CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP120340

Project Title:
Arginine Methylation Link to HPV-16-Induced Cervical Cancer

Award Mechanism:
High Impact/High Risk

Principal Investigator:
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Entity:
The University of Texas Southwestern Medical Center

Lay Summary:

Human papillomavirus (HPV)-induced cervical cancer is one of the leading causes of death in women worldwide. In addition, HPV is causally associated with head-and-neck and oral cancers that have recently emerged as sexually transmitted diseases. Nevertheless, only a dozen HPVs are linked to cancer from over 100 types of HPVs so far identified. Many “low-risk” HPVs only induce benign warts that rarely, if ever, progress into cancer. Accordingly, it is important to understand why only “high-risk” HPVs, such as HPV-16 and HPV-18, cause cervical cancer, whereas low-risk HPVs, including HPV-6 and HPV-11, induce primarily warts. Over the past few years, prophylactic vaccines that “prevent” four major types of genital HPV infection (HPV-6, HPV-11, HPV-16 and HPV-18) have become available and are recommended for vaccination of girls over nine years old. However, “therapeutic” vaccines that can “cure” HPV infection are still not available. This barrier lies in our lack of knowledge about the molecular targets and gene control mechanisms unique to cancer-causing HPVs. To unravel the functional differences between high-risk and low-risk HPVs, we have developed screening assays to examine whether HPV-produced proteins may exhibit “structural” features uniquely found in “high-risk”, but not “low-risk”, viral proteins. Indeed, we found a chemical group (called methylation) is linked to a basic amino acid (arginine) uniquely present in HPV-16 E6 protein (16E6), but not in HPV-11 E6. This finding indicates that arginine methylation may increase the cancer-inducing activity of 16E6 found in over 50% of cervical cancer patients. Our goal here is to establish the functional role of 16E6 methylation by identifying cellular proteins that recognize this chemical modification. If successful, we will be able to use this mark for future screening of HPV-induced cervical cancer and facilitate the development of drug inhibitors against HPV propagation.