

Immunotoxicity

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Immunotoxicity

Human

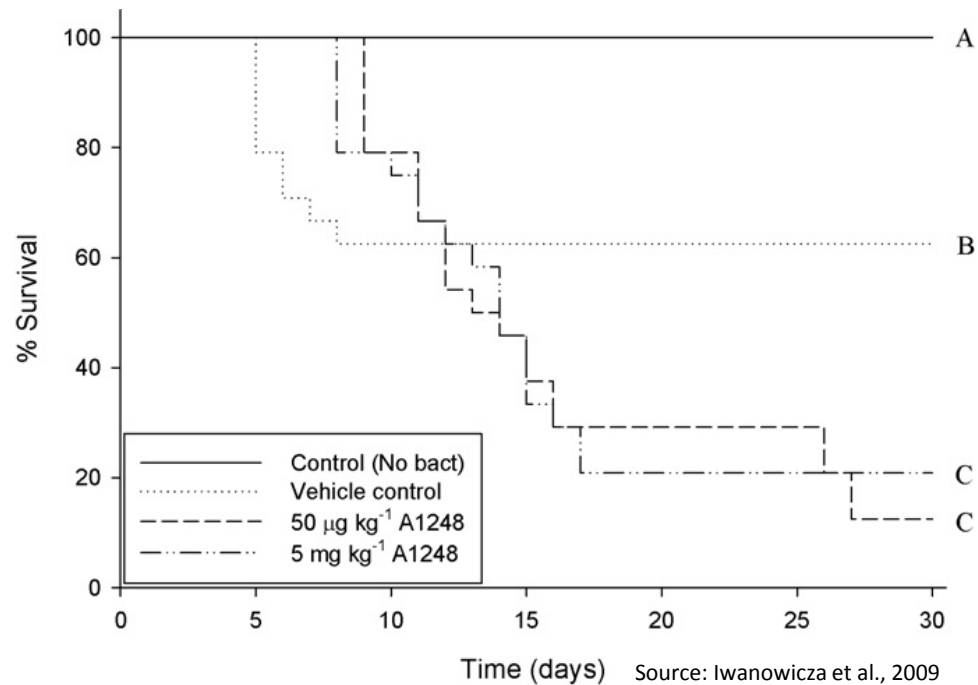
- well documented; data since 1970s
- tiered testing frameworks to assess immunotox. effects; rely on a range of immunological tests and endpoints

Ecotoxicology

- rarely considered in ecotoxicological risk assessment
- no established inventory for the...
 - ...detection of immunomodulation
 - ...evaluation of associated consequences

