

Internship Proposal

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Project Title:

Biochemical and structural studies of anticoagulant molecules

Level:

Master

Project Summary:

We study the properties of natural (from blood-feeding organisms) and engineered peptide anticoagulants, mostly targeting thrombin. For this, we characterize their properties in vitro and ex vivo, with the ultimate aim of understanding their molecular mechanism of action and the regulation of their physiological activity.

Work to be developed by the student:

Protein expression and purification; Macromolecular crystallization; Biochemical (activity assays; kinetic characterization) and biophysical (measurement of binding properties; structural determination) characterization.

References:

Agten, S.M. et al. (2021) Potent trivalent inhibitors of thrombin through hybridization of salivary sulfopeptides from hematophagous arthropods. *Angew Chem, Int. Ed. Engl.* 60, 5348-56. DOI: 10.1002/anie.202015127

Calisto, B.M. et al. (2021) Sulfotyrosine-Mediated Recognition of Human Thrombin by a Tsetse Fly Anticoagulant Mimics Physiological Substrates. *Cell Chem Biol* 28, 26-33. DOI: 10.1016/j.chembiol.2020.10.002

Watson, E.E. et al. (2019) Rapid Assembly and Profiling of an Anticoagulant Sulfoprotein Library. *Proc Natl Acad Sci USA* 116, 13873-8. DOI: 10.1073/pnas.1905177116

Thompson, R.E. et al. (2017) Tyrosine sulfation modulates activity of tick-derived thrombin inhibitors. *Nat Chem* 9, 909-17. DOI: 10.1038/nchem.2744

Figueiredo, A.C. et al. (2012) Unique thrombin inhibition mechanism by anophelin, an anticoagulant from the malaria vector. Proc Natl Acad Sci USA 109, E3649-58. DOI: 10.1073/pnas.1211614109



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