Cell Cycle Regulation. We are working to understand how yeast regulate the cell cycle in response to external signals. Cell cycle regulation is an important process in that improper cell cycle regulation can lead to cancer. It is also an important in biology because organized regulation of proliferative growth is a fundamental requirement for an organism, and absolutely required for the proper development of multicellular structures. More specifically, we are studying the connections between external signals and the conserved cyclin/cyclin dependent kinase (CDK) pathway that is thought to regulate progress from the G1 phase of the cell cycle into S phase. Yeast have proteins that are homologs to the products of the human p21 ras oncogenes that are associated with many cancers. In yeast, the mitogen signal that regulates Ras is glucose. We are interested in how signals that control proliferation in yeast are coupled through Ras activity to the machinery of the cell cycle. Recently, we have identified the Cln3, a G1 cyclin, as a major target for the Ras/cAMP pathway in yeast. We are also studying the transcriptional regulation of a number of yeast cell cycle genes to better understand how signals that produce proliferation in yeast control movement from G1 to S phase.

Developmental Toxicology. We are interested in studying the molecular mechanisms by which TCDD (dioxin) disrupts the normal developmental programing of fish. TCDD is a widespread environmental toxicant that accumulates in the food chain. TCDD activates a transcription factor, the arylhydrocarbon receptor (AhR) that in turn alters the pattern of gene expression. While it is assumed that alterations in gene expression lead to the toxic effects, it is not known what genes are critical in this response. Early life stage fish are more sensitive to TCDD than any other known organism. Because of their well known utility in genetic and developmental studies, we have established the zebrafish as a model system for studying this toxicity. In an attempt to identify genes that play a role in TCDD toxicity, we have initiated a selection for zebrafish mutants that are resistant to TCDD lethality.