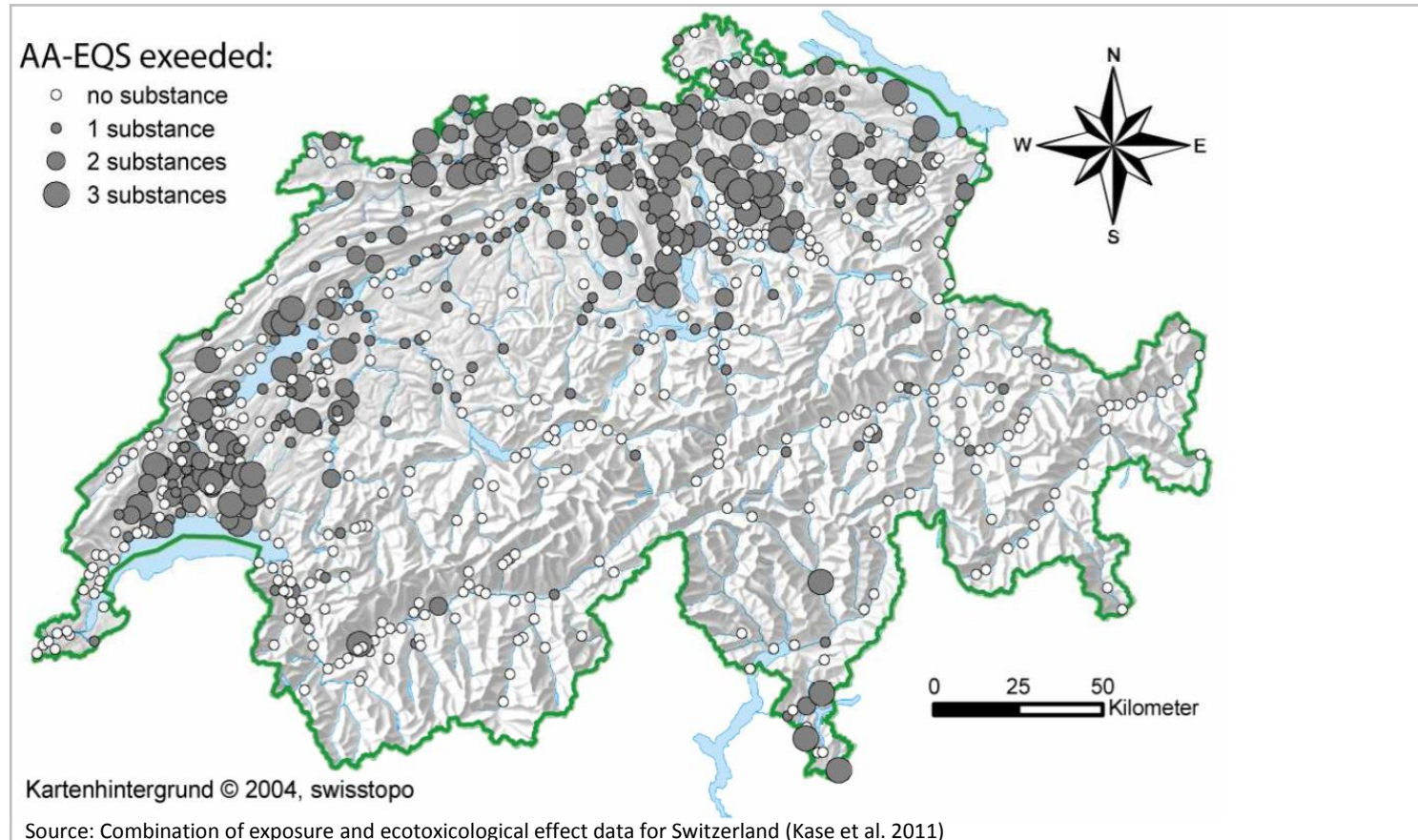
Why studying fish immunotoxicity?

Essential for fitness and survival:



Numerous legacy & emerging contaminants are (potentially) immunotoxic

There is an environmental relevance!



=> 543 water sections downstream of sewage treatment plants

=> atenolol, benzotriazole, carbamazepine, clarithromycin, diclofenac & sulfamethoxazole

What is an immunotoxic substance?

Definition problematic -> numerous substances can have an impact

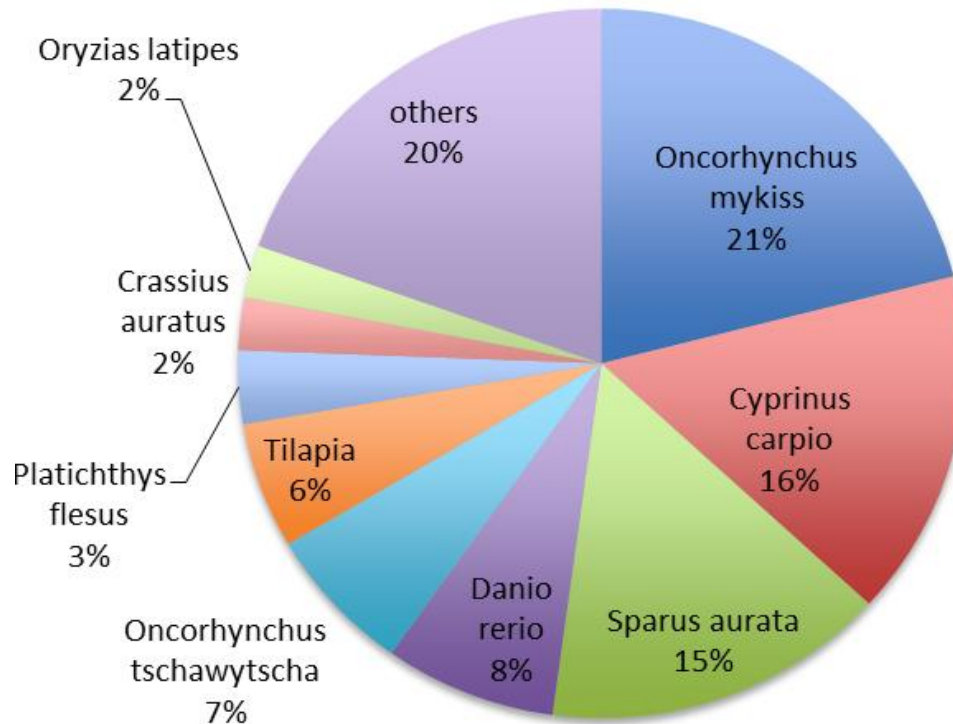
Side / secondary effect of general toxicity?!

