Detection of abnormalities in squamous cells

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Screening for squamous cell carcinomas is routinely being carried out for the human cervix, the bladder and –increasingly– for the oral cavity. Standard cytological screening methods rely on visual inspection of slides of stained cells containing between 10^3 and 10^4 cells. Such visual inspection is time consuming, and relies on subjective interpretation of parameters such as nuclear-to-cytoplasmic (N/C) ratio, staining patterns and cell morphology. Consequently, the interobserver reproducibility and overall accuracy[1] of visual interpretation are as low as ca. 60 %.

We have previously reported spectral analyses of squamous cells to establish the sensitivity and reproducibility by infrared micro-spectroscopy of individual cells.[2,3] To this end, we have analyzed human oral mucosa (buccal) cells to establish the normal heterogeneity of squamous cell spectra.[2] Furthermore, we have established in an animal model that hormonal changes change the maturation of cervical cells, and that the degree of maturation can be followed spectroscopically.[3] More recently, we have shown that different cell types can be distinguished among exfoliated cells: we found that the urothelial cells lining the inside of the human bladder have distinctly different spectra than those of the squamous cells lining the distal urethra. Both these cell types constitute the majority of cells found in normal human urine, and are, therefore, amenable to a screening test for bladder cancer. Cancerous urothelial cells, obtained from a resected bladder specimen, show significantly different spectral patterns than normal urothelial cells.

Finally, for the interpretation of human cervical cells, we have collected about three thousand spectra of individual human (ecto-cervical) squamous cells. In contrast to the buccal cell samples, which nearly exclusively contain superficial squamous cells, the cervical samples contain variable fractions of less mature (parabasal and intermediate) squamous cells. The distribution of mature vs. immature cells in normal cervical cell exfoliates is hormone level dependent. Unsupervised multivariate analysis of the spectral patterns of individual cells was used to classify the observed spectral changes.

In addition to single cell infrared spectral and statistical analysis of squamous cells, we have collected important aspects of cell morphology, as well as the distribution of cellular components via confocal Raman micro-spectroscopy.

References

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[2] M.Romeo, B.Mohlenhoff and M.Diem "Infrared Micro-Spectroscopy of Human Cells: Causes for the Spectral Variance of Oral Mucosa (Buccal) Cells", (2006) *Vibrational Spectrosc.*, **42**, 9-14.

[3] M.Romeo, B.Mohlenhoff, M.Jennings and M.Diem, "Infrared micro-spectroscopic studies of epithelial cells", (2006) *Biochimica et Biophysica Acta*, **1758,** 915–922.