CASCADE - Chemicals as contaminants in the food chain: a network of excellence for research, risk assessment, and education.

Mattias Öberg[1], Helen Håkansson[1], Ingemar Pongratz[2], Jan-Åke Gustavsson[2]

[1]Karolinska Institutet, Institute of Environmental Medicine, Stockholm
[2]Karolinska Institutet, Dep. of Biosciences, Huddinge

Introduction

Harmful effects of chemical contaminants in food are of major health concern in Europe today. Lack of integration between basic research, risk assessment, and education severely hampers the efforts to reach European excellence in this area. The research activities that are carried out are small in scale and are not well integrated into a coherent structure. To tackle the fragmentation problems and to achieve synergistic effects and full European research potential, the European Commission has initiated a Network of Excellence called CASCADE or "Chemicals as contaminants in the food chain: a network of excellence for research, risk assessment, and education" The contract is running for five years and is worth over €14 million with partners from eighteen research centres. The network has the potential and goal to be a world force in knowledge on health issues related to chemical contaminants in food. Focus is on chemical residues that act via and/or interfere with cell regulation at the level of nuclear receptors. The risk assessment integration parts of the network aim to increase the awareness among scientists and others of the need to bring multiple aspects of scientific information into use in risk assessment.

Structure of the CASCADE network of excellence

Today, European research in the area of endocrine disrupters is obsolete and fragmented. To enhance the state of the art of this research area 18 participants have joined in CASCADE. The participants consist of 23 research groups which are devoted to integration and improvement of European Research area led by following partners (Table 1).

Table 1: List of partners in the CASCADE network of excellence

Participant name	Country	Group leader
Karolinska Institutet	SE	J.-Å. Gustavsson
Karolinska Institutet	SE	H. Håkansson
Karolinska Institutet	SE	O. Söder
KaroBio AB	SE	A. Berkenstam
Johannes Gutenberg Universität	DE	C. Behl
Bereich Humanmedizin Georg-August Universität	DE	W. Wuttke
GSF Forschungszentrum für Umwelt und Gesundheit	DE	M. Göttlicher
GSF Forschungszentrum für Umwelt und Gesundheit	DE	K.W. Schramm
Universität Tübingen	DE	G. Gauglitz
Ecole Normale Supérieure de Lyon	FR	V. Laudet
Ecole Normale Supérieure de Lyon	FR	F. Flammant
Centre National De La Recherche Scienifique	FR	B. Demeniex
Institut National de la Recherche Agronomique	FR	J.-P. Cravedi
Institut National de la Recherche Agronomique	FR	P. Prunet
Università degli Studi di Milano	IT	A. Maggi
Instituto di Ricerche Farmacologiche ”Mario Negri”	IT	E. Benfenati
Instituto Nazionale di Ricerca per gli Alimenti e la Nutrizione	IT	F. Branca
Turun yliopisto	FI	S. Mäkelä
Helsingin yliopisto	FI	O. Jänne
Universidad de Granada	ES	N. Olea
Puleva Biotech SA	ES	J.J. Lopez
Rijkinstituut vor Volkgezondheid en milieu (RIVM)	NL	W. Slob
Pécsi Tudományegyetem	HU	J. Garai

Around a hub of management CASCADE will work with a set of joint research projects dealing with identification of target tissues and receptors as well as functional analysis, spreading of excellence by meetings and other dissemination activities, education by e.g. summer schools, as well as improving the risk assessment within the field. In this abstract we have mainly focused on the work concerning risk assessment.

The overall objectives of CASCADE is to provide European consumers with reliable information on health risks that are associated with exposure to chemical residues in the food. Focus is on the chemical residues that act via and/or interfere with cellular regulation at the level of nuclear receptors (eg. AhR). In order to fulfil this, the joint scientific programme will:

- Provide novel qualitative and quantitative information regarding the mechanism of action of contaminants(e.g. dioxin) in food.
- Develop mechanism- and/or effect/disease-based *in vivo*, *in vitro* and *in silico* test methods to screen food extracts for the presence of a broad range of chemical residues and metabolites of chemical residues, which have the potential to interfere with nuclear receptor signalling pathways.

- Identify biological markers of exposure.
- Provide mechanistic information regarding disease development caused by chemical exposure.

