Barth Lab EPFL (SV / IBI) / Ludwig Institute for Cancer Research

PhD project. Engineering powerful proteins with novel functions for synthetic cell biology and therapeutic applications

Protein design has made tremendous progress in recent years and is becoming central to synthetic biology applications including cell engineering approaches. For example, engineered proteins with customized signaling responses to disease-associated molecules provide promising and powerful new therapeutic agents for cancer immunotherapy, regenerative medicine and autoimmune disorders.

Our lab is developing and applying computational-experimental protein design approaches for engineering proteins with a wide range of novel functions, including chemosensors, mechanosensors, signaling switches and chemogenetic probes. The technologies have been validated on several proof of concepts (e.g. Feng et al., *Nat Chem Biol* 2017; Arber et al., *Curr Opin Biotech* 2017; Keri et al., *Curr Opin Struct Biol* 2018; Young et al., *PNAS* 2018; Chen et al., *Nat Chem Biol* 2020*; Yin et al., Nature* 2020). Using these approaches, we now aim at designing innovative and powerful protein nanomachines towards building synthetic living cells or enhancing the anti-tumor functions of engineered immune cells in cancer immunotherapies.

Specific projects typically involve some aspects of computational protein modeling and design using the techniques developed in the lab complemented by the directed evolution of desired protein functions and validation of engineered cells using a variety of cell biology approaches. Collaboration with laboratories at the CHUV/UniL/Ludwig Institute for Cancer Research (e.g. Caroline Arber, George Coukos) are in place for testing engineered molecules and cells in mouse xenograft models before potential translation to the clinic. Marrying empirical and computational protein engineering approaches has the unique potential to design a broad spectrum of cellular functions for engineering powerful cells with novel synthetic or sustained anti-tumor responses.