

## **Student project Epidemiology**

Dr. Annemarie Boleij, Prof. Iris Nagtegaal, Department of Pathology, Radboudumc.  
Annemarie.Boleij@radboudumc.nl

### **Title: Influence of microbiome modulating drugs on tumor downstaging and regression following pre-operative chemoradiation**

Pre-operative chemoradiation (CRT) has become the standard of care in locally advanced rectal cancer (LARC), despite being effective only in 60% of patients. To date we do not fully understand the mechanisms that lead towards tumor response. The tumor-microenvironment influences response to CRT, with the presence of lymphocytes resulting in tumor downstaging. In contrast, tumor budding (formation of single tumor cells and small clusters of tumor cells) is associated with a poor response to therapy. Further exploration of the tumor-microenvironment in regulation of the tumor response is essential to increase effectiveness of CRT or to select patients that benefit from this therapy.

The mucosal microbiome is an underestimated factor in the tumor-microenvironment, which has shown to influence proliferation, inflammation, immunity as well as response to therapy. The microbiome critically modulates the effectiveness of both chemotherapy and immunotherapy; however, it is unknown how certain microbiome modulating drugs, such as antibiotics, NSAIDs, corticosteroids, proton-pump inhibitors, and immunosuppressive drugs influence the tumor-microenvironment and host-response to CRT. These drugs could alter microbiome composition and function or the host-response to the microbiome and might be direct treatment options to use or avoid before and during CRT.

#### **Aim**

- To understand effects of microbiome modulating drugs on therapy response of LARC patients in order to increase effectiveness of CRT

#### **Plan of investigation**

For this study we will use a large national **cohort** of over 4000 LARC patients of which microbiome modulating medication, tumor characteristics and response to therapy are available. We will mine these registry data on microbiome-modulating drugs in the months preceding the CRT to identify microbiome-modulating drugs that could affect tumor downstaging and regression. Pathology and tumor data from PALGA and IKNL (including tumor response) will be linked to medication data from Pharmo Research to find pharmacological options to tweak the microbiome for a better response to CRT.

#### **Goals for the student (~6 months internship)**

- Literature study (evidence for drugs related to microbiome & CRT outcome)
- Coupling data from Pharmo research with PALGA and IKNL databases
- Univariate and multivariate analysis approaches
- Identifying potential confounders
- Writing a concept article

#### **Expected output**

Pharmacological options to tweak the microbiome for better response to CRT in LARC