Detection of Biomarkers for Developmental Toxicity in Zebrafish using Microarray, Gene Expression Profiling, and Pathway Analysis

Introduction:

Zebrafish and mammalian toxicity profiles are highly comparable (Celine et al 2012), making the Zebrafish model , when combined with microarray and pathways analysis, an extremely useful tool for the detection of potential biomarkers of developmental toxicity and for the investigation of the mode of action (MoA) of toxicants.

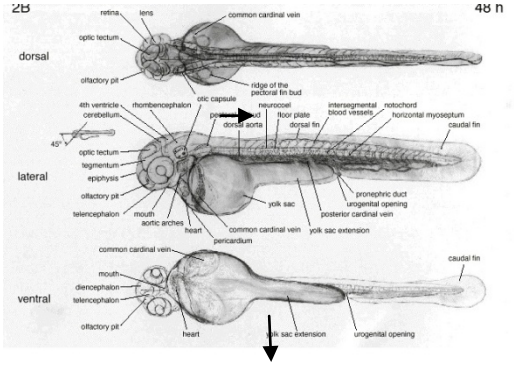
Advantages:

- Cost effective when compared to two generation toxicity bioassays.
- Time effective- ,quick organogenesis process (<5 days)
- Aligns with 3 Rs- Replacement, Reduction and Refinement.
- Transparent embryos/larva facilitates investigation at structural and functional level within the same individual.
- Cross-species conservation of developmental processes and pathways.
- Development of mechanism-based hypotheses based on statistical and pathways analysis of microarray data.

Zebrafish embryos

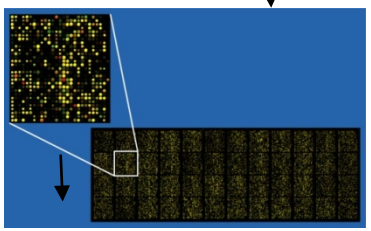
Culture fish embryos in multi-well plates + tested compound

Eg Developmental malformations:



Evaluate fish embryo development at desired stages (*Image permission of :Haffter et al,"The Company of Biologists" 1996)*

RNA Extraction



Microarray gene expression profiling

In house-developed statistical software and pathway analysis

References:

1. Sipes NS, Padilla S, Knudsen TB, 2011. Zebrafish: as an integrative model for twenty-first century toxicity testing. Birth Defects Res C Embryo Today. 2011 Sep;93(3):256-67. doi: 10.1002/bdrc.20214
2. McGrath P, Li CQ, 2008. Zebrafish: a predictive model for assessing drug-induced toxicity. Drug Discov Today. 2008 May;13(9-10):394-401. doi: 10.1016/j.drudis.2008.03.002.Epub 2008 Apr 22.
3. Scholz S, Fischer S, Gündel U, Küster E, Luckenbach T, Voelker D., 2008. The zebrafish embryo model in environmental risk assessment--applications beyond acute toxicity testing. Environ Sci Pollut Res Int. 2008 Jul;15(5):394-404. doi: 10.1007/s11356-008-0018-z. Epub 2008 Jun 25

Detect potential biomarkers for developmental toxicity and to investigate the MoA of toxicants.