Zebrafish – a model organism for human disease

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Fish as Model Organisms

- Share common molecular pathways with mammals
- Excellent models for developmental toxicology studies
  - lots of offspring
  - extrauterine development
  - transparent chorion
  - rapid growth
    http://www.youtube.com/watch?v=eQNxHGpK7Wc
  - short generation time
  - absorb compounds from water
  - low cost
- Share common diseases
Common Fish used in Toxicology

Photo Courtesy of Utah Division of Wildlife Resources

Photo Courtesy of Johnny Foster

Photo Courtesy of www.arkive.org

Photo Courtesy of Warwick Stoll / peturepl.com
LETTER

A systematic genome-wide analysis of zebrafish protein-coding gene function

Ross N. W. Kettleborough1, Elisabeth M. Busch-Nettwich1, Steven A. Harvey1, Christopher M. Dooley1, Ewaart de Bruin2, Freek van Eenennaam1, Ian Sealy1, Richard J. White1, Colin Hend1, Isaac J. Nijman1, Prusia Fenyves1, Selina Mehrotra1, Catherine Schafft1, Richard Gibbons1, Neha Wal1, Samuel Carruthers1, Amanda Hall1, Jennifer Voo1, Edwina Cupp1 & Derek L. Stemple1

do:10.1038/nature11992

LETTER

The zebrafish reference genome sequence and its relationship to the human genome

Kerstin Howe1, Matthew D. Clark3,4, Carlos F. Torrejón1, James Torrance1, Camille Berthelot4,5,6, Matthias Muffato2, John E. Collins3, Sean Humpherys1, Karen McLaren1, Lucy Matthews1, Stuart McLaren1, Ian Sealy1, Mario Caccamo1, Colin Hall1, Paul Hooper1, James B. Keen1, John A. Kedra1, John H. Kedra1, Michael Kistler1, Tom Leaf1, Abdul Mahdi1, James Musser1, Christopher V. Nazer1, Samuel Smith1, Sue Taylor1, Paul Turner1, Tim White1, Robert Wilm1, James Wood1 & Tawaue Woods4

April 2013
Browse 19335 Zebrafish Lines at ZIRC
Transgenic Fish

DOMINIK PAQUET, THE ROCKEFELLER UNIVERSITY

http://dellairelab.medicine.dal.ca, Dalhousie University
Brain Activity Map

- http://www.youtube.com/watch?v=KE9mVEimQVU
Fetal Origins of Adult Diseases

- Epigenome is vulnerable to:
  - maternal diets
  - nutrients
  - ethanol consumption
  - cigarette smoking

- Aberrant epigenetic marks deposited early in life will have lifelong effect on:
  - gene expression
  - increase risks of adult diseases

- Early embryo development is a critical time
Benzo(a)pyrene (BaP)

- Model polycyclic aromatic hydrocarbon (PAH)
- Environmental contaminant
- Recognized human and animal carcinogen
- Reproductive and developmental toxicity
  - mental retardation, increase CVD and cancer risk
Multi- and/or Transgenerational Toxicology

Exposure

$P_0$

$F_1$
daughter

$F_2$
granddaughter

$F_3$
great granddaughter

$F_1$ fetus contains $F_2$ germ cells

$1^{st}$ “un”exposed generation
Transgenerational Effects of Dietary BaP Exposure

- Adult Po zebrafish were fed for 21 days
  - $2 \ ♀$ & $2 \ ♂$ / tank, 10 tanks/ group
- Determine for Po (exposed), F1, F2, F3, & F4:
  - Reproductive success
  - Embryo survival
  - Hatching rate
  - Deformities (96 hpf)
  - Gonad differentiation
  - Tumorigenesis
  - Changes in the transcriptome and epigenome
    - (liver, gonad, heart, brain)
Adverse Outcome Pathways

Toxicant - BaP
- Chemical Properties

Macro-Molecular Interactions
- Receptor/Ligand
- DNA Binding
- Protein Oxidation
- Epigenetic Change

Cellular Responses
- Gene Activation
- Protein Synthesis
- Altered Signaling

Organ Responses
- Altered Physiology
- Disrupted Homeostasis
- Altered Tissue Development/Function

Organism Responses
- Lethality
- Impaired Development
- Impaired Reproduction

Population Responses
- Structure
- Extinction

Vasa Promoter Methylation

???
Zebrafish Educational Resources

http://www.fishforscience.com/

http://www.neuro.uoregon.edu/k12/zfk12.html

http://www.zfic.org/