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Vaccine therapy for lymphomas: From bench to bedside and back

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Follicular lymphoma (FL) is the most common low-grade B-cell lymphoma, comprising 22% of all non-Hodgkin's lymphoma cases worldwide. Despite advances in therapy that usually achieve complete remission initially, most patients with advanced stage FL eventually relapse and die of their disease, so novel therapeutic strategies are needed to eliminate minimal residual disease. The clonal tumor immunoglobulin expressed on the surface of malignant B cells, termed idiotype (Id), has been found to be safe and immunogenic as a tumor-specific antigen for therapeutic vaccination in Phase I/II trials against FL and other B-cell malignancies. In a recently completed randomized, double-blind, controlled, multicenter phase III clinical trial, vaccination with patient-specific tumor-derived Id protein significantly prolonged disease-free survival by 14 months, compared with the control group that received a non-specific immune stimulant, providing the first positive result for a Phase III vaccine trial against lymphoma. To further improve the efficacy of therapeutic vaccines in follicular lymphoma, my laboratory is now focused on defining the dominant immunosuppressive mechanisms in the tumor microenvironment. We have identified regulatory T cells and PD-1/PD-ligand pathway as important negative regulatory pathways that inhibit T-cell function in follicular lymphoma. The relative contributions of these inhibitory processes will be reviewed and novel approaches to enhance the efficacy of therapeutic vaccination strategies in human lymphomas will be discussed.

Biography

Dr. Sattva Neelapu completed his clinical fellowship in Medical Oncology and postdoctoral fellowship in tumor immunology and immunotherapy at the National Cancer Institute, National Institutes of Health, Bethesda, MD. In 2004, he joined the faculty of the Department of Lymphoma and Myeloma at The University of Texas M. D. Anderson Cancer Center, Houston, TX and has continued his clinical and laboratory research in immunotherapy and tumor immunology. He has conducted numerous therapeutic cancer vaccine clinical trials in patients with lymphoma and myeloma. His laboratory is now focused on characterization of immunoregulatory mechanisms in the tumor microenvironment in patients with lymphoma.