Combating age related diseases

The influence food can have on our health…

Cancer, cardiovascular disease (CVD) and diabetes are the main causes of morbidity and mortality in the general population. In developed nations, unsuitable diets as well as smoking have been identified as outstanding avoidable detrimental factors. During the last decade, there has also been a dramatic increase in the incidence of atherosclerotic diseases as well as of diabetes, a development that has been linked to changes in food habits. European consumers ranked food safety as their number one priority, followed by secure and fair standards for farmers. Considering that at least 25% of cancers in the Western world can be related to food habits, it is not surprising that food safety has become a European research priority.

Is there hope for a change in that trend? Yes, because edible plants such as vegetables and fruits contain beneficiary constituents, antioxidants and other cancer protective agents. Further, diabetes and CVD are closely interlinked and also, to a certain extent, to the mechanisms in cancer; therefore, the protective agents in food can be expected to exert positive health outcomes against the diseases that are age related. Even a modest decrease in the prevalence of these maladies translates into millions of lives saved. The way of achieving such a goal is to enrich those constituents in food that exhibit protective activities and, at the same time, identify and minimise carcinogenic agents in the diet.

How can this be accomplished? The Department of Genetics, Microbiology and Toxicology (GMT), Stockholm University, Sweden, is a multidisciplinary organisation that utilises the knowledge of their basic research into a collaborative applied research project. In strong competition, Professor and Head of Department Dag Jenssen with his colleagues and international collaborators were together beneficiaries of funding from the EU under the food safety programme of the 7th Framework Programme 'Development of functional foods and ingredients'. This EU call was focused on medium-scale collaborative projects carried out in coordination with funding from the Department of Biotechnology, Ministry of Science and Technology in India.

In view of the globalisation of the food industry and the fact that many food products are imported into the EU market, cooperation beyond EU borders is being prioritised by the EU community. Cooperation with India is encouraged due to the fact that food science has a long tradition in the eastern part of the world and research organisations here constitute competent and experienced partners in this research area. The project 'Impact of agents with potential use in functional foods on biomarkers for induction of age related diseases' (FUNCFOOD, http://funcfood.gmt.su.se) has five participants within EU and three partners in India.

What is the intention of the FUNFOOD project? Although a number of epidemiological studies have consistently demonstrated the protective effects of fruits and vegetables with respect to several age related diseases, the objective of the FUNCFOOD project is to investigate the protective action of agents with potential use as functional food constituents with respect to cancer, diabetes and CVD. In collaboration between EU and Indian research centres, the proposal features a multipronged approach, where the protective action of various non-toxic agents are studied in vitro as well as in rodent models with respect to induction of DNA lesions, tumours and biomarkers for the development of diabetes, diabetic retinopathy and atherosclerosis. In addition, reduced availability of carcinogens and inhibition of their metabolic activation are investigated. Testing of the protective efficacy of functional food constituents in intervention crossover studies in humans exposed to carcinogens, which are normally present at significant levels in the environment, represents an approach that has rarely been resorted to, and will be implemented under this project in Europe as well as in India using 'biomarkers' utilising sophisticated molecular, cytogenetic and other analytical methods.

The challenge posed by the FUNFOOD project is to enhance the health benefit from diets beyond the traditional nutrients it contains by means of the addition of bioactive ingredients. This goal will be achieved by a step-wise approach providing robust scientific evidence for selecting active ingredients appropriate for inclusion in functional foods. In a first step, a candidate list of potential chemoprotective agents are selected based on the grounds that solid data concerning their protective effects in human is lacking, followed by screening tests applying high throughput in vitro model systems to find and select the best candidates for further testing in more complex system, eg. using animal models. The results of the animal studies will lead to conclusions concerning which are the best candidates for further testing in human intervention studies. In these

studies, validated and sensitive biomarkers for the different diseases will be utilised.

What do we expect in terms of outcome from FUNCFOOD? Although there has been remarkable progress in our understanding of the processes that lead to neoplasia, diabetes and CVD, the mechanisms underlying chemoprevention of these diseases, in general, is little understood. The results from this project are expected to provide an improved insight with respect to this topic and in the studies that directly concern people. The dissemination process will focus on stakeholders in the food industry that will be encouraged to use the results of FUNCFOOD in new food products.

How do we know what levels of harmful components in food are low enough to be safe? Safety measures are not only a matter of identifying the harmful agent. It is very much a matter of the levels that we are exposed to, ingested or inhaled, and the time doing so. Estimation of dose is the basis for risk evaluations; a theory that was once proposed in the 18th Century by the Renaissance man Philippus Aureolus Theophrastus Bombastus von Hohenheim-Paracelsus. To be able to put limits on exposure to harmful chemicals or radiation, we need to know to what levels. Unfortunately, our experimental models do not necessarily allow investigations of the levels humans are exposed to in real life.

Another important factor here is that people have very different sensitivity towards both radiation and chemicals. Historically, the research on radiation has taken the lead in this research compared to the safety regulations of chemicals. At Department of GMT, an EU project is coordinated within this discipline by Professor Andrzej Wojcik. With the acronym MULTIBIODOSE (www.multibiodose.eu), the project involving 15 European beneficiaries will provide 'Multi-disciplinary biodosimetric tools to manage high scale radiological casualties', which is an

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essential tool that can provide timely assessment of radiation exposure to the general population and enable the identification of those people, who have been exposed and should receive immediate medical treatment. A number of biosimetric tools are potentially available, but they must be adapted and tested for a large-scale emergency scenario. These methods differ in their specificity and sensitivity to radiation, the stability of signal and speed of performance. A large scale radiological emergency can take different forms. Based on the emergency scenario, different biosimetric tools should be applied so that the dosimetric information can be made available with optimal speed and precision.

Another EU project at GMT related to this area of research is DoReMi, which is linked to MELODI (www.melodi-online.eu) in which Professor Mats Harms-Ringdahl, Head of Centre for Radiation Protection Research (CRPR), is participating. The main objective of MELODI is to develop a strategic research agenda for low dose research in Europe. DoReMi is a complement to MELODI, aiming to achieve fairly short term results and to contribute to the development of MELODI. DoReMi is concerned with the scientific issues of the shape of the dose effect relationship, the individual radiation sensitivity and non-cancer effects of radiation, respectively, and will produce scientific deliverables from their research and training operational activities. These results as well as the experience feedback from such should also contribute to the goals of MELODI. The experience from these projects will also be embedded in chemical safety regulations.

The activities at GMT also include many other projects in different fields from projects involved in mechanisms for translation, horizontal gene transfer, population genetics of natural whale and seal populations, how to defeat malaria with biological methods and studies on the relation between DNA damage response and cancer as tools, to the development of more efficient cancer drugs.

Stockholm University

Professor Dag Jenssen
Head

Department of Genetics, Microbiology and Toxicology (GMT)
Stockholm University
Svante Arrhenius vag 20C
SE-106 91 Stockholm
Sweden

Tel: +46 8 16 31 08
Mobile: +46 70 610 31 08

dag.jenssen@gmt.su.se
www.gmt.su.se