Dissecting the association of the human palatine tonsil microbiome and HPV-driven oropharyngeal squamous cell carcinoma

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Oropharyngeal squamous cell carcinoma (OPSCC) can be caused by viral transformation of epithelial cells in the oropharynx such as high risk-human papilloma virus (HR-HPV). Importantly, the incidence of OPSCC has been increasing during the last decades although tumors with biologically active infection by HR-HPV exhibit a distinct biology and improved treatment response leading to better patient outcome. Recent studies have suggested that the containment of HR-HPV can be influenced by the microbiome present at mucosal surfaces and by microbial agents that persist within immune cells and thereby alter immune responses against the pathogen. Hence, we hypothesize that the microbiome of human palatine tonsils contributes to the establishment and persistence of HPV infection leading to malignant transformation and development of OPSCC. In particular, we assume that the microbial composition in left and right tonsils from the healthy individual is identical or at least very similar. Moreover, we expect to detect differences between the diseased and healthy tonsils of patients affected by OPSCC.

We plan to characterize the microbial composition of tonsillar surfaces and crypts in healthy individuals suffering from sleep apnea using next generation sequencing of 16S V5-V6 rDNA amplicons. We expect that this initial part of the study will fill a critical gap in the knowledge on the microbiome present in different compartments in tonsils of healthy adults. Next, we plan to profile the tonsillar microbiome of patients suffering from HPV-associated OPSCC and OPSCC that is not linked to HPV infection. We expect that evaluation of next generation sequencing and clinical data will provide novel knowledge on microbiome-HPV interaction and will form the basis for further prospective clinical studies. Finally, we plan to assess whether a distinct intracellular microbiome exists in immune cells within the tonsillar lymphoid tissue using multi-parameter flow cytometric analysis and cell sorting. We anticipate that these analyses will reveal whether and to what extent bacterial communities are associated with immune cells in human tonsils.

Overall, the outlined project will provide hitherto unknown information on the microbiome of different compartments in human tonsils, support design of future prospective clinical studies to clarify the role of the microbiome in HPV-driven OPSCC and direct future analyses of immune cell-commensal bacteria interaction in tonsillar lymphoid tissue.
keywords
Human papilloma virus, oropharyngeal carcinoma, microbiome, tonsil, macrophages

type of project
fundamental research

status
ongoing - recruiting phase

start of project
2017

end of project
2018

project manager
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