Woods Hole Oceanographic Institution

Biology Department Seminar

Thursday, March 31, 2016
Redfield Auditorium – 12:00 Noon

Engineering fish genomes to understand environmental interactions

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The exposure of fish and other marine organisms to industrial and pharmaceutical pollutants (xenobiotics) is of global concern. In most cases the mechanisms of response and adverse outcomes to those exposures are still poorly known. The pregnane x receptor (PXR; also known as the steroid and xenobiotic receptor) is a nuclear receptor activated by a range of pharmaceutical and industrial compounds. The downstream consequence of activated PXR is transcriptional induction of many enzymes involved in the metabolism of xenobiotics, including the cytochrome P450 enzyme, CYP3A. The precise molecular interactions and ligand specificity of PXR in fish is much less well understood than in humans. We have been using zebrafish (*Danio rerio*) as a laboratory test species to tease out the principles underlying the important chemical defense role PXR plays in wild fish populations. Recent advances in genetic engineering, namely CRISPR-Cas9, have made it possible to precisely alter the genome of a number of species from fungi to animals. Taking advantage of the CRISPR-Cas9 system we are able to modulate gene expression and function through editing of the organism's genome, and have employed CRISPR-Cas9 to modify the PXR gene in zebrafish, as well as other xenobiotic-interacting genes. Genome editing has the potential to help us define detailed roles for xenobiotic sensing proteins, elucidate underlying transcriptional programs, and even identify 'design principals' that may be shared in wild fish populations.