UNIVERSITY OF RHODE ISLAND
Department of Chemistry
SEMINAR

3:00 PM, Monday, March 27, 2023
Room 105 – Beaupre Center

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Engineering Biomolecules to Mitigate Viral Pathogenesis and Tumor Progression

HOST

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Chemistry Department Seminar, University of Rhode Island
March 27th, 2023

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Title: Engineering Biomolecules to Mitigate Viral Pathogenesis and Tumor Progression

Abstract:

The cell surface is decorated with a myriad of molecules involved in signaling, structure, protection, and recognition of 'self'. Pathogenic viruses and tumors have evolved to co-opt these molecular signals to gain access to healthy host cells, causing an array of diseases and a significant burden on public health. Thus, identifying and characterizing such interactions enables the development of tools that disrupt them and ultimately prevent infection and disease. Biomolecules themselves are great templates for the development of such inhibitory agents; we are able to manipulate these templates, from DNA to proteins, using design principles and engineering techniques informed by each interaction. This seminar will discuss two approaches to engineering biomolecules that prevent cell surface interactions underpinning pathogenesis and disease: **rational design** and **directed evolution**.

Using a **rational design** approach, we generated nucleic acid nanostructures to rapidly sense and inhibit Dengue virus, which causes an estimate of 390 million cases of Dengue fever and 96 million hospitalizations per year. Leveraging the predictable nature of DNA base pairing, inhibitory elements were arranged in a geometric pattern that precisely mimics the symmetrical arrangement of infectious proteins on the virus surface. Using a **directed evolution** approach, proteins were evolved to bind the Thomsen-Friedenreich (TF) antigen, a tumor cell surface disaccharide linked to cancer survival and progression. A randomly generated protein library was sampled to identify molecules that bind the TF antigen, and lead candidates were further engineered by site-directed mutagenesis, oligomerization, and modification with fluorescent handles to fine tune desired properties towards.

These orthogonal approaches, rational design and directed evolution, are incredibly powerful tools in the engineering of biomolecules to combat disease at the cell surface interface. Both are poised to provide insights into molecular determinants of infection, generate compounds that prevent disease, and increase public health worldwide. The Kizer lab will continue to leverage these approaches in the Chemistry Department at Brown University, tackling new targets and interactions involved in human health and disease.