# *Spectral cytopathology: Observing biochemical changes within normal looking squamous cells of the oral cavity and cervical epithelium*

Jennifer M. Schubert[a], Kostas Papamarkakis[a], Benjamin Bird[a], Miloš Miljković[a], Kristi Bedrossian[b], Nora Laver[b], Max Diem[a]

[a] Laboratory for Spectral Diagnosis, Department of Chemistry and Chemical Biology, Northeastern University, 306 Huntington Avenue, Boston, MA USA
[b] Department of Pathology, Tufts Medical Center, 800 Washington Street, Boston, MA USA
E-mail: jmschubert@gmail.com

We present two benchmark studies in which individual oral and cervical exfoliated cells were classified with a high degree of sensitivity by analyzing infrared spectral signatures unique to anatomical region, hormonal influences, viral infection, and cancer. The methodology utilized, Fourier Transform Infrared Micro-Spectroscopy and Principal Component Analysis, is referred to as Spectral Cytopathology, SCP.

Squamous cells were employed in both studies. Oral SCP successfully differentiated squamous cells from the oral cavity according to anatomical region (i.e. tongue, gums, palate, cheeks, etc.). Cells with normal morphology, but collected from virally infected (herpes simplex virus) patients could clearly be distinguished from uninfected cells. Squamous cells with normal morphology, but from patients diagnosed with pre-cancer and cancer, and squamous carcinoma cells, generally showed spectra quite different from those of truly normal samples. The observation that morphologically normal cells from cancer patients exhibit abnormal spectra was interpreted in terms of "malignancy associated changes" (MACs), which indicate changes in cellular behavior even before morphological changes are observable.

Squamous cells from clinical cervical samples from women on hormonal contraceptives, which had a pathological diagnosis of normal or low grade dysplasia, were successfully correlated by SCP with their clinical diagnosis. SCP also detected abnormal spectral changes in samples with a normal clinical diagnosis, but who had a history of abnormal cervical cytology. The spectral changes observed in the morphologically normal looking cells from abnormal samples are most likely due to a human papillomavirus infection.

The limitations of conventional medical cytological methods are well-recognized and acknowledged within the pathology community. SCP manifests extensive potential as an accommodating tool for cytopathologists for the accurate and reproducible detection of cells in all states of disease, especially transitional and reactive states that are not diagnostic. There is serious potential, therefore, in the detection of initial biochemical variations by SCP, for the contribution of preventative diagnostics.

**References:**

K. Papamarkakis, B. Bird, J. M. Schubert, M. Miljković, R. Wein, K. Bedrossian, N. Laver, M. Diem, *Laboratory Investigation*, Submitted.

J. M. Schubert, B. Bird, K. Papamarkakis, M. Miljković, K. Bedrossian, N. Laver, M. Diem, *Laboratory Investigation*, Submitted.