Understanding Allosteric Regulation within SIRT1

Enzymes, proteins that can catalyze reactions, are commonly compared to machines in a factory. While we’re used to thinking of enzymes as static, 3-D structures, it’s easy to forget that, like machines, enzymes have many moving parts. Furthermore, unlike the fixed, rigid structures of machines, many regions of proteins are soft and flexible, some regions have no permanent structures at all and are master shape-shifters. As scientists, we’re slowly starting to realize that these flexible, shape-shifting regions are fundamentally important for the fine-tuning of enzyme activity levels. However, little is known about the exact mechanism for which these regions carry out such regulations.

In the Wang lab, we venture away from the active site and study how flexible, even unstructured regions far away from the active site of enzymes can allosterically change their catalytic activity. This talk will focus on what we’ve found by studying SIRT1, a lysine deacetylase that plays an important role in many cellular pathways, and the role its N-terminal region plays in regulating the enzyme activity. Using biochemical and biophysical techniques, we are trying to uncover the mystery of how two different domains in this region can change the activity at the far-away active site in SIRT1 by interacting with small molecules or other enzymes and undergoing various types of conformational changes.