

# IMMUNODOMINANCE, DECEPTIVE IMPRINTING AND IMMUNE REFOCUSING TECHNOLOGY: BLUE PRINT FOR DERIVING NEXT GENERATION BIOLOGICALS FOR DIFFICULT MICROBES

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Over the last 250 years, the use of vaccines, a mainstay of preventative medicine and public health mainly in the infectious diseases area has proven to be one of the most successful and cost-effective medical interventions ever discovered. Despite these great advances to human and animal health of the past 5 decades; the basic immunologic principals and technology does not work for the most part against the many remaining pathogens and many cancers of humans and animals. This is mainly due to a combination of evolved host evading strategies of both infectious pathogens and cancer cells and the yet unappreciated aleatory characteristics inherent within the vertebrate immune system. These combined make them inherently more capable of outsmarting the host defense systems. Phenomena such as strain- and serotype-restricted immunity, antigenic variation/mutation, poor anamnestic memory, disease-enhancement and incomplete immunity, all are major gaps in our understanding of the complex host evasion mechanisms that have evolved. Deceptive imprinting is at the heart of a new understanding of how the hosts response to mutable infectious pathogens and cancer cells to create a molecular diversion (decoy) at the level of both the innate and acquired immune host defense systems, much like how metallic chaff would confuse a radar system trying to locate a missile or plane. On an immunologic level, immunodominance, repertoire sculpting and antigenic variation are coupled such that host immune responses are directed to more immunodominant and non-protective structures resulting non-protective B and T cell immune responses. To circumvent this host evading mechanism, we have developed a first generation technology called immune refocusing that has been designed specifically to reorder the non-protective immunodominance by identifying/mapping the decoy epitopes and molecularly removing or attenuating it thus redirecting the host immune system to the more protective regions of the microbe. This lecture will bring together those aspects learned from studying infectious diseases pathogens in new paradigm shifting first principals of deceptive imprinting and immunology and those of cancer biology in hopes of developing new insights from querying pathogen genomes through pressure point technology and application of the technology of immune refocusing. These paradigm shifting scientific insights have opened up fresh new approaches to technical advancement and the development of new antigens that can be used for vaccines and deriving new monoclonal antibodies toward inducing improved and broader protective immunity for both infectious diseases and cancer.

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