Variation of immunotoxic effects across the life cycle

Effects not always obvious -> resting vs. activated immune system

The immune system is complex!

Zebrafish are frequently used in immunotoxicological studies



Zebrafish are frequently used in immunotoxicological studies



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THE IMPACT OF ENDOCRINE-DISRUPTING CHEMICALS ON OXIDATIVE STRESS AND INNATE IMMUNE RESPONSE IN ZEBRAFISH EMBRYOS

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Abstract: Bisphenol A (BPA) and nonylphenol (NP) are well known endocrine-disrupting chemicals (EDCs) ubiquitous in the aquatic environment and are an ecotoxicological risk for the health of aquatic organisms. Limited attention has been given to the immunotoxicity of these chemicals. The present study revealed a concentration-dependent increase of reactive oxygen species content and an induced expression of redox-sensitive transcription factors in zebrafish embryos after exposure to various concentrations of BPA, NP, and BPA/NP mixture for 4 h to 168 h postfertilization. Transcription of genes related to the immune response, including *IFN γ* , *IL1 β* , *IL10*, *Mx*, *TNF α* , *CC-chemokine*, and *CXCL-clc*, were significantly up-regulated on exposure to EDCs. A significant induction of concentrations of proinflammatory mediator, nitric oxide, accompanied by an increase in the activity of nitric oxide synthase (NOS) and an upregulation of inducible NOS gene expression, was detected in zebrafish embryos on exposures to EDCs. To elucidate the potential mechanisms by which BPA and NP activate the innate immune response, expression profiles of genes related to the Toll-like receptors (TLRs) signaling pathway were examined. Expressions of *TLR3*, *TRIF*, *MyD88*, *SARM*, *IRAK4*, and *TRAF6* were altered on exposure to EDCs. The authors' results demonstrate that exposure to BPA and NP significantly affects the expression of genes related to immune response in zebrafish embryos following oxidative stress. *Environ Toxicol Chem* 2013;32:1793–1799. © 2013 SETAC

Keywords: Environmental estrogen

Bisphenol A

Nonylphenol

Oxidative stress

Immune system

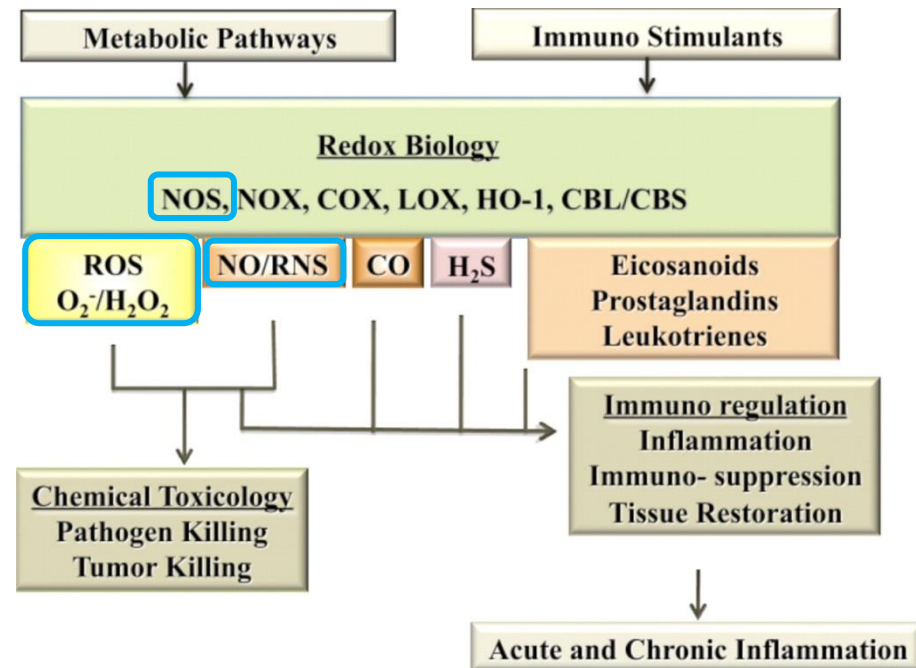
Methods for the detection of immunotoxic effects

