

Title: **Evaluation of the mechanisms involved in the patho-physiological alterations of the abomasal mucosa in cattle infected with *Ostertagia ostertagi*.**

Mihi Belgacem; Manuela Rinaldi; Edwin Claerebout; Jozef Vercruyse; Bruno Goddeeris; Peter Geldhof

Laboratory for Parasitology- Department of Virology, Parasitology & Immunology- Ghent University

Infections with the gastrointestinal nematode *Ostertagia ostertagi* remain in cattle an important economic problem in the temperate regions of the world, causing loss in animal production. The infection results in profound physio-morphological changes of the abomasal mucosa including mucus cell hyperplasia and cell de-differentiation, accompanied by increased gastric pH and hypergastrinemia. The causes and the mechanisms behind these alterations are still unclear. Therefore the aim of the current study was to determine the pathways involved in the observed cell hyperplasia and dedifferentiation during an infection with *O. ostertagi*. Further, an attempt was made to evaluate if increase in gastric pH may be due to a decrease number of mature acid-producing parietal cells in the mucosa and if this can be linked to the alteration in the gastric cell population during infection. Transcription levels of several molecules belonging to the EGFs, WNT, and FGF signaling pathways, involved in the onset of cell hyperplasia and cell dedifferentiation, were found to be up-regulated at 24 days post-infection (dpi). On the other hand, gene transcription levels of ATP4A and AQP4, two specific markers for parietal cells activity, showed a significant down-regulation only after 60 days of exposure to *Ostertagia*. In consistent with these findings, immunostaining showed that cell hyperplasia in the abomasal mucosa occurs earlier compare to the loss of mature acid-producing parietal cell, suggesting that alteration in cell population leads to a decrease in number of parietal cells in the infected mucosa. This may explain the increase in gastric pH measured after infection. Additionally several pro-inflammatory factors such as IL8, IL1 β , IL6 and COX-2 were found to be up-regulated during the infection starting at 9 dpi. These cytokines may have a direct inhibitory effect on parietal cells and they may also play a role in cell migration and maturation.