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Efficacy of combination mucosal vaccination and immunotherapy strategies for the treatment of HPV-associated cancers

Virology

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High-risk human papillomaviruses (most frequently HPV-16) are sexually transmitted infections responsible for preand cancerous lesions of cervix as well as a high percentage of anal, vaginal, vulvar, penile and oropharyngeal cancers. Effective vaccines based on the HPV core protein L1 currently approved for prevention of new HPV infections in young adults are ineffective to treat existing infections/lesions which predominantly express the viral E6 and E7 oncogenes but not L1. Therapeutic vaccines based on the E6 and E7 tumor antigens are urgently needed, especially for people in the developing world to combat HPV diseases. We discovered specific HPV-16 E6 and E7 peptides for which memory T cell immunity is associated with recurrence-free survival in women treated for HPV pre-cancerous cervical lesions. In mouse model studies, mucosal intranasal immunization employing these E6 and E7 peptides admixed with novel adjuvants induced HPV-specific systemic and mucosal effector CD4/CD8 T cell responses that prevented HPV+ tumor formation. Therapeutic mucosal intranasal vaccination with these peptides in combination with adjuvants significantly reduced HPV tumor growth in mice affording long term survival advantage. Furthermore, combination of intranasal vaccination with the E6 and E7 peptides with immune check point blockade antibody treatmentresulted in significant tumor regression leading to eradication. These data support future clinicaltesting of combination vaccine immunotherapy strategies for effective treatment and possibly eradication of preand cancerous HPV lesions.

Biography

Jagan Sastry is a professor in the departments of Immunology and Veterinary Sciences at The University of Texas MD Anderson Cancer Center, Houston, TX. His research over the past 25+ years, supported by NIH, industrial and private funding in the broad areas of viral oncology and immunology, focuses on understanding the biology, pathology, immunology and genetics of HPV-associated cancers and HIV-induced AIDS. The overall goals are to develop vaccines and therapeutics for prediction, treatment and prevention. He actively mentors graduate/undergraduate students and post-doctoral fellows as well as serves on NIH study sections and editorial boards of scientific journals.

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