Award ID:
RP100612

Project Title:
Molecular Engineering and Preclinical Evaluation of High Potency
Therapeutic Antibodies for the Treatment of Cancer

Award Mechanism:
High Impact/High Risk

Principal Investigator:
Georgiou, George

Entity:
The University of Texas at Austin

Lay Summary:

Antibody therapeutics such as rituximab (Rituxan, anti-CD20), trastuzumab (Herceptin, anti-Her2/neu), cetixumab/pantitumumab (Erbitux /Vectibix, anti-EGFR) have revolutionized cancer treatment. While each antibody therapeutic promotes the elimination of cancer cells by various routes, they all share a common and critical mechanism of clinical significance that relies on the recruitment of immune cells to attack and kill the tumor, a process termed antibody dependent cell cytotoxicity (ADCC). This process depends on the recognition of the anti-cancer antibodies by protein receptors on the immune cells. There are two kinds of such antibody receptors: "activating receptors" that turn-on the tumor cell killing machinery of immune cells and "inhibitory" that suppress tumor cell killing. Because the existing antibodies bind to both the activating and inhibitory receptors on immune cells, they are unable to unleash their full cancer cell killing potential. The Georgiou lab has developed engineered antibodies that only engage the activating receptors on immune cells and demonstrated that these antibodies now display novel and very promising mechanisms of action in the killing of breast cancer cells. Importantly, their engineered antibodies can be produced inexpensively in bacterial cells. The objectives of this grant are: (i) to further fine-tune the potency of the engineered antibodies and (ii) to evaluate their efficacy in tumor killing in animal models having a human-like immune system. These studies will open the way for the subsequent deployment of engineered antibodies in the clinic.