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Expert Neuroscience Research, Advancing Drug Development

Zebrafish models

Zebrafish as a Model Organism

Zebrafish provides unprecedented opportunities for the study of vertebrate development for several reasons: the genome of this organism is well characterized, the animal can be easily reared in laboratory settings, and techniques, such as CRISPR/Cas9 and TALEN, have been developed for genetic manipulations of specific genes of interest. Also of great importance, the embryo remains translucent throughout much of its development, so that it can be studied in detail under the microscope. Such study includes ingenious methods that have been developed for tagging the protein products of specific genes with fluorescent markers.

NeuroDetective– *1422 Hopeland Rd., Wyncote, PA 19095, U.S.A.*
+1. 215. 536. 8757 – *info@ndineuro.com*

Muscle formation

This model focuses on sarcomeres, the basic contractile units in skeletal and cardiac muscles. The proteins Smyd1 and Hsp90a1 have recently been shown to play vital roles in sarcomeres assembly. Genetic knockdown of Smyd1 or Hsp90a1 results in paralyzed fish embryos with defective sarcomeres organization in skeletal and/or cardiac muscles.

Functional assessment of genes associated with Type 2 Diabetes

This model uses a semi-high throughput screening method that employs transient gene knockdown in transgenic zebrafish embryos, to assess how each individual gene contributes to the production of pancreatic β-cells, a cell type that is central to diabetes pathogenesis. A subset of genes that is necessary for production of β-cells have been identified as potential drug targets.

Modeling of metabolic traits in ciliopathies

Ciliopathies are disorders caused by defects in small cellular protrusions called cilia. This model focuses on the role that cilia genes play in the production of two major cell populations that are important for regulation of energy balance. The first is endocrine cells in the pancreas which are important in regulation of glucose levels. The second is neuronal populations in the hypothalamus that regulate food intake.

Identification of genes associated with lipid traits

This model targets defective lipid metabolism in zebrafish, including hypercholesterolemia and non-alcoholic fatty liver disease. We have developed assays that combine suppression of putative disease genes with or without the introduction of high fat diets. Using this genetic model, we are able to functionally characterize genes found in human genomic regions associated with lipid traits with the goal of identifying new susceptibility genes.

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