Science-based histopathological diagnosis of oral borderline malignancies

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It has been almost sixty years since Danely Slaughter, a pathologist in Chicago, first introduced the concept of “field cancerization” based on his histopathological observation that one oral cancer lesion contained multiple foci of carcinoma *in-situ* (CIS) which were not continuous with each other, and which neighbored dysplastic or normal epithelia. During the intervening years, there have been numerous advances in cancer science, yet it is still challenging to histopathologically distinguish CIS from epithelial dysplasia or from microinvasive carcinoma. The boundaries between different grade foci are not always discernible on hematoxylin and eosin-stained sections, though some molecular events of “cell competition” must occur between cells belonging to the different grades of malignancy, which is considered to be one of the most interesting subjects in modern cell biology. It is therefore meaningful to demonstrate phenotypic differences between malignant foci and their neighboring not-yet malignant foci in the oral mucosa, namely what oral CIS is, from the diagnostic point of view. This might be the basic attitude of pathologists who want to make objective diagnoses. In this talk, I will introduce some of my scientific evidence on which I For instance, CIS can be distinguished by its immunohistochemical positivity for keratin (K) 17, which is reciprocal to that for K13. The border between a K17 positive (+) and K13 not positive (-) area and a K17-/K13+ area can be recognized as a lateral invasion front of CIS. The expression of K17 is related to cell proliferation and migration. K17+ keratin pearls in CIS are generated by hemophagocytosis of CIS cells, which is caused by extravasation of erythrocytes from collapsed intraepithelial blood vessels. Some other biological subjects investigated as backgrounds for characteristic histopathological features of CIS will be presented as scientific reasons for why the histopathological diagnosis of oral CIS is possible.