UCMERCED | CHEMISTRY & BIOCHEMISTRY

DATE 05/03/2024 | TIME 01:30pm | LOCATION COB1 110

CHEMISTRY & BIOCHEMISTRY SEMINAR SERIES:

Exploring the molecular mechanisms of temperature sensing by Cdc-2-like-Kinases

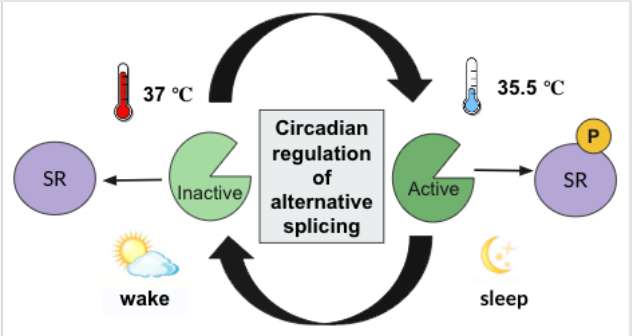
Abstract:

Organisms from all domains of life can sense and respond to temperature changes. Cdc2-like-kinase (CLKs) are highly tuned "molecular thermometers" whose catalytic activity changes in response to subtle fluctuations in physiological temperature. CLK orthologs, found in mammals, reptiles, insects, and plants, have a conserved function as biochemical temperature sensors, whose dynamic ranges are tuned by evolution to an organism's physiological temperature. The structural rearrangements that allow these enzymes to change their signaling output in response to small fluctuations in temperature do not involve global protein unfolding, and the underlying conformational changes remain elusive because existing CLK crystal structures have universally been determined at cryogenic temperatures (~100 K), masking relevant transitions between the active and inactive states of the kinase. To overcome this limitation, we are determining X-ray crystal structures of CLKs across their respective physiological temperature ranges in order to observe the conformational changes that modulate activity. In conjunction, we are using kinetic assays to quantify changes in the catalytic properties as a function of physiological temperature. To better understand how evolutionary sequence variation can tune the sensitivity of a molecular thermometer, we are studying CLKs from the Hawaiian leafhopper (Nesophrosynesp.), an organism that has undergone speciation across a naturally occurring thermal gradient ranging from 24 ℃ in the coastal region to 4 ℃ in the sub-alpine habitats. Our study of CLK sequence variation across cold and warm-adapted leafhopper species will reveal the mechanistic and evolutionary principles that underlie thermosensory function in this widespread family of kinase enzymes.

Luisa R. Garcia Michel

Graduate Student, Chemistry & Biochemistry

UC Merced



About the Speaker:

Luisa is a UC Merced Chemistry and Biochemistry graduate student from Mexico. She earned her Chemistry degree and STEM research minor from the University of Mary in Bismarck, ND. She studied allosteric communication in extracellular signal-regulated kinase 2 (ERK2) and its mutants using computational modeling and molecular simulations in Dr. Daniel Barr's lab. During her undergraduate, she pioneered the Learning Assistant (LA) program for Chemistry classes and was involved in a variety of language and science teaching opportunities. In Fall 2021 Luisa joined the Thompson lab to study the temperature-regulation of Cdc2-like-kinases (CLKs). She continues to be passionate about kinase allostery and science education.