Department of Molecular and Cellular Biology

Graduate Seminar MCB*6500

Friday, September 20th, 2024 @ 12:00 p.m.

presented by:

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(Advisors: Dr. Siavash Vahidi and Dr. Robert Harkness)

"Assessing the efficacy of deep-learning tools for *de novo* protein design"

De novo protein design aims to create tailor-made proteins with new-to-nature functions. Historically, *de novo* protein design has proven to be extremely challenging due to the complexity and high computational costs of efficiently and accurately evaluating the vast sequence and structural search space. Recently, however, advances in artificial intelligence and deep learning have significantly accelerated progress in this field. Deep learning-based approaches offer several advantages over traditional methods and can be used for a wide variety of design tasks including enzyme active site scaffolding, design of symmetric oligomers, and protein binder design. These emerging tools hold significant promise but must be validated more broadly to fully understand the scope of their capabilities. My proposed research will specifically assess the performance of RFdiffusion, one of the leading deep-learning models for *de novo* protein design. My research will evaluate the ability of RFdiffusion to generate unconditional protein designs as well as protein binders that engage a specific target. The focus for binder design will be on targeting the 20S core particle of the mycobacterial proteasome, a well-established virulence factor and drug target in *Mycobacterium tuberculosis*. The generation of *de novo* binders of the mycobacterial proteasome could reveal novel interactions that modulate the catalytic activity of the proteasome and advance our understanding of this clinically relevant system.