research on ageing-relevant redox topics: (a) exploring redox-active substances and their ability in the human body to maintain biological functions (e.g. cardiovascular, type II diabetes, nervous system, inflammation); (b) studying redox active nutritional and physiological components, and their general impact on cellular signalling and the epigenome; (c) assessing redox-active substances and their impact on the gut microbiota; (d) analysing transformation of nutrients in the gut (activation, inactivation, bioavailability); and (e) collaborating for redox mechanistic studies. The international, multi-site NutRedOx Centre of Excellence will be useful to exchange mutually accessible methods, techniques, and experienced personnel, as well as to support secondments of Ph.D. students or postdoctoral research fellows, as well as via specific, designated NutriOx lectureships for junior faculty members, and to promote staff mobility between the different sites, including participants from less research-intensive inclusiveness target countries.

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## References

- [1] United Nations. Department of economic and social affairs. Population division. New York: World Population Ageing; 2015.
- [2] Leslie W, Hankey C. Aging, nutritional status and health. *Healthcare*. 2015;3:648–658.
- [3] Trachootham D, Lu W, Ogasawara MA, et al. Redox regulation of cell survival. *Antioxid Redox Signal*. 2008;10:1343–1374.
- [4] Calabrese V, Cornelius C, Mancuso C, et al. Redox homeostasis and cellular stress response in aging and neurodegeneration. *Methods Mol Biol*. 2010;610:285–308.
- [5] Ray PD, Huang BW, Tsuji Y. Reactive oxygen species (ROS) homeostasis and redox regulation in cellular signaling. *Cell Signal*. 2012;24:981–990.
- [6] Lobo V, Patil A, Phatak A, et al. Free radicals, antioxidants and functional foods: impact on human health. *Pharmacogn Rev*. 2010;4:118–126.
- [7] Chambial S, Dwivedi S, Shukla KK, et al. Vitamin C in disease prevention and cure: an overview. *Indian J Clin Biochem*. 2013;28:314–328.
- [8] Ursini F, Maiorino M, Forman HJ. Redox homeostasis: the Golden Mean of healthy living. *Redox Biol*. 2016;8:205–215.
- [9] Mak TN, Louro-Caldera S. The Role of Nutrition in Active and Healthy Ageing: for prevention and treatment of age-related diseases: evidence so far. Luxembourg: Publications Office of the European Union; 2014.
- [10] Lorenzo-López L, Maseda A, de Labra C, et al. Nutritional determinants of frailty in older adults: a systematic review. *BMC Geriatr*. 2017;17:108.
- [11] Ticinesi A, Lauretani F, Milani C, et al. Aging gut microbiota at the cross-road between nutrition, physical frailty, and sarcopenia: is there a gut-muscle axis? *Nutrients*. 2017;9:1303.
- [12] Marín L, Miguélez EM, Villar CJ, et al. Bioavailability of dietary polyphenols and gut microbiota metabolism: antimicrobial properties. *BioMed Res Int*. 2015;2015:905215.
- [13] Karas M, Jakubczyk A, Szymanowska U, et al. Digestion and bioavailability of bioactive phytochemicals. *Food Sci Technol*. 2017;52:291–305.
- [14] Ozen AE, Pons A, Tur JA. Worldwide consumption of functional foods: a systematic review. *Nutr Rev*. 2012;70:472–481.
- [15] Beaulieu M, Schaefer HM. The proper time for antioxidant consumption. *Physiol Behav*. 2014;128:54–59.
- [16] Özen AE, Bibiloni Mdel M, Pons A, et al. Consumption of functional foods in Europe; a systematic review. *Nutr Hosp*. 2014;29:470–478.
- [17] NU\_AGE study. Available from: <http://www.nu-age.eu/home>. [cited 05 April 2018].
- [18] POSITIVEe study. Available from: <https://www6.inra.fr/cost-positive>. [cited 05 April 2018].
- [19] Seyedsadjadi N, Berg J, Bilgin AA, et al. Significant relationships between a simple marker of redox balance and lifestyle behaviours; relevance to the Framingham risk score. *PLOS ONE*. 2017;12:e0187713.
- [20] Duda-Chodak A, Tarko T, Satora P, et al. Interaction of dietary compounds, especially polyphenols, with the intestinal microbiota: a review. *Eur J Nutr*. 2015;54:325–341.
- [21] Pray L, Pillsbury L, Tomayka E. The human microbiome, diet, and health workshop summary. Washington DC: Institute of Medicine, The National Academies Press; 2013.
- [22] David LA, Maurice CF, Carmody RN, et al. Diet rapidly and reproducibly alters the human gut microbiome. *Nature*. 2014;505:559–563.
- [23] Voreades N, Kozil A, Weir TL. Diet and the development of the human intestinal microbiome. *Front Microbiol*. 2014;5:494.
- [24] Conlon MA, Bird AR. The impact of diet and lifestyle on gut microbiota and human health. *Nutrients*. 2014;7:17–44.
- [25] Singh RK, Chang HW, Yan D, et al. Influence of diet on the gut microbiome and implications for human health. *J Transl Med*. 2017;15:73.