Epigenetic studies of oral lichen planus as a model for inflammation-mediated cancer development via malignant reprogramming

Fazel N, Tepper C G, Izumiya Y, Murphy W J and Davari P
University of California, Davis, USA

Oral lichen planus (OLP) is an oral mucosal disease considered to be a pre-malignant condition with risk of malignant transformation to oral squamous cell carcinoma (SCC) at varying rates ranging from 0.8% to >5%. Studies of loss of heterozygosity and microsatellite instability indicate that OLP is molecularly distinct from oral dysplasias and SCC. The operating hypothesis for our studies is that tumors, such as SCC, arise through “malignant reprogramming” driven by a combination of both genetic and epigenetic changes. The primary goal of this pilot study is to identify key sites of aberrant epigenetic regulation in OLP by defining the entire repertoire of differentially-expressed genes and regulatory non-coding (ncRNAs) in OLP lesions. This is accomplished by performing state-of-the-art next-generation sequencing (NGS)-based whole transcriptome profiling (RNA-Seq) analyses of matched pairs of lesional and perilesional normal appearing tissue samples. The specimens were sectioned for RNA extraction, chromatin immunoprecipitation (ChIP), and immunohistological studies. Sequencing libraries prepared from the total RNA samples were sequenced on an Illumina HiSeq 2000 to yield ~30 million reads per sample, which will then be processed with our automated analysis pipeline. Subsequently, integrative bioinformatics was applied to define an OLP-specific gene expression signature, as well as application of gene set enrichment analysis to define potential overrepresentation of functional groups, including immune system and inflammatory pathway-related genes. Insight into the mechanistic basis engendering these expression changes was obtained by correlation with the occurrence of somatic mutations (variant analysis) and epigenetic changes, such as histone modifications. We anticipate that characterization of the latter will lead to the identification of the responsible histone-modifying enzymes, which can then be exploited as novel therapeutic targets.

Biography

Fazel N, MD, DDS, MAS, Associate Professor of Dermatology, completed her medical school training at the University of Michigan, Ann Arbor followed by her dermatology training at Henry Ford Health System in Detroit, Michigan. Prior to her medical training she completed her dentistry training at Northwestern University Dental School. She has a unique background with dual certification in dermatology and dentistry. She has a special interest in the medical management of oral mucous membrane disease and soft tissue pathology. Her background in dentistry provides for insight into the pathophysiology and treatment of aphthous ulcers, burning mouth syndrome, oral lichen planus, and oral vesiculobullous disease (e.g., pemphigus and pemphigoid). She is regarded as a leading expert in the field of oral mucosal disease by many colleagues who refer these difficult and challenging conditions to her.

nasim.fazel@ucdmc.ucdavis.edu

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