

College of Liberal Arts and Sciences
Spring 2021 Chemistry Seminar Series
Friday, April 30th

Zachary Hill, PhD
Co-Founder and Chief Scientific Officer
Soteria Biotherapeutics

Generation and Application of Novel Chemically Induced Dimerization Domains

Abstract:

Chemically induced dimerizers (CIDs) allow for temporal control of biological processes through the addition of a small-molecule dimerizing agent. CIDs have proven to be invaluable tools for studying biology, controlling synthetic biological circuits, and most recently as safety switches for cell therapies. Unfortunately, the classical FKBP/FRB CID system utilizes the small molecule rapamycin, which is both toxic and immunosuppressant, making it undesirable for use with cell therapies. Orthogonal “rapalogs” show reduced toxicity, but have undesirable PK properties, greatly reducing their utility in regulating cell therapies. Several plant-based CID systems have been developed, but the non-human nature of these proteins results in immunogenicity issues if incorporated into a cell therapy. For applications of CIDs in therapeutics to reach their full potential, it is critical that new human-protein-based CIDs be developed that utilize small molecules with drug-like properties. I will present our development of a general strategy to generate CIDs from existing human-protein/small-molecule complexes and protein diversity libraries. Using this technique we have generated novel human-based CIDs and applied them to regulating a number of therapeutic applications. In addition to therapeutic applications we believe that our general strategy of CID development will lead to the creation of new orthogonal tools to enable synthetic and cellular biologists.

Bio:

Zachary Hill, PhD, is co-founder and Chief Scientific Officer of Soteria Biotherapeutics, an immuno-oncology company focused on developing a next generation of switchable bispecific t-cell engaging antibodies to treat cancer patients with solid tumors. Prior to founding Soteria, Zach was a postdoctoral fellow in the laboratory of Professor Jim Wells at the University of California San Francisco. While at UCSF, Zach was a Helen Hay Whitney Fellow, as well as the recipient of a NIH K99/R00 Transition Award from the NCI. Zach received his PhD in Organic Chemistry from the University of Washington, where he worked under the direction of Professor Dustin Maly on the development of bivalent inhibitors of protein kinases. Zach’s scientific interests sit at the interface of protein engineering and small molecules, with an emphasis on developing novel therapeutics.