doi:10.2533/chimia.2008.316 CHIMIA **2008**, *62*, No. 5

Chimia 62 (2008) 316–317

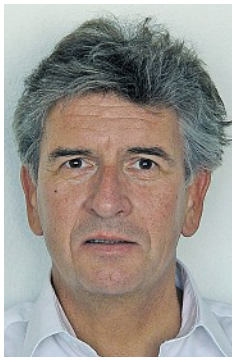
ISSN 0009–4293

Editorial

Endocrine Disruptors: Relevance to Humans, Animals and Ecosystems

Research Highlights from the National Research Programme NRP50

Guest Editors: Felix R. Althaus*, Konrad Hungerbühler[a], Susan Jobling[b], Urs Ruegg[c], Ana Soto[d] Christoph Studer[e]

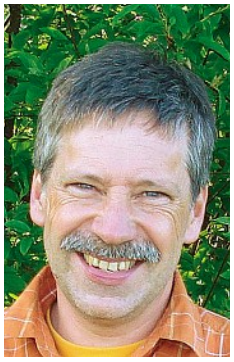

F. R. Althaus


K. Hungerbühler


S. Jobling


U. Ruegg


A. Soto


C. Studer

Endocrine disruptors (sometimes also referred to as hormonally active agents) are exogenous substances that act like hormones in the endocrine system and disrupt the physiological function of endogenous hormones. Endocrine disruptors exhibit a completely new type of toxic action that had gone largely unnoticed in conventional toxicological tests until relatively recently. Endocrine disruptors act like 'stealth chemicals', *i.e.* they act below the 'radar' of toxicity monitoring that has been in place worldwide for toxic chemicals. The term 'stealth' illustrates the fact that:

i) These chemicals may act at concentrations several orders of magnitudes below the threshold of conventional toxicity.
ii) The action of these chemicals is most deleterious in a narrow time window when an organism goes through specific steps of embryonic, fetal or postnatal development ('developmental toxicity'), by disrupting organizational events. Outside of these critical windows, the developing organism becomes less sensitive to this type of action even at concentrations of chemicals several orders of magnitudes higher than those causing early developmental toxicity.

*Correspondence:
Prof. F. R. Althaus, University of Zurich, Vetsuisse Faculty, CH-8057 Zürich, Switzerland, E-mail: fra@vetpharm.uzh.ch
[a]Institute for Chemical and Bioengineering, ETH Zurich, CH-8093 Zurich, Switzerland
[b]Department of Biological Sciences, Brunel University, Uxbridge, Middlesex, UK
[c]Geneva-Lausanne School of Pharmaceutical Sciences, Univ. of Geneva, CH-1211 Geneva, Switzerland
[d]Department of Anatomy and Cellular Biology, Tufts University School of Medicine, Boston, MA 02111, USA
[e]Federal Office for the Environment, FOEN, CH-3003 Bern, Switzerland

iii) The actions of endocrine disruptors exhibit concentration additivity if they share a common receptor target. This means that low inactive concentrations of individual compounds in a mixture may jointly add up to achieve a receptor response ('something out of nothing'). In addition, their dose-response curves are often non-monotonic.

iv) Endocrine disruptors might cause heritable (but non-genetic) alterations in an organism. A recent discovery by Michael K. Skinner's laboratory[1–3] demonstrated that endocrine disruptors may affect the F1 through F4 generations of a single pregnant mother animal exposed during a sensitive time window to endocrine disruptors. Skinner and collaborators have demonstrated that these transgenerational effects were due to epigenetic mechanisms, *i.e.* 'heritable' alterations in the gene expression program of the offspring. There are both maternal and paternal modes of inheritance. These aspects brought about a paradigm change in biology as well as in toxicology, in particular the way we explain the action of xenobiotics on living organisms.

The results of the National Research Programme on *Endocrine Disruptors: Relevance to Humans, Animals and Ecosystems (NRP50)* need to be viewed against this background. In the public (media) perception, the most tangible result was the geographic distribution of male reproductive health problems in a study involving Swiss army conscripts. Exposures to endocrine disruptors at the place of conception and pregnancy are inferred as a possible cause as has been convincingly demonstrated in animal studies. The results of the NRP50 in conjunction with US studies highlight the potential risks of human exposure, and if animal studies are taken at face value, early gestational exposure may contribute to 'fetal-origin-late-onset-adult-disease' in other major areas, such as cancer, obesity, diabetes, urogenital disorders and fertility. NRP50 research discovered new chemicals as endocrine disruptors (*e.g.* UV filters), new targets (such as corticoid receptor and PPAR signaling), and new detection methods (nanoelectrospray ionization mass spectrometry, high density oligonucleotide microarrays, *in silico* prediction of structure-activity relationships). NRP50 research identified potential routes of exposure (breast milk, food intake and aqueous environment) and factors affecting the environmental processing of endocrine disruptors. Finally, integrative risk assessment techniques allowed for the identification of chemical hot spots in the environment as well as the exclusion of others.

With these results at hand, NRP50 established consensus platforms between science, industry and regulators in order to direct future action regarding endocrine disrupting chemicals. Two of these platforms were targeting specific chemical groups (UV Filters and Flame Retardants), and one of them was system-oriented (aquatic system). The results of these platforms are summarized in the last chapter of this special issue on endocrine disruptors.

[1] M. D. Anway, A. S. Cupp, M. Uzumcu, M. K. Skinner, *Science* **2005**, *308*, 1466.
[2] R. L. Jirtle, M. K. Skinner, *Nat. Rev. Genet.* **2007**, *8*, 253.
[3] E. E. Nilsson, M. D. Anway, J. Stanfield, M. K. Skinner, *Reproduction* **2008**, *135*, 713.

It is with great pleasure that the Editorial Board of CHIMIA warmly thanks Prof Dr. Felix Althaus and his fellow guest editors for their efforts in the planning and successful realisation of this interesting and topical issue on 'Endocrine Disruptors: Relevance to Humans, Animals and Ecosystems'.