

Yeast and Zebrafish in Pharmacy School

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Rational drug design and the development of high throughput drug screening require an understanding of biological processes at the molecular level. One approach is to use simple model systems to make links between molecular mechanisms and biological function. In my lab we use zebrafish (*Danio rerio*) to understand the impact of dioxin on the development of the embryonic heart, and we use the yeast *Saccharomyces cerevisiae* to study how cells move from quiescence to growth. Dioxin, a well-known toxic chemical waste product, is an agonist for the ligand-activated transcription factor AHR. We find ppb levels of dioxin produces profound malformation in the embryonic zebrafish heart. This effect is limited to only a few days during heart development: adult and juvenile fish are insensitive. One of the effects that dioxin produces is arrested cell division in the developing heart. We have used another model, the yeast *Saccharomyces cerevisiae*, to understand how cells move from a quiescent state to an actively multiplying state. Yeast cells become quiescent as the culture medium is expended, yet will resume active growth if glucose is added to the culture. Resumption of growth is accompanied by the induction of approximately 1,000 genes only 10 minutes after glucose addition. Computer analysis of these gene sequences reveals that many carry a regulatory sequence called RRPE 5' of the ORF. We have characterized the RRPE and used a high-throughput screen of yeast-GST fusion proteins to identify a protein, Stb3, that binds to RRPEs *in vivo* and *in vitro*. Work linking Stb3 to Ras- and Tor-mediated glucose signals will be discussed. By using models such as yeast and zebrafish we can understand biological processes that have relevance to human biology.