A close-up of colon cancer
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Preface: a close-up of colon cancer
Cancer has become the number one cause of death in the Netherlands and colon cancer is one of the most prevalent cancers, responsible for significant morbidity and mortality. In past decades, research on colon cancer has greatly increased our knowledge about this disease. The exact mechanism of development however remains largely elusive. An increased effort to implement screening programs for colonic adenomas (precursor lesions that may develop into cancer) and early stage colorectal cancer is likely to decrease the burden of colorectal cancer. However, in a significant number of patients the disease has already spread beyond the confines of the colon to locoregional lymph nodes or more distant metastatic sites. Finding an effective treatment against metastasized disease remains therefore the holy grail of treatment. Nowadays and for the past 20 years, treatment has remained virtually unchanged, consisting of surgical resection, frequently accompanied by chemotherapy that attacks dividing cells and thus often has severe side effects.

To better understand and eventually treat colon cancer, in the following thesis, two different research strategies are used. The first strategy aims at understanding cancer, through gaining knowledge of the intestine during normal and healthy homeostasis. After all, if one intends to comprehend a disease in which so many control systems have failed, it is important to first understand the role of these systems before they fail. In the **first part** of this thesis, three chapters are presented in which normal intestinal epithelial homeostasis is analyzed. On the other hand, epidemiological data may identify factors with an important role in the development of colon cancer such as obesity, smoking, a diet rich in red meat and male gender. Despite the fact that many of such factors have been identified, the reason for the association with the disease or mechanism of action often remains unclear. One of the factors that have repeatedly been identified to alter colon cancer susceptibility is gender. Therefore, in the **second part** of this thesis, external influences, mainly gender differences are investigated during tumor development in the experimental setting.

Looking at colon cancer from both perspectives is necessary for improved understanding of this disease and however modest, this thesis is a minute contribution to unravel and eventually to better treat this disease.