A NEW IN VITRO MODEL TO STUDY HOST-MICROBE INTERACTIONS IN CHEMOTHERAPY-INDUCED MUCOSITIS

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Introduction and Objectives
Alimentary mucositis is a common side effect of chemo- and radiotherapy. It not only majorly affects the quality of life of patients but also often causes a cessation of the treatment. Unfortunately, no treatment is available yet. Although the role of microbiota on the development of mucositis is not clear, there are indications they could play an important role. Our objective is to explore the host-microbe interactions during chemotherapy-induced mucositis by means of a new in-house developed in vitro model.

Materials and Methods
The model consists of a 24-well Transwell plate with removable inserts in which an oral or fecal-derived biofilm can be cultured separately from a monolayer of epithelial cells in presence or absence of chemotherapeutic agents such as 5-Fluorouracil (5-FU) or irinotecan (SN-38). The impact on the epithelial cells of both the microbiota and the chemotherapeutic agents is investigated using a wound healing assay.

Results and Discussion
We show that microbiota have a generally negative impact on wound closure of oral TR146 cells, irrespective of the presence of 5-FU. In contrast, using small intestinal IEC6 cells a significantly negative impact of microbiota on wound healing is observed in absence of SN-38, which is abolished when SN-38 was present. The model is also useful for the study of changes in the composition of the biofilm after treatment with chemotherapeutic agents. DGGE analysis and 16S sequencing of insert samples show that a shift in the microbiome occur after 5-FU and SN-38 exposure.
In conclusion, using our in vitro mucositis model we were able to identify functional and mechanistic changes in host-microbe interactions after exposure to chemotherapeutic agents. Therefore, the model will be helpful in further characterising the pathobiology of mucositis and in the development of new treatment strategies.