



High-Throughput Screening with ZEBROS (Zebrafish Reactive Oxidative Species)

Application

- ◆ *Scientific model using zebrafish*
- ◆ *Ability to study a variety of introduced diseases*

Advantages

- ◆ *Rapid development*
- ◆ *Profuse reproductive capacity*
- ◆ *Relatively transparent and hardy for study*

Introduction

Zebrafish have rapidly become a major scientific model to study diseases because of their transparent embryos that allow detailed morphological observations, rapid development from externally fertilized eggs, prolific reproductive capacity (usually over 100 eggs per clutch), and modest maintenance requirements. They are physically large enough to isolate significant amounts of specific tissues, especially skeletal muscle, yet are sufficiently small to allow for substantial "economies of scale." The biological resources for zebrafish continue to expand, including the ongoing sequencing of its genome. Single cell embryos go through a rapid phase of development until age 24 hours when a full vertebrate body structure has been formed. The embryos hatch from their chorionic shells by day 3 and are then free swimming fry. During this time they are relatively transparent and hardy, so a variety of chemical probes can be used to illuminate various biological functions. In the past few years, Glenn Gerhard, MD has been using zebrafish as a model organism to study reactive oxidative species (ROS) due to these research benefits.

Geisinger's intellectual property focuses on a high-throughput screening tool to study the effects of introduced target drug compounds on fish embryos in a large system (such as 96 well plate). For example, Dr. Gerhard has used probes to measure reactive oxygen species and mitochondrial function in zebrafish embryos. Zebrafish fry grow rapidly and become reproductively mature by 3 months of age, making them an ideal candidate for rapid testing against pharmaceutical compounds. Fish can be specifically tailored for certain purposes and studied en masse. For example, Geisinger researchers have designed red and green fluorescent fish to study muscular deformities associated with Amyotrophic Lateral Sclerosis (ALS) in a high-throughput manner. Changes in these abnormalities including colorimetric changes can be used to screen for drugable compounds.

The ZEBROS system has been tested with support from Bucknell University staff and students. Specifically, bioengineering students have helped identify process improvements to facilitate transport of nutrients to and export of waste away from the well plates.

CONTACT



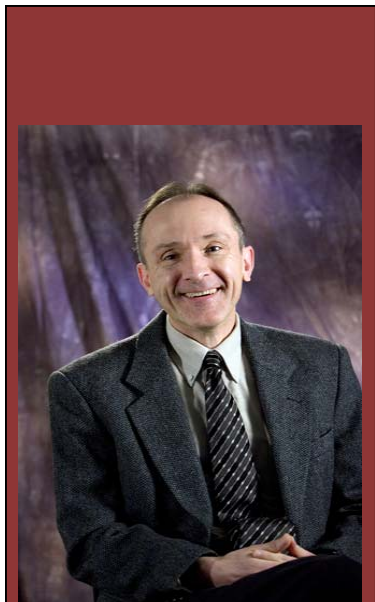
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About the Inventor

Glenn Gerhard, MD is a board certified Clinical Pathologist with research training in Human Genetics at the University of Pennsylvania and residency training in Pathology at Dartmouth. He serves as the Director of the Geisinger Clinic Genomics Core, Staff Scientist at the Weis Center for Research, and Associate Medical Director of the Geisinger Molecular Diagnostics Laboratory in the Department of Pathology and Laboratory Medicine at Geisinger. Dr. Gerhard is a co-inventor on two patent applications filed in May 2006 and May 2007. In 1997, he co-Founded Targeted GastroIntestinal Therapeutics (TGIT), a firm based upon developing diagnostics and therapeutics for hereditary hemochromatosis, a disorder of iron.

Selected publications includes:

1. Grundy MA, Gorman N, Sinclair PR, Chorney MJ, **Gerhard GS**. High-throughput non-heme iron assay for animal tissues. *J Biochem Biophys Methods*. 2004 May 31;59(2):195-200.
2. **Gerhard, GS**, and Kasales, CJ. Aging and kyphosis. *Journal of Gerontology: Biological Sciences*, Nov; 58(11): 968, 2003.
3. **Gerhard, GS**. Comparative aspects of zebrafish as a model for aging research. *Experimental Gerontology*, Nov-Dec; 38(11-12): 1333-41, 2003. Zacharski, L. and Gerhard, GS. Atherosclerosis: a Manifestation of Chronic Iron Toxicity? *Vascular Medicine*, 8:153-5, 2003.
4. Chorney, MJ, Yoshida, Y, Meyer, PN, Yoshida, M and **Gerhard, GS**. The Enigmatic Role of the Hemochromatosis Protein in Iron Absorption. *Trends in Molecular Medicine*, Mar; 9(3):118-25, 2003.
5. Sinclair, PR, Gorman, N, Trask, H, Bement, J, Szakacs, JG, Elder, GE, Balestra, D, Sinclair, JF, and **Gerhard, GS**. Uroporphyrin caused by ethanol in HFE (-/-) mice as a model for porphyria cutanea tarda. *Hepatology*, Feb; 37(2):351-8, 2003.
6. **Gerhard, GS** and Cheng, KC. A call to fins! Zebrafish as a gerontological model. *Aging Cell* 1(2), 104-111, 2002.
7. **Gerhard, GS**, Kauffman, EJ, Wang, X, Stewart, R, Moore, J, Kasales, CJ, Demidenko, E, and Cheng, KC. Life spans and senescent phenotypes in two strains of Zebrafish (*Danio rerio*). *Experimental Gerontology*, Aug(8-9):1055, 2002.



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