**Protein Binding Therapeutic/Diagnostic RFA**

Since their first description over 50 years ago, protein targeting agents, most commonly monoclonal antibodies, have revolutionized the treatment of multiple different diseases including cancer. These entities have exquisite sensitivity and specificity for binding targets, which can be exploited by use of the naked antibody or delivery of a payload. Additionally, investigators have used the binding moieties of antibodies to generate single chain variable fragments that are critical to the binding of chimeric antigen receptor-modified T cells. However, despite their promise there are challenges with the use of antibody technology therapeutically. Antibodies are generated in animals and require the model organism to generate the reagent. This limits the ability to broadly generate new targets. Antibodies poorly penetrate into certain regions of the body due to their size, and the presence of the Fc portion of the antibody can lead to off target toxicities with antibody therapy.

Over the past decade, new approaches to generate protein binding entities have been described and characterized. These entities utilize Ig or non-Ig scaffolds to generate domains that can bind to surface structures via display technologies. Additionally, new computational approaches are available to characterize the surface of cells to identify potential therapeutic targets. Finally, powerful software based on recent advances in machine learning has been developed to model the interactions between protein binders and targets that can be used to enhance the development of protein-binding therapeutics.

Recently, we created a new shared resource that provides access to protein binding technology to investigators focusing on developing novel cancer therapy targets. This resource can assist investigators in the development of protein binding reagents and the characterization of tumor targets amenable to protein binding therapeutics. As part of the development of this resource, we are initiating an RFA for proposals to use this shared resource. This RFA will cover the following types of project:

1. Development of a protein therapeutic against a previously vetted cancer target
2. Characterization of tumor targets in pancreatic or breast cancer for protein-based therapeutics
3. Assistance in the development of entities that can be used to by T cells to target tumor cells

This RFA will utilize the standard Innovation Award process and provide up to $100,000 of grant funding per year for 2 years with the opportunity for a third year of funding for promising proposals that could lead to a therapeutic. All proposals must have a collaborative interaction between research work performed in the PIs laboratory and the use of the shared resource. The work in the SR could include target identification, protein engineering or enhancement of the function of current protein binders/mAb.