UC DAVIS HEALTH | SCHOOL OF MEDICINE

Department of
Cell Biology and Human Anatomy

iBIO: Integrated Biomedical Sciences Seminar Series

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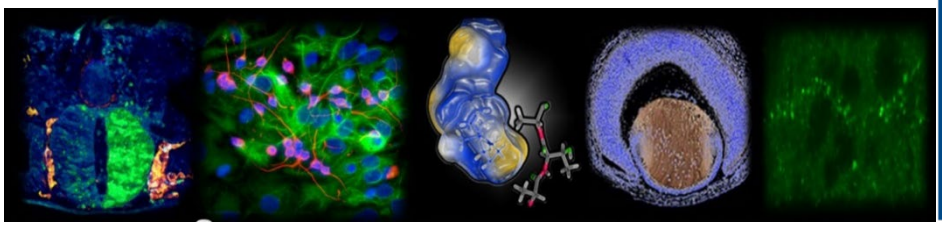
"New regulation in WNT/β-catenin signaling – probing beyond the core signaling module through haploid genetic screens"

WNT signaling is a fundamental pathway that encodes positional information in animals, orchestrates patterning and morphogenesis during embryonic development, and promotes tissue renewal and regeneration in adults. Dysregulation of WNT signaling has been implicated in many diseases, most notably cancer. Signaling pathways have evolved regulatory adaptations superimposed on conserved, core signaling modules. The premise of our research is that discovering and understanding such regulatory mechanisms will illuminate how WNT signaling is deployed to execute different biological functions, and that targeting regulatory adaptations may help overcome some of the therapeutic challenges associated with inhibiting core pathway components. Through unbiased, forward genetic screens and follow-up studies in haploid human cells, we discovered new regulatory mechanisms at various steps of the WNT signaling cascade, including ligand reception, signal transduction and transcriptional regulation. In one mechanism, the ubiquitin ligase HUWE1 potentiates WNT/β-catenin signaling through a process mediated by the β-catenin destruction complex scaffolds APC and AXIN1, which is distinct from the control of β-catenin protein stability by the destruction complex. In another mechanism, the secreted stem cell growth factor R-spondin 3 regulates WNT receptor levels through heparan sulfate proteoglycans independently of LGR receptors, which were thought to be required for all R-spondin signaling.

Tuesday, April 26, 2022
GBSF Auditorium and Zoom
10 a.m.



April
26

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