Treponema denticola chymotrypsin-like proteinase may contribute to orodigestive carcinogenesis through immunomodulation

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Background:Periodontal pathogens have been linked to oral and gastrointestinal (orodigestive) carcinogenesis. However, the exact mechanisms remain unknown. Treponema denticola (Td) is associated with severe periodontitis, a chronic inflammatory disease leading to tooth loss. The anaerobic spirochete Td is an invasive bacteria due to its major virulence factor chymotrypsin-like proteinase. Here we aimed to investigate the presence of Td chymotrypsin-like proteinase (Td-CTLP) in major orodigestive tumours and to elucidate potential mechanisms for Td to contribute to carcinogenesis.Methods:The presence of Td-CTLP within orodigestive tumour tissues was examined using immunohistochemistry. Oral, tonsillar, and oesophageal squamous cell carcinomas, alongside gastric, pancreatic, and colon adenocarcinomas were stained with a Td-CTLP-specific antibody. Gingival tissue from periodontitis patients served as positive controls. SDS-PAGE and immunoblot were used to analyse the immumodulatory activity of Td-CTLP in vitro.Results:Td-CTLP was present in majority of orodigestive tumour samples. Td-CTLP was found to convert pro MMP-8

and -9 into their active forms. In addition, Td-CTLP was able to degrade the proteinase inhibitors TIMP-1, TIMP-2, and ?-1-antichymotrypsin, as well as complement C1q.Conclusions:Because of its presence within tumours and regulatory activity on proteins critical for the regulation of tumour microenvironment and inflammation, the Td-CTLP may contribute to orodigestive carcinogenesis.