Spectral cytopathology: Towards relating spectroscopic changes with their biological source

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Efforts in the Laboratory for Spectral Diagnosis at Northeastern University (Boston, MA USA) have focused upon the diagnosis of disease by analyzing exfoliated cells using infrared micro-spectroscopy and unsupervised multivariate methods of analysis. This approach, coined Spectral Cytopathology or SCP, has been applied successfully on cells exfoliated from several tissue origins including the cervix, oral cavity, and nasopharynx. For each case, spectroscopic differences were detected between cells from normal samples and morphologically normal looking cells from samples diagnosed with disease. The cause of these spectroscopic differences related to biochemical changes on the sub-cellular level has been of large interest in the pursuit of this project.

In the case of cervical cancer, infection with high-risk or oncogenic strains of human papillomavirus (HPV) is a critical step in cervical carcinogenesis and usually leads to the development of cervical intraepithelial lesions. A large scale study was launched in order to investigate if the spectral changes between normal and abnormal cervical samples were due to HPV infection. A total of 48 samples of exfoliated cervical cells collected during routine gynecological examinations were analyzed by SCP. The SCP results were placed in juxtaposition with the results from an HPV test in which a positive outcome indicated an infection with any of the 13 most common high-risk HPV strains (Digene Hybrid Capture II test). The sensitivity of SCP in this study was evaluated at 88% and specificity at 43%.

Although the HPV study allowed us to generally correlate the spectroscopic changes with HPV infection, it is still unknown to whether these changes are due to the presence of the virus itself or viral load (concentration), expression of viral proteins or viral products, or changes within the cells as the result of a combination of these. In order to explore these questions further, cells from an ovarian cancer cell line, SKOV-3, were cultured and subsequently transfected with green fluorescent protein plasmid, fixed, and analyzed by SCP. Spectroscopic changes observed between cells transfected with different concentrations of the plasmid would be analogous to infection with different numbers of viral copies of HPV (more viral copies indicates an active infection).