Risk Assessment development

The risk assessment component of the joint Scientific Programme (Figure 1) focuses on the development of exposure assessment methodology, mathematical modelling of experimental data, and the development of novel tools and concepts, which are needed to improve the health risk assessment of chemical residues and contaminants in the food.

During the coming year CASCADE will use mathematical approaches to improve and develop more efficient exposure assessment methods and perform more detailed exposure evaluations based on existing information. CASCADE aim for a better understanding of the exposure in the general population as well as in specific sub-groups, e.g. children, elderly and specific consumers. CASCADE will also clarify several underlying issues of the benchmark dose methodology.

In addition, CASCADE intends to scrutinise the methodological concepts and assumptions as well as management aspects in the existing risk assessment decisions for dioxin-like compounds.

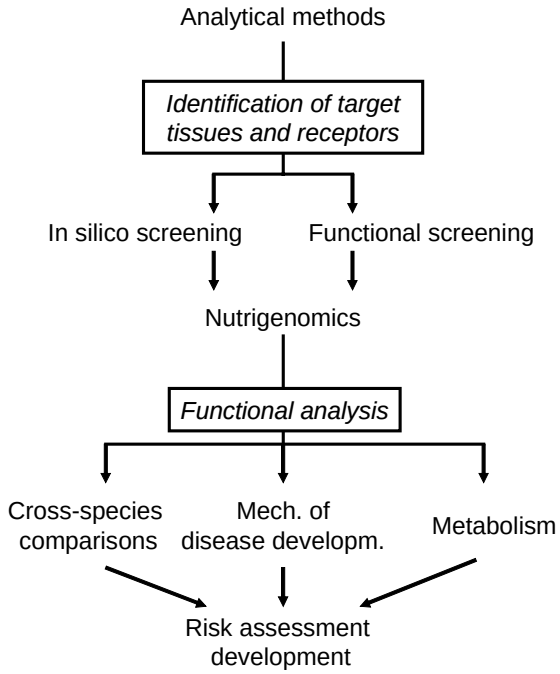

Figure 1: Graphical presentation of work packages that contributes to reliable information on health risks that are associated with exposure to chemical residues in the food. Focus is on the chemical residues that act via and/or interfere with cellular regulation at the level of nuclear receptors (eg. AhR).

Risk Assessment Intergration

To clarify the role of CASCADE in the international arena one objective is to establish firm contacts between CASCADE and other networks such as CREDO, SAFEFOOD, NewS, and relevant individual FP5 EU-funded projects related to endocrine disruption. A network will be formed between individuals in different EU-funded projects that are actually working hands-on with quantitative risk assessment research and development. A similar network will be formed for experts in exposure assessment. Major tasks during the first year for these networks will be to identify experimental data which are suitable for mathematical modelling and to provide a state-of-the-art review of the methodology to evaluate exposure to chemical residues in the food. Summary documents describing the health risk assessment status of the four model compounds selected for the experimental CASCADE work (including TCDD), will be prepared, including existing exposure data. These documents will be used to identify data gaps, set priorities and indicate additional risk assessment work.

To further integrate a research training programme in Environmental Health Risk Assessment will be organised. The first course will be held in Italy during the spring 2005. The full course program will correspond to at least 10 weeks of full-time studies and includes subjects like environmental chemistry, exposure assessment, statistical methods, risk philosophy and communication, regulatory toxicology as well as an international practice period.

Summary

CASCADE was established in the spring of 2004 to provide Europeans with durable, comprehensive and independent network of excellence in research, risk assessment, and education concerning endocrine disrupting chemicals in food. Activities include state-of-the-art research from the best European research centres in the field, innovative training programmes, relevant information to consumers and reliable assessments to legislators concerning risks of chemicals in food. The focus on nuclear receptors is highly relevant not only since these transcription factors span all aspects of human disease from growth and development to reproduction, but also because many food contaminants interfere with the nuclear receptor signalling pathway. The CASCADE network of excellence is not static. It is to be continuously enriched with valuable activities that can add strength and competitiveness. Research centres, organisations, policy makers, and the public are always welcome to contact us and discuss collaboration.

References

1 EU Framework Programme 6, Priority 5: “Food quality and safety”, Topic 41
2 EU Contract no. FOOD-CT-2003-506319