Karlsruhe Institute of Technology

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Impacts of noxa on the early stages of vertebrate development: a systems biology approach

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Question

This project addresses the question, how and to what extend noxa interact on very early processes and pathways during vertebrate development. Two substances (Ethanol and Bisphenol A) have been chosen to study their effect on early differentiation in zebrafish (*Danio rerio*). Processes of early vertebrate development are highly synchronized and depend on complex signaling cascades. They control the differentiation and coordinative movement of cells and cell clusters. The final aim of this project is to visualize *in vivo* the disrupting interaction between the noxa and processes of early vertebrate differentiation.

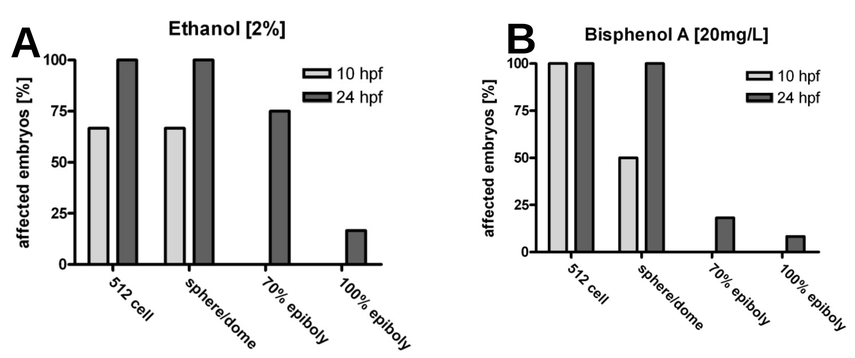

Fig. 1 Effects of different exposure scenario

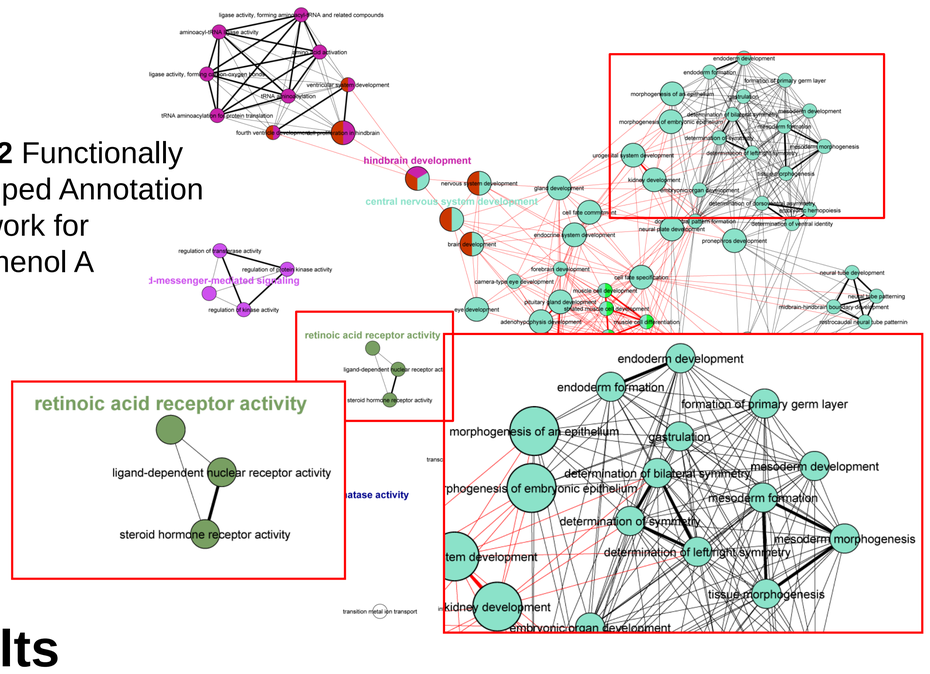

Fig. 2 Functionally Grouped Annotation Network for Bisphenol A

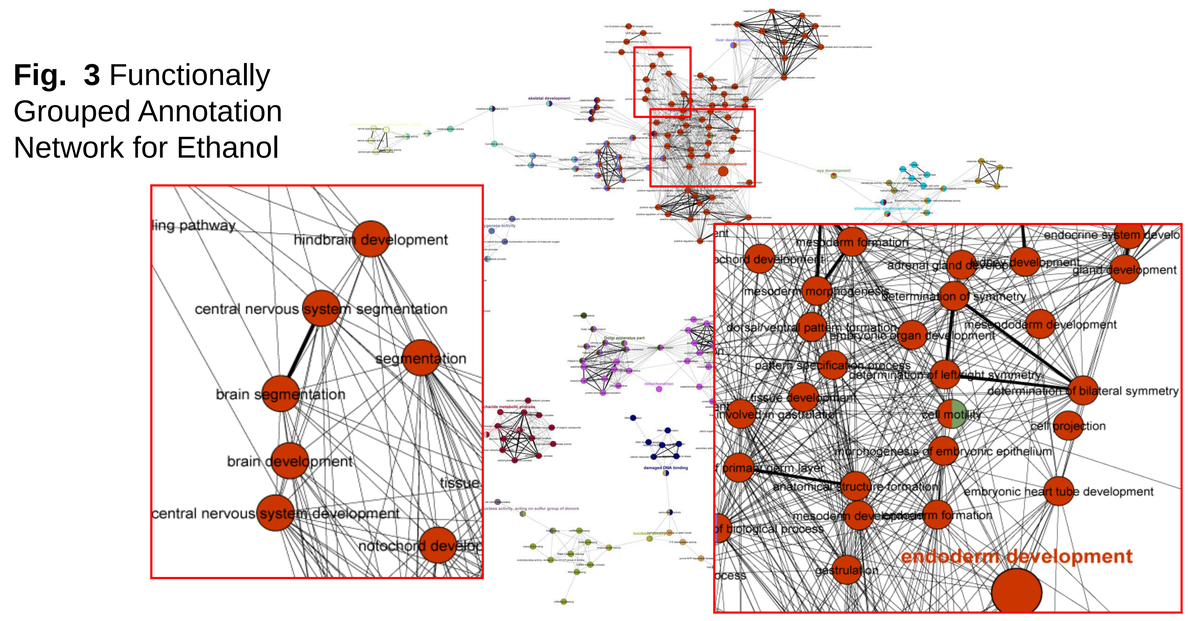

Fig. 3 Functionally Grouped Annotation Network for Ethanol

Results

