CASCADES

SEMINAR SERIES

Professor Kathryn Cole

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"Structural Studies of Protein-Inhibitor Complexes: Towards the Development of New Anticancer Therapeutics"

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2:30 PM ET

Hahn Hall North 402

Histone deacetylases (HDACs) catalyze the hydrolysis of acetylated lysine side chains in histone and non-histone proteins. Abnormal HDAC activity is linked to various diseases, including several cancers, making these enzymes important drug targets. Four HDAC inhibitors (HDACi) have been approved by the FDA as chemotherapy agents, including the depsipeptide Romidepsin (Istodax,® Celgene Corporation). While depsipeptides are some of the strongest HDACi known to date, there is limited structural information for their binding.

Tubulin is another anticancer target. It is involved in many cellular functions, including cell shape, mitosis, migration, and movement of organelles. While anti-tubulin drugs have been used to treat cancer for ~70 years, the currently approved drugs tend to be complex molecules derived from natural products, and suffer from multidrug resistance, low solubility, toxicity issues, and/or the lack of multi-cancer efficacy. Therefore, there is renewed energy in developing new generations of tubulin inhibitors that (1) are less toxic, (2) combat drug resistance, and/or (3) are effective against more types of cancers.

As such, my lab uses molecular modeling and molecular dynamics, to study protein-inhibitor complexes. Our in-silico results will help to predict favorable binding interactions and inform the design and synthesis of future analogues to improve overall binding and potency.