Quantitative Raman Imaging of Nucleic Acids and Tryptophan for Distinction of Normal Human Skin Cells and Tumorigenic Keratinocytes

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At present, tumor diagnostic imaging is commonly based on hematoxylin and eosin or immunohistochemical staining of biopsies, which requires tissue excision, fixation, and staining with exogenous marker molecules. Here, we report on label-free tumor imaging using confocal spontaneous Raman scattering microspectroscopy, which exploits the intrinsic vibrational contrast of endogenous biomolecular species. We present a chemically specific and quantitative approach to monitoring normal human skin cells (keratinocytes and fibroblasts) as well as the human HaCaT in vitro skin carcinogenesis model and the tumor-derived MET in vivo skin cancer progression model. Mapping the amplitudes of two spectrally well isolated Raman bands at 752 and 785 cm⁻¹ allowed for direct visualization of the distributions representative of tryptophan-rich proteins and nucleic acids, respectively, with subcellular spatial resolution (see Fig. 1).

Using these Raman markers, it was feasible to discriminate between normal human epidermal keratinocytes (NHEK) and dermal fibroblasts (NHDF) and to confine all tumorigenic cells from both the NHEK and NHDF. First evidence for the successful application of the proposed intracellular nucleic acid and tryptophan Raman signatures for skin cancer diagnosis was further demonstrated in an organotypic cutaneous squamous cell carcinomas model, allowing for the identification of tumor cells and their surrounding stroma in the tissue context [1].

References