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**A potential biological mechanism for the association between periodontal disease and pancreatic cancer – porphyromonas gingivalis**

*Saba E, Farhat M, Daoud A*, et al*.*[*Oral bacteria accelerate pancreatic cancer development in mice*](https://gut.bmj.com/content/73/5/770)Gut *2024; 73: 770-786. doi: 10.1136/gutjnl-2023-330941.*

In the context of a dismal prognosis, the need to unearth additional modifiable risk factors for, and to understand their contribution to, pancreatic ductal adenocarcinoma (PDAC) is imperative. Presence within the oral cavity of Porphyromonas gingivalis (P. gingivalis), often associated with periodontal disease, has been suggested as one such risk factor, supported by associations shown in epidemiological studies alongside its detection in PDAC tumour tissue itself. Saba et al., hypothesised that translocation of P. gingivalis from oral cavity to pancreas, facilitating cooperation on a local level with oncogenic (including Kras; Kirsten rat sarcoma viral oncogene homolog) mutations in pancreatic acinar cells, may represent a mechanism to explain potential accelerated PDAC development.

Following oral administration of P. gingivalis to both wild-type and genetically-engineered (GEM) mice (Kras+/ LSL-G12D; Ptf1a-CreER, iKC), pancreatic samples were obtained surgically from seven subjects to firstly confirm bacterial translocation, and subsequently facilitate study of direct effect in vitro.

P. gingivalis was found to migrate from the oral cavity to the pancreas, with P. gingivalis DNA found in all mice, and cell-associated P. gingivalis confirmed in six subjects (in areas of healthy pancreas and pancreatic intraepithelial neoplasia [PanIN]). In wild-type mice, as well as shifting composition of the intrapancreatic microbiome, repeated P. gingivalis administration induced pancreatic acinar-to-ductal metaplasia (ADM); in genetically engineered iKC mice, P. gingivalis hastened progression of PanIN to PDAC. Finally, in the setting of in vitro hypoxia and nutrient stress, it also shielded PDAC cells from reactive oxygen species (ROS)-mediated cell death.

In support of earlier epidemiological data, this laboratory-based mouse study provides evidence for a possible causal biological mechanism – local direct effect of P. gingivalis following translocation to the pancreas – for the previously described association between pancreatic malignancy and the common modifiable entity of periodontal disease, alongside prompting exploration of direct targeting of intracellular P. gingivalis as a new therapeutic approach in this area.