



CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP140664

Project Title:
Development of Therapeutic Antibodies Having Both Fc[gamma] and Fc[Alpha] Effector Functions and Displaying Potent Cancer Cell Killing

Award Mechanism:
High Impact/High Risk

Principal Investigator:
Georgiou, George

Entity:
The University of Texas at Austin

Lay Summary:

Antibody therapeutics constitute the most significant advance in clinical oncology of the last 20 years. Antibodies are proteins that are normally produced by the immune system but can also be made by cells in bioreactors. They are Y shaped molecules in which the two "ends" of the Y molecule bind to targets on the surface of cancer cells. The "stem" region of the molecule then serves to recruit white blood (immune) cells that kill the antibody-bound cancer cell. Extensive clinical data has demonstrated that the ability of antibodies to recruit white blood cells is very important for cancer therapy. Scientists have developed ways to engineer the "stem" region of the Y-shaped antibody molecule for improved recruitment of white blood cells and hence, better cancer clearance. In fact, one approved cancer antibody therapeutic and more than 15 antibody drugs in advanced clinical trials have been engineered in this manner. The two most abundant types of antibodies in humans are called IgG and IgA. All antibody therapeutics developed so far, are of the IgG type which is much easier to manufacture and which is able to recruit a wide variety of white blood cells. However, some kinds of white blood cells, such as neutrophils, the most abundant white blood cells, are recruited onto tumors much more efficiently by IgA-type antibodies than by IgG-type antibodies. We recognize that the ability to recruit to tumors white blood cells that cannot be engaged by IgG type antibodies can be very important for effective therapy. We thus engineered a completely novel molecule, we call IgGA, that combines the favorable therapeutic properties of both IgG and IgA type antibodies. IgGA is remarkably effective in killing cancer cells in the test tube. The proposed studies are now aimed to rigorously evaluate this novel antibody molecule in animal models of cancer and pave the way for clinical development.