Differential expression of PD1 and PDL1 in oral potentially malignant lesions and oral squamous cell carcinoma: a pilot study

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Background

Programmed cell death protein 1 (PD-1, CD279) is a 50-55 kDa type I transmembrane receptor expressed by activated T and B cells, as well as subset of monocytes and dendritic cells (DCs). PD-1 and its ligands (PDL1, PDL2) are part of “checkpoint” immune recognition and peripheral tolerance system that emerged as a critical signaling pathway in cancer. PDL1 is expressed in various types of cancers and activation of PD1-PDL1 inhibits T-cell mediated cancer surveillance. Here we describe a quantitative, reproducible 2-color fluorescence-based protocol to determine the differential expression of PD1/PDL1 in oral biopsy specimens.

Methods

Histopathological samples with a diagnosis of hyperkeratosis (HK), OMPL (mild, moderate, severe dysplasia) and squamous cell carcinoma (OSCC) were selected from the archives of the Toronto Oral Pathology service, University of Toronto. FFPE sections were stained with monoclonal antibodies for PD1 and PDL1 (Abcam) and Alexa Fluor-labelled secondary antibodies allowing visualization of both proteins in the same section using a spinning disk confocal microscope (Quorum). PDL1 staining was assessed in basal/spinous layers of the epithelium while PD1 staining was assessed in inflammatory cells in tumor stroma/lamina propria. The mean fluorescent intensity (MFI) was quantified and normalized against background signal.

Results

Our results show a significant increase in PD1 expression in inflammatory cells in dysplasia and OSCC compared to hyperkeratosis. PDL1 expression in epithelial cells was significantly increased in OSCC but not in dysplasia or HK. The results suggest that PD1 increase in inflammatory cells precedes malignant transformation while PDL1 overexpression in epithelial cells only occurs after malignant transformation.

Conclusion

We developed a new quantitative method to study PD1/PDL1 expression in FFPE oral biopsy samples. The expression of PD1 and PDL1 may be used as predictive markers of transformation and the data may be used to develop early intervention in OPML using PD1 inhibitors.