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Exploiting synergy between TNFR and TLR4 signaling for the development of adjuvant systems

Protein-based subunit vaccines against cancer and infections are attractive because of their safety as well as rapid, cost-effective, and large-scale production. However, they are weakly immunogenic and their immunogenicity is further compromised by various immune evasion mechanisms employed by cancer and chronic infections. Accumulating evidence suggest that prophylactic and therapeutic vaccines may benefit from adjuvants modulating innate, adaptive, and regulatory arms of the immune system. In this context, subunit vaccines efficacy 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 co-stimulatory molecule, SA-4-1BBL, having pleiotropic effects on various cells of the immune system. As adjuvant component of subunit-based vaccines, SA-4-1BBL was effective in eradicating tumors in preclinical models. Therapeutic efficacy was associated with a robust increase in T effectors and down-regulation of various immune evasion mechanisms. SA-4-1BBL has recently been used in combination with a TLR4 agonist as adjuvant component of tumor associated antigen-based subunit vaccine in cervical and lung cancer preclinical models with robust therapeutic efficacy. These studies provide a strong rationale for using SA-4-1BBL as a platform to design adjuvant systems for the development of 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 Post-doctoral 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 has more than 100 peer-reviewed papers, an inventor on 16 worldwide patents, organized and lectured at numerous national/international conferences, and served on study sections for national and international federal and nonfederal funding agencies. He is the Executive Editor for the *Journal of Clinical and Cellular Immunology* and on the editorial boards of a dozen of scientific journals. He is member of several national and international societies and recipient of various awards.

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