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The age of rational antigen design: Deceptive imprinting and immune refocusing as a blueprint for future vaccines, immunobiotics and immunotheranostics

Over the last 200 years, the use of vaccines have been one of the mainstays of preventative medicine and public health and has proven to be one of the most successful and cost-effective medical interventions ever. Despite these great advances to human and animal health, the use of native-like antigens that has enabled us to control many important pathogens has failed in the development of new vaccines against pathogens that stimulate sub-optimal immune responses. The remaining large list of human and major animal disease-causing microbes is inherently resistant to current vaccine technologies and the founding basic immune and vaccine principles (Jenner-1796 and Pasteur-1885) upon which they were based. The selected genetic instability of the pathogen leading to antigenic variation, coupled with non-protective immunodominance stands as one of the major obstacles in vaccine design today. The immune defense system of the host operates by surveying the "antigenic space" (relative foreignness) through shapes and linear sequences of chemical information. It appears that microbial pathogens for which we have poor or no vaccines have evolved to exploit shortcomings in our immune systems by coupling immunodominance with epitopes that are unlinked to the inhibition of infection or replication. These pathogens take advantage of the propensity of the immune system to respond to a small number of immunodominant epitopes and, due to antigenic hierarchy, ignore subdominant epitopes which could stimulate improve protective immunity. Thus, some pathogens such as HIV-1 and influenza stimulate strain-specific immunity, dengue and ebola stimulate disease-enhancing immunity, and most bacterial pathogens stimulate immune responses lacking anti-bacterial activities.

Recently ,significant, paradigm-shifting discoveries of a new law and first principle of immunity ("Deceptive Imprinting") and vaccination (Immune Refocusing Technology, IRT) have been made. Work in the area of Deceptive Imprinting suggests that these strain-specific or nonprotective epitopes are preferentially recognized due to mechanisms that are deeply ingrained within our B and T cell repertoire and act as decoys to prevent protective immunity. IRT attempts to design improved antigens that re-assort the antigenic and immunological hierarchies by redirecting immunity to protective epitopes that were previously subdominant. IRT utilizes a multi-faceted algorithm to identify and selectively dampen the decoy epitopes while preserving the structure and formation of important conformational epitopes. The methods for characterizing the decoy epitopes are continually being improved through the fields of computational biology, bioinformatics, structural biology, theoretical/statistical physics, immunology, microbiology, immunogenetics and comparative medicine. The directed goals of these efforts are to forge new pathways for discovery in developing novel approaches for infectious diseases, cancer, auto-immune, idiopathic diseases and allergic conditions.

Biography

Gregory J. Tobin, PhD. is Chief Scientific Officer and VP of Biological Mimetics, Inc. (BMI). Dr. Tobin is dedicated to developing novel vaccines against "vaccine-resistant" pathogens by investigating mechanisms of host immunity and pathogen evolution. Dr Tobin has developed the Immune Refocusing Technology (IRT) to design novel vaccines that stimulate improved cross-strain and protective immune responses. IRT uses a multifaceted algorithm to identify and dampen strain-restricted or non-protective epitopes (decotopes). The resulting antigens stimulate improved immune responses directed to previously subdominant epitopes that convey enhanced protective or broadened cross-strain immunity. Through a collaborative network of academic, institutional, and industrial scientists, Dr. Tobin designs and oversees multiple projects to increase our understanding of how pathogens evade immune pressure and to develop improved vaccines against human and veterinary pathogens. Dr. Tobin continues to investigate the design of broadened vaccines against influenza, HIV-1, rhinoviruses, Dengue Virus, S. mutans, FMDV, ISAV, PRRS, and other viral and bacterial agents. Prior to joining BMI in 1999, Dr. Tobin was a Senior Scientist and Group Leader (Gene Expression and Regulation Group) for SAIC-Frederick at the National Cancer Institute. While at the NCI, Dr. Tobin led projects related to development of virus-like particle (VLP) based vaccines for HIV-1, optimization of recombinant protein expression, development of animal models for AIDS and cancer, and investigations into the pathobiology and molecular mechanisms of HIV-1, bovine immunodeficiency virus (BIV) and visna virus.