Measurement of:

Reactive Oxygen Species (ROS), Nitric Oxide (NO)
and Nitric Oxide Synthase (NOS)

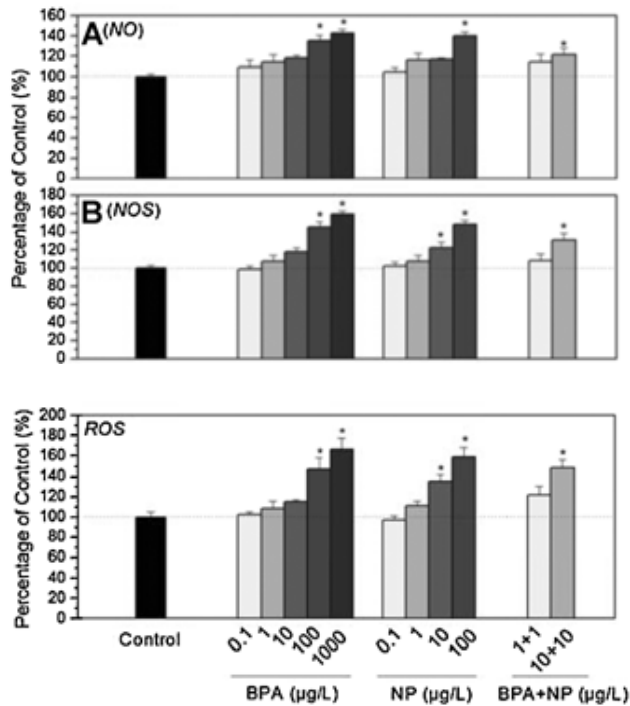
Expression of immune-related
genes via qPCR analysis

Advantage:
whole-body analysis was done

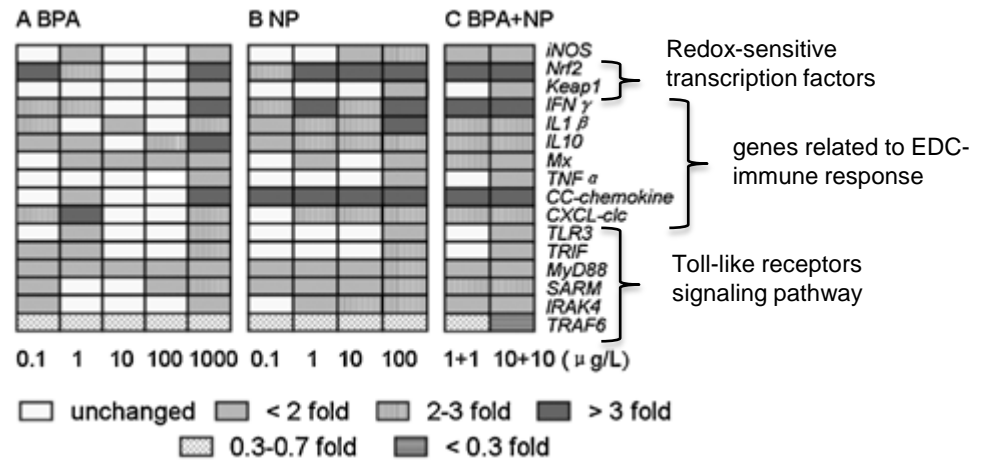


The impact of BPA and NP on zebrafish embryos

Immunoassays:



qPCR analysis:



Take home message

from the zebrafish / toxicology lessons

- Environmental chemicals can be a direct, non-infectious cause of disease
- Environmental chemicals can also indirectly cause diseases, for instances by compromising the immune system (this can increase the susceptibility)
- Zebrafish is a suitable model to assess mechanisms of toxicity, as well as adverse consequences (in view of the high diversity of fishes in particular, and vertebrates in general, model species are essential)

