

BCHM 421/422 – 2018/2019

Project #1 Outline: Eukaryotic cells require a regulated balance between protein synthesis and protein degradation. The rate of protein synthesis is controlled through a variety of pathways, one of which is the eukaryotic elongation factor 2 kinase (eEF2K). Given its fundamental role in protein synthesis, it is not surprising that eEF2K is considered as a drug target in cancer, cardiovascular and neurodegenerative diseases. eEF2K's activity is absolutely dependent on calmodulin (CaM)/Ca²⁺. However, the structural basis of CaM/Ca²⁺-mediated activation is unknown. We plan to determine the structure of eEF2K in complex with CaM/Ca²⁺ to reveal whether conformational changes triggered by CaM/Ca²⁺ binding is responsible for activation. We will also characterize other domains and structure elements in eEF2K's function and regulation using kinase and ATPase assays, as well as, biophysical techniques.

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Project Title: Structure and functional characterization of eukaryotic elongation factor 2 kinase

Keywords (3-5):

- 1. Kinase**
- 2. Calmodulin**
- 3. Protein crystallography**
- 4. Activation**
- 5. Activity**

Project Goals: This project's main goal is to determine the structures of various constructs of eEF2K in complex with CaM/Ca²⁺, in addition to characterizing other components of eEF2K involved in kinase activity and regulation.

Experimental Approaches: Cloning, protein expression and purification, crystallization, kinase assay, ATPase assay, binding studies using biophysical techniques.

References:

- C Proud. (2015) Regulation and roles of elongation factor 2 kinase. *Biochem Soc Trans* 43, 328-332
- Lui, R. & Proud, C. (2016) Eukaryotic elongation factor 2 kinase as a drug target in cancer, and in cardiovascular and neurodegenerative diseases. *Acta Pharmacologica Sinica* 37, 285-294.