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Anatomical Pathology

THE MICROBIOME AND ORAL CANCER: DRIVER OR PASSENGER

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Microbes as carcinogens have been in and out of favour for centuries. We now accept that ~13% of human neoplasms are caused directly by micro-organisms.[1] Obvious examples are high-risk (hr) genotypes of human papillomaviruses (HPVs) for cervical, anogenital and oropharyngeal carcinomas, and *H. pylori* for stomach cancer.

Since the advent of gene sequencing technologies there has been an explosion of information, initially using 16s RNA amplifications which do not capture every sequence present in a tissue, and now – at greater expense – metagenomic screening. A substantial literature concerning squamous cell carcinomas of the mouth has developed quickly.

It is essential to consider the total microbiota present, indeed the whole functional microbiome. Viruses, bacteria and fungi are all important. Specific hrHPVs, predominantly type-16, are responsible for a minority of cancers within the oral cavity, but a majority of those in the oropharynx. The role of Epstein-Barr virus and of human herpes viruses remains elusive. There are associations, but it cannot be said too often that associations do not prove cause and effect. *Candida albicans* is strongly associated and there are plausible mechanisms. Amongst bacteria, studies have revealed a range of consortia: all have in common a pro-inflammatory metabolism. Do these consortia actually *drive* neoplastic transformation or does the presence of an invasive lesion provide an environment in which they flourish, as *passengers* – perhaps in a positive feedback promoting tumour progression?[2] Circumstantial evidence[3] comes from observations that the microbiome associated with potentially malignant disorders resembles that in cancer.

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ORAL POTENTIALLY MALIGNANT DISORDERS: A CLINICIAN'S PERSPECTIVE

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The ability to predict which oral potentially malignant disorder will progress to squamous cell carcinoma remains the ultimate challenge facing clinicians managing patients with oral diseases. Currently oral epithelial dysplasia graded by pathologists holds a strong bearing on the risk of malignant transformation of a lesion; with high-grade lesions indicative of higher risk of malignant transformation, while low-grade lesions very rarely transforming to malignancy. However, repeated studies and real-world cases have shown that oral squamous cell carcinoma can occur in lesions with no epithelial dysplasia. There still remains an unmet need among clinicians managing patients with oral diseases for effective tools to predict risk of malignant progression. This presentation will aim to explore the real-world dilemmas faced in clinical diagnosis and management of patients with oral potentially malignant disorders and discuss developments in technology including diagnostic adjuncts and artificial intelligence that may assist in resolving this clinical dilemma.

COUNTING MITOSES: SI(ZE) MATTERS

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The assessment of proliferative activity by counting mitoses is something that most if not all histopathologists practice, as it is required for diagnosis and/or grading of many tumours. In the past, mitoses were often counted 'per high power field', which was convenient, but was regarded as scientifically questionable even 40 years ago, as it ignored the fact that microscope fields may differ substantially, even at the same high power (×400) magnification.[1] Other features such as vessels, cell numbers or apoptoses are also counted in some circumstances, and the same issues apply. The problem has been compounded by digital pathology, where fields are rectangular, and also vary substantially in the area displayed. There is considerable potential for error,

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