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Intramuscular vaccination targeting mucosal tumor draining lymph node enhances integrins-mediated Cd8+ T Cell infiltration to control mucosal tumor growth

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Objective: Mucosal immunization is suggested to be crucial at for controlling tumors in the mucosal region; however, therapeutic DNA vaccination with electroporation in various mucosal sites has yet to become clinically adaptable. Since tumor-draining lymph nodes (tdLNs) have been suggested as immune-educated sites that can be utilized to mount a potent antitumor immune response, we examined whether intramuscular DNA vaccination with electroporation at sites that target the mucosal tdLNs could elicit mucosal immune response to restrict tumor growth.

Methods: The efficacy and mechanism of intramuscular administration of a therapeutic DNA vaccine with electroporation at different sites was examined by lymphocyte analysis, tumor growth, mouse survival, as well as integrin expression, in mice bearing orthotopic HPV16 E6/E7+ syngeneic TC-1 tumors in various mucosal areas.

Results: While provoking comparable systemic CD8+ T cell responses, intramuscular hind leg vaccination generated stronger responses in cervicovaginal-draining LNs to control cervicovaginal tumors, whereas intramuscular front leg vaccination generated stronger responses in oral-draining LNs to control buccal tumors. Surgical removal of tdLNs abolished the antitumor effects of therapeutic vaccination. Mucosal-tdLN-targeted intramuscular vaccination induced the expression of mucosal-homing integrins LPAM-1 and CD49a by tumor-specific CD8+ T cells in the tdLNs. Inhibition of these integrins abolished the therapeutic effects of vaccination and the infiltration of tumor-specific CD8+ T cells into mucosal tumors.

Conclusions: Our findings demonstrate that tumor draining lymph nodetdLNs -targeted intramuscular immunization can effectively control mucosal tumors, which represents a readily adaptable strategy for treating mucosal cancers in humans.

Biography

Chien-Fu Hung is an associate professor of pathology and oncology and a professor of gynecology and obstetrics at the Johns Hopkins University School of Medicine. He is a member of the Johns Hopkins Kimmel Cancer Center. His research focuses on the prevention and treatment of cervical and ovarian cancers. His team is currently using an ascitogenic ovarian/peritoneal tumor model to investigate DNA vaccine strategies encoding ovarian tumor antigens identified by microarray and SAGE. He earned his Ph.D. in molecular biology from the University of Illinois. He completed a fellowship in pharmacology at the University of Pennsylvania and a fellowship in pathology at the Johns Hopkins University.

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