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*2005 Program
New Investigator (3-year project)*

Project Title: Association of Smoking, HPV infection and Aberrant Methylation in Cervical Cancer Carcinogenesis

Project Summary: Cervical cancer is a major public health issue among women world-wide, including women in the state of Florida. Over the past decade, researchers have identified that an infection of the cervix with Human Papillomavirus (HPV) will cause cervical cancer. However, most HPV infections are cleared by a woman's immune system and never cause any disease. Only a small number of HPV infections will cause changes to the cervical tissue that are detected by a Pap smear screen. It has been shown that smoking is a behavior that puts women with an HPV infection at a higher risk of cervical cancer compared to nonsmoking women that have an HPV infection. Women who smoke tend to have a harder time clearing the virus and have a greater risk of more advanced cervical disease. There are many ways that tobacco can cause damage to the cervix that would allow for the virus to remain active in the cervical cells. One proposed pathway of smoking damage is changing the control of gene expression and even turning important genes off. The expression of a gene is turned off when a methyl group is added to a specific DNA base, known as DNA methylation. There is little known about this pathway of gene silencing through DNA methylation among smokers as an HPV infection develops into cervical abnormalities which can lead to cancer of the cervix among women.

The project goals are to increase the understanding of the relationship between smoking and DNA methylation among women with cervical lesions or cancer and the possibility of using DNA methylation changes as a new test for women at risk of developing cervical cancer. The long-term goal of this research is to help develop a strong cervical cancer prevention message encouraging women to quit smoking, especially when DNA methylation changes are found. The aims of this study are to 1) determine the relationship between DNA methylation of six genes and risk of cervical disease, 2) to further understand how smoking influences this relationship, and 3) to compare methylation changes found in cervical cells to DNA found in blood. Women that are seeing a health care provider after having an abnormal Pap smear test will be asked to participate in this study, with an estimated 260 women participating each year. All women will fill out a questionnaire, donate blood and will have a Pap smear sample taken for research. This study will measure methylation of six genes and compare the level by smoking behavior and the diagnosis of cervical abnormalities. This study will provide important information about the use of DNA methylation as a possible new test for the early detection of cervical cancer, especially among women who smoke.