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SA-4-1BBL as a novel adjuvant for the development of therapeutic vaccines

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Protein-based subunit vaccines against cancer and infections are attractive because of their safety profile as well as rapid, cost-effective, and large-scale production. However, they are weekly immunogenic and their immunogenicity is further compromised by various immune evasion mechanisms employed by cancer and chronic infections. Importantly, accumulating evidence suggests that both prophylactic and therapeutic vaccines may benefit from their ability in modulating all the three arms of the immune system; innate, adaptive, and regulatory. In this context, the efficacy of subunit vaccines may require formulations that include adjuvants having pleiotropic effects on various cells of the immune system. We have recently generated a novel form the 4-1BBL costimulatory molecule, SA-4-1BBL, that has robust immune stimulatory activity in soluble form and affects selected cells of innate, adaptive, and regulatory immunity. As the adjuvant component of tumor associated antigens based subunit vaccines, SA-4-1BBL was effective in eradicating established tumors in mouse models. The therapeutic efficacy of the vaccine was realized by the pleiotropic effects of SA-4-1BBL on various cells of the immune system, resulting in a net increase in CD8+ T effector (Teff) cells over CD4+CD25+FoxP3+ T regulatory (Treg) cells, which serve as a major barrier for the efficacy of cancer vaccines. Importantly, 4-1BBL not only overcame the inhibitory function of Treg cells, but also blocked the conversion of Teff cells into inducted Treg cells by the tumor. These studies provide a strong rationale for further developing SA-4-1BBL costimulatory molecule as adjuvant for the development of prophylactic/therapeutic vaccines.

Biography

Haval Shirwan is Dr. Michael and Joan Hamilton Endowed Chair in Autoimmune Disease, Professor of Microbiology and Immunology, director of Molecular Immunomodulation Program at the Institute for Cellular Therapeutics. He conducted his graduate studies at the University of California in Santa Barbara, CA, and postdoctoral studies at California Institute of Technology in Pasadena, CA. He joined the University of Louisville in 1998 after holding academic appointments at various institutions in the United States. His research focuses on the modulation of immune system for the treatment of immune-based diseases with particular focus on type 1 diabetes, transplantation, and vaccines. He is an inventor on 16 worldwide patens, widely published, lectured at numerous national/international conferences, served on study sections for various federal and non-profit funding agencies, and is on the editorial board of 16 scientific journals. He is member of several national and international societies and recipient of various awards.

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