

Models for experimental Colitis and *in vitro* approaches on patient intestinal resection material

Background

The Department of Gastroenterology and Hepatology of the Academic Medical Center in Amsterdam is an expert and referral centre for IBD and has a longstanding tradition of excellent patient care combined with both clinical and fundamental research activities. Since several years now its fundamental IBD-research is bundled in the Tytgat Institute where it is part of the research theme of 3 different principle investigators (GR van den Brink, AA te Velde and WJ de Jonge). The close collaboration between the Tytgat Institute and clinicians of the Gastroenterology department is an important strength of our approach.

The models

Routinely used models in our lab are:

- DSS colitis
- TNBS colitis
- CD45RB^{high} Tcell transfer colitis (Powrie model)

Results with the models

In the Netherlands, but also internationally, the AMC fulfils a leading role in the treatment of IBD. In the past we introduced the concept to treat patients with Crohn's disease with antibodies against tumor necrosis factor (anti-TNF), a breakthrough in the therapy of this disabling disease. Over the years, other novel insights in the pathogenesis and genetics of IBD have been introduced, including the importance of IL-10 as potential treatment. The latter has led to the generation of genetically manipulated lactobacillae producing IL-10 (tested in patients with Crohn's disease). At present the clinical IBD group is headed by Prof G. D'Haens who plays a crucial and coordinating role in phase I and II clinical trials evaluating the therapeutic potential of new biologicals. His internationally acclaimed expertise ensures timely 'bench to bedside' translation of results obtained in the Tytgat Institute.

At the Tytgat Institute state of the art *in vitro* assays and *in vivo* models (used on a routine basis) allow us to investigate the role of pathways relevant to the development of IBD. In a large number of publications we not only used conventional mouse models like DSS- and TNBS-colitis but also the CD45RB T cell transfer model that most closely reflects human IBD. These models were used to establish basic mechanisms in IBD as well as pharmacological and dietary intervention strategies.

Since we have broad access to patient tissues and isolated cells we also validate our experimental data by immunological phenotyping and activation of mucosal lymphocytes, dendritic cells and macrophages. Data obtained in these *in vitro* investigations can be correlated with clinical phenotype and genetic profile.

Potential use for research partner

These models are optimized for testing of pharmaca, biological, or nutritional interventions to relieve the severity of colitis. An *in vivo* mouse endoscope has been recently set up to be able to perform life imaging of the colitic lesions, and the recovery due to experimental treatment. Human resection material can be processed in MLII environments. All ethical approval is in place for the use of human material in test setting in our lab.