Early- to mid-gastruation stages have been identified as sensitive stages for Ethanol and Bisphenol A exposure (Fig.1). Following up, microarray analysis were performed using custom designed expression analysis of treated and vehicle treated embryos. Publicly available databases like GO were used for further analysis of obtained gene lists (Fig. 2+3). Specific pathways of early development were identified and are currently further evaluated by *in situ* analysis (Fig. 4). Disturbed processes/patterning after Bisphenol A treatment include mainly brain development, dorsal/ventral differentiation and conversion & extension movements. These processes will be target for following quantitative *in vivo* microscopy of flourescent reporter lines.

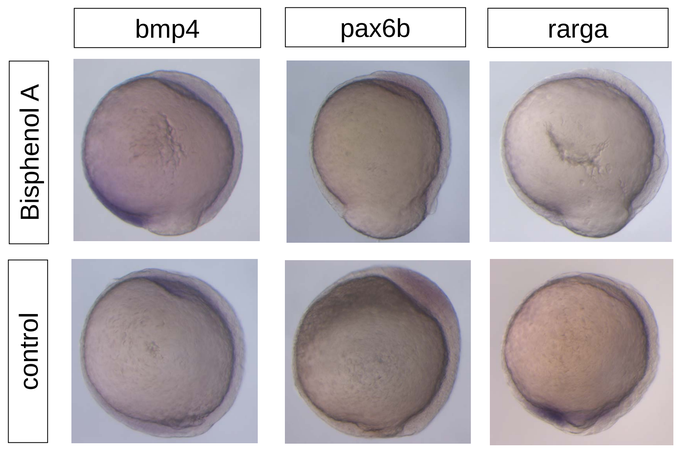

Fig. 4 *In situ* Hybridisation of selected transcripts

Computational challenges

Challenges of handling and processing huge datasets (>10TB) are coming along with this approach of *in vivo* microscopy.

1. DataBrowser: This is an application for managing, analyzing and visualizing large amounts of data and its meta data. The data are stored on the Large Scale Data Facility (LSDF) @ KIT which provides up to 6PB of storage in a first step.

2. Imaging Project: 4D image raw data can be processed on a user defined imaging pipeline with currently more than 200 operators available. Plug-Ins of almost any language can be easily integrated to this C++ based program. Finally, the image analysis can be computed on a single workstation or on a HADOOP-cluster with more than 400 cores.