Diagnostics and Treatments for High-Risk Human Papillomavirus (HR HPV) Infections

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Technology description

Understanding cellular pathways affected by HR HPV

Technology Overview

HR HPV is required for cervical and other anogenital cancer development. Although there are effective vaccines to protect against certain HR HPV types, they are not therapeutic. This leaves adults, adolescents, and children previously exposed to HR HPV at risk for future disease, morbidity, and mortality, regardless of their vaccination status. HR HPV type16 (HPV 16) encodes two viral oncoproteins (16E6 and 16E7), which bind to host cell proteins to dysregulate and disrupt apoptosis, senescence, growth and differentiation in infected keratinocytes. These pathways are important for the viral life cycle, which depends upon both epithelial cell differentiation and continued cell cycling, and for cancer development. The Katzenellenbogen lab is interested in how HPV uncouples cellular differentiation from cell cycle arrest in host cells during HPV infection.

Dr. Katzenellenbogen is also studying mechanisms by which HR HPV activates telomerase, an enzyme that is universally expressed in HPV-associated cancers. Recent work in the Katzenellenbogen lab has focused on the interaction of 16E6 with the cellular protein NFX1-123. Together, these two proteins post-transcriptionally increase expression of the catalytic subunit of telomerase, hTERT. NFX1-123 interacts with and stabilizes hTERT mRNA, leading to increased telomerase activity and the avoidance of cellular senescence. The lab has also shown that 16E6 and NFX1-123 collaboratively increase the growth and differentiation master regulator, Notch1. These results led to a model in which 16E6, NFX1-123, and Notch1 collaborate to establish a “differentiating with dividing” phenotype, which is an ideal host cell environment for a long-lived and productive HPV infection.

Dr. Katzenellenbogen is currently evaluating the effects of disrupting the E6-NFX1-123 interaction. Future studies will include evaluating the normal cellular function and range of expression of NFX1-123 in healthy women, and changes in NFX1-123 expression over time and during cancer progression. HPV can serve as a model for universal pathways in cancer development and can help define the critical steps in oncogenesis that might serve as targets for screening and treatment. Dr. Katzenellenbogen would be interested in industry collaborations aimed at developing potential diagnostics or parallel predictive risk tools for HPV-associated and other cancers.

Institution

Seattle Children's Research Institute

Inventors

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