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Editorial

Microbiota and Pancreatic Ductal Cancer

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The most common malignancy of exocrine pancreas is pancreatic ductal cancer (PDC). PDC is one of the most aggressive cancers. For the majority of patients, it remains a lethal disease, and is the 4th leading cause of cancer death in Europe. There is no effective screening diagnostic test and most patients have advanced disease at presentation, therefore the lack of biomarkers for early detection contributes to poor outcomes. Identification of modifiable risk factors and an effective primary prevention strategy could become critical to reducing the aggressiveness of this malignancy.

The ecological community of commensal, symbiotic, and pathogenic microorganisms present in our body is known as the microbiota. The microbiome is the entire genome sequence of this microbial community. A limited body of evidence suggest that there may be an association between microbiota imbalance and PDC. Microbiota imbalance (also known as dysbiosis or dysbacteriosis) has been linked to dysregulation of immune effector cells and activation of inflammatory cytokines, playing a role in several inflammatory diseases. Moreoever, *Fusobacterium nucleatum, Bacteroides clarus* and *Roseburia intestinalis* have been successfully identified patients with colorectal cancer, which gives hope to the development of a novel diagnostic biomarker.

Regarding PDC, there is evidence suggesting significant higher antibody levels of periodontal pathogen *Porphyromonas gingivalis* in these patients. The highest concentration of *Porphyromonas gingivalis* is associated with a twofold increase in PDC risk. Moreover, higher levels of antibodies to commensal oral to a lower

risk of PDC. *Porphyromonas gingivalis* is the main microorganism involved in periodontal disease, a very common oral disorder affecting around 90% of general population. In addition, other publications have found a link between an increase of *Bacteroides* and the risk of developing PDC. Converserly, levels of *Neisseria elongata* and *Streptococcus mitis* are reported to be lower in PDC patients, while *Granulicatella adiacens* is reported to be higher. Finally, several groups have analysed *Helicobacter pylori* as risk factor for the development of PDC. However, reports are inconsistent, with several meta-analyses finding an association between *Helicobacter pylori* and PDC, with others reporting no association.

Further investigation is required to confirm these findings, and to explore clinical implications such as screening and therapeutic possibilities. In fact, microbial abnormalities may be explored as early biomarkers for PDC and therefore may potentially have a significant impact on the long-term survival of these patients. For instance, the identified salivary biomarkers have high specificity and sensitivity for the detection of PDC.

To conclude, the potential role of microbiota imbalance in PDC is an emerging topic of increasing interest, which may open a new avenue for biomarkers and targeted therapies of this lethal disease.