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Courses offered: BIOL302 Molecular Cell Biology I: Cellular Biochemistry and Molecular Biology, BIOL507 Advanced Biological Chemistry, BIOL582 Graduate Seminar

Research interests: Research in my laboratory focuses on mechanisms and regulation of signaling initiated by G protein-coupled receptors (GPCR). Human GPCRs mediate responses to light, odor, taste, hormones, and neurotransmitters. Defects in GPCR signaling pathways can cause a multitude of human diseases including hypertension, heart failure, and cancer. A better understanding of the mechanisms regulating GPCR signaling pathways will aid in our ability to define targets for therapeutic intervention, and could eventually lead to an entirely new class of pharmaceuticals.

The GPCR signaling pathways are highly conserved across evolution, which allows us to use the simplest eukaryotic organism, the budding yeast Saccharomyces cerevisiae, as a model system. The yeast experimental system offers the powerful genetic and biochemical tools unavailable in any other eukaryotic systems. Currently, we are studying a novel mechanism by which GPCR signaling pathways are regulated, namely through stimulus-dependent ubiquitination of signaling components. We have found stimulus-dependent ubiquitination of key components of the pathway including G proteins and MAP kinases, and we are using genetic and biochemical methods to study how these modifications contribute to signaling regulation. We are also interested in identifying the molecular machinery that carries out these modifications and how GPCR signaling might in turn regulate their activities.

Another project in my laboratory focuses on function and substrate specificity of a deubiquitinating enzyme Ubp3. Recently we discovered that yeast Ubp3 is a novel regulator of protein kinase C (PKC), serine/threonine kinases that play important roles in many cellular processes, including proliferation, differentiation and cell survival. We are now conducting biochemical analysis to elucidate the molecular mechanisms by which Ubp3 regulates PKC. We are also planning on extending our work to other systems including human cell lines and pathogenic fungus to test whether PKCs are similarly regulated by deubiquitinating enzymes in these systems. Insights gained here could potentially open up an exciting possibility of targeting deubiquitinating enzymes as a strategy for developing novel therapeutics against cancer or fungal infections.

Research opportunities: I welcome highly motivated students interested in molecular biology, cell regulation, and signal transduction to pursue graduate study in my laboratory. Ample research opportunities exist for motivated undergraduate students.

Representative publications:

Zhu M\*, Torres MP, Kelley J, Dohlman HG, Wang Y. Pheromone- and Rsp5-dependent ubiquitination of the G protein beta subunit Ste4 in yeast. Journal of Biological Chemistry. 286(31):27147-55, 2011. Epub on Jun 17, 2011. (\*Graduate Student at SLU)

Wang Y, Abu Irqeba A\*\*, Ayalew M, and Suntay K\*\*. Sumoylation of a transcription factor Tec1 regulates signaling of mitogen-activated protein kinase pathways in yeast. PLoS ONE. 4(10): e7456. 2009. (\*\* undergraduate student at SLU)

Wang Y, Zhu M\*, Ayalew M, Ruff JA\*\*. Down-regulation of Pkc1-mediated signaling by the deubiquitinating enzyme Ubp3. Journal of Biological Chemistry. 283(4):1954-61, 2008. (\* graduate student at SLU; \*\* undergraduate student at SLU)

Wang Y, Dohlman HG. Regulation of G protein and MAP kinase signaling by ubiquitination - insights from model organisms. Circulation Research. 99:1305-1314, 2006.

Esch KR, Wang Y, Errede B. Pheromone induced degradation of Ste12 contributes to signal attenuation and the specificity of developmental fate. Eukaryotic Cell. 5(12):2147-2160, 2006.

Wang Y, Dohlman HG. Pheromone-regulated sumoylation of transcription factors that mediate the invasive to mating developmental switch in yeast. Journal of Biological Chemistry. 281:1964-1969, 2006.

Wang Y, Marotti LA, Lee MJ, Dohlman HG. Differential regulation of G protein alpha subunit Gpa1 trafficking by mono- and poly-ubiquitination. Journal of Biological Chemistry. 280(1):284-291, 2005.

Wang Y, Dohlman HG. Pheromone signaling mechanisms in yeast: a prototypical sex machine. Science. 306(5701):1508-1509, 2004.

Wang Y, Ge Q, Houston D, Thorner J, Errede B, Dohlman HG. Regulation of Ste7 ubiquitination by Ste11 phosphorylation and the Skp1-Cullin-F-box complex. Journal of Biological Chemistry. 278(25):22284-22289, 2003.

Wang Y, Dohlman HG. Pheromone-dependent ubiquitination of the mitogen-activated protein kinase kinase Ste7. Journal of Biological Chemistry. 277(18):15766-72, 2002.

Marotti LA, Newitt R, Wang Y, Aebersold R, Dohlman HG. Direct identification of a G protein ubiquitination site by mass spectrometry. Biochemistry 41(16):5067-74, 2002.

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