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ProtEx™ technology as a novel and practical alternative to gene therapy for immunomodulation

Gene therapy through the introduction of recombinant DNA/RNA into the cell holds great potential as a therapeutic approach for the treatment of various immune-based disorders. Despite this great promise, there remain many barriers to the routine application of gene therapy to the clinic. Inasmuch as immune decisions are made through receptor/ligand interactions on the cell surface in a relatively short period of time (minutes to hours), this raises the question whether selected goals of gene therapy for immunomodulation can be achieved by the transient display of exogenous immunological ligands on the cell surface. Towards this end, we developed a novel approach designated as ProtEx™ taking advantage of the high affinity interaction (Kd=10-15 M) between streptavidin and biotin. Once formed, this complex dissociates very slowly, allowing long-term display of proteins chimeric with streptavidin on biotinylated cell membrane. ProtEx™ involves the generation of chimeric proteins with core streptavidin, biotinylation of cells under physiological conditions, and engineering of biotinylated cells, tissues or organs with chimeric proteins. In testing this concept, we generated several recombinant proteins with well-defined immune functions. These proteins were displayed on the surface of primary and established cell lines, tissues, and organs under physiological conditions within 2 hrs without detectable toxicity. The immunomodulatory efficacy of ProtEx™ technology was demonstrated in various experimental models of transplantation, diabetes, and therapeutic cancer vaccines. Rapid and durable cell-surface display of functional proteins offers an entirely new means of immunomodulation with significant potential for the development of prophylactic and therapeutic vaccines against infections and cancer.

Biography

Dr. Shirwan is Dr. Michael and Joan Hamilton Endowed Chair in Autoimmune Disease, Professor of Microbiology and Immunology, the Director of the Molecular Immunomodulation Program at the Institute for Cellular Therapeutics, and member of James Brown Cancer Center, University of Louisville, KY. Dr. Shirwan is also the Founder and CSO of ApoVax, Inc., Louisville, KY. Dr. Shirwan is widely published and, lectured at numerous national/international conferences, served on study sections for various federal and non-profit funding agencies, and is on the editorial boards of 12 scientific journals. He is member of several national and international societies and recipient of various awards.

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