Research

Ubiquitination rivals phosphorylation in its widespread importance in many processes. Degradation, vesicular transport and the DNA damage response are all regulated by ubiquitination. Our lab has a long-standing interest in two ubiquitin ligases, the APC and the SCF. Both the APC and the SCF are Cullin Ring ubiquitin ligases with core catalytic subunits and specificity factors that recruit substrates. Both have important roles in cell cycle progression, as well as other processes. We have developed methods to identify substrates of these ligases, and are applying these to both yeast and human cells. Importantly, ubiquitin ligases represent an important class of both oncogenes and tumor suppressors.

Recent and ongoing projects in the lab:

**CRISPR screens to identify functions of orphan ubiquitin ligases.** There are more than 600 ubiquitin ligases encoded by the human genome. Many of these are poorly understood. We have used CRISPR screening to identify the roles of many of these uncharacterized genes.

**Identification of substrates of ubiquitin ligases in yeast and human cells.** Our laboratory has performed a large number of screens focused on either a biological process or a particular ubiquitin ligase. Subsequent projects have involved identifying the relevant substrates of that ligase, and determining the importance of that targeting event.

**Proteome-wide characterization of post-translational modifications.** We have performed a great number of proteomic screens for substrates of ubiquitin ligases, kinases and acetyltransferases. These have brought us into many areas, including cell cycle regulation, DNA repair, metabolism, and transcription.

**Characterization of the functions of atypical polyubiquitin chains.** Ubiquitin forms chains on
substrates. While the best-characterized chains involve the addition of a ubiquitin to lysine 48 of a previously added ubiquitin, many other chain types exist. We have explored this primarily genetically, but also through biochemistry.

**ROTATIONS PROJECTS INCLUDE FOLLOWING UP ON GENES WE HAVE IDENTIFIED WITH ROLES IN G1/S PROGRESSION AND MITOSIS IN HUMAN CELLS.**