Benjamin Groth  
UC Davis  
Microbiology Graduate Group  
Exit Seminar  

"The Roles of the Histone Deacetylases Rpd3 and Hst1 in the regulation of de novo NAD+ metabolism."

Wednesday, October 26th, 2022  
4:10 pm  
Green Hall 1022 (formerly LS1022) - In-Person Only

Abstract: Nicotinamide adenine dinucleotide (NAD+) is an enzymatic cofactor with a large variety of crucial roles in metabolism and signaling. Perturbations to NAD+ metabolism are associated with a diverse set of diseases, ranging from cancer to neurological damage. As a result, NAD+ metabolism is an eminent topic of interest. However, the complex network of factors interacting with NAD+ metabolism is not completely elaborated. To clarify and investigate the regulation of NAD+ metabolism, genetic screens were developed to quantitate altered release of NAD+ precursors in yeast strains of interest. This allowed for the observation that deletion of the histone deacetylase (HDAC) RPD3 causes stark reduction in release of the intermediate of de novo NAD+ biosynthesis, QA (quinolinic acid). It was found that that Rpd3 interacts in an antagonistic fashion with the class III HDAC Hst1, a repressor of the de novo-mediating BNA genes. The two HDACs are responsible for the production of differential chromatin modifications at the BNA2 promoter. Moreover, Rpd3 and Hst1, along with the transcription activator Pho2, link the regulation of de novo NAD+ biosynthesis with regulation of genes in the phosphate (Pi) sensing PHO pathway. Pi sensing was shown to interact in a variety of complex ways with de novo NAD+ metabolism and NR salvage, establishing a considerable degree of coordination between these pathways. Altogether, these results highlight a critical role for Rpd3 as a positive regulator of de novo NAD+ metabolism.