



CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP160827

Project Title:
A platform technology for the isolation of anti-cancer monoclonal antibodies from chickens

Award Mechanism:
High Impact/High Risk

Principal Investigator:
Chen, Zhilei

Entity:
Texas A&M University System Health Science Center

Lay Summary:

Antibody-based therapy has transformed modern cancer treatment. However, to realize the full potential of antibodies in the fight against cancer, new and better cancer-cell-specific antibodies are urgently needed. All current therapeutic antibodies are derived from murine host. Mouse and human are both mammals and many of our proteins share high homology. Homologous regions likely play important cellular functions and thus are preserved through evolution. Hence, homologous regions on a cancer receptor are potentially good targets for cancer therapy. However, animals cannot generate antibodies against proteins of their own (a.k.a. "anti-self"). Consequently, it is not possible to obtain murine antibodies targeting highly homologous regions from a human protein. Chickens diverged from mammals about 300 million years ago, making chickens far better immune hosts for therapeutic antibody engineering than any mammal. However, currently there is no facile technology to isolate target-specific chicken monoclonal antibody. The current project aims to develop a novel technology to isolate chicken monoclonal antibody targeting human cell surface cancer receptor. Using human hCD20 as our model cancer receptor, we will first elicit chicken polyclonal antibodies using a recently developed antibody-guided immunization strategy. B-cells from immunized animals will be harvested and a paired heavy and light chain single chain antibody (scFv) library will be generated and displayed on mammalian cells. These cells will subsequently undergo iterative rounds of negative-positive selection to enrich hCD20-specific scFv. Finally, selected scFvs will be converted to chimeric human antibodies and their ability to kill hCD20+ cancerous B cells will be evaluated. Successful completion of this study will not only result in a facile technology for engineering chicken antibody against cancer receptors, but also a set of novel anti-hCD20 antibodies for treating B-cell lymphoma.