Semi maturation of bovine monocyte-derived dendritic cells after incubation with *Giardia duodenalis*

G. H. Grit[1], S. Van Coppernolle[1], B. Devriendt[1], T. Geurden[1], J. Hope[2], J. Vercruysse[1], P. Geldhof[1], E. Cox[1], E. Claerebout[1]

[1]Department of Virology, Parasitology & Immunology, Faculty of Veterinary Medicine, Ghent University, Salisburylaan 133, 9820 Merelbeke, Belgium
[2]The Roslin Institute, University of Edinburgh, Easter Bush, Midlothian, EH25 9RG, UK

Giardia duodenalis is an important intestinal parasite in animals and humans. The role of dendritic cells in the immune response against *G. duodenalis* is poorly documented and has only been studied in the mouse, which is not a natural host for this parasite. In this study we addressed the effect of *G. duodenalis* trophozoites and excretion/secretion (ES) products on the expression of maturation markers and cytokine production by bovine monocyte-derived dendritic cells (MoDCs) *in vitro*. Moreover, the ability of stimulated MoDCs to take up antigen and to induce mononuclear cell (MC) proliferation was assessed.
Although none of the maturation markers CD40, CD80 and MHCII were up-regulated in MoDC cultures after stimulation with *Giardia* trophozoites or ES, a dose-dependent decrease of ovalbumin uptake was observed. IL-15 transcription was significantly increased after 24h of stimulation with *Giardia* trophozoites. Other cytokines were not significantly up- or down-regulated. MoDCs stimulated with *Giardia* trophozoites or ES induced a dose-dependent proliferation of allogenic γδ-T-cells and TCRαβ$^+$ CD4$^+$ and -CD8$^+$ T-cells *in vitro*, compared to cultures with unstimulated MoDCs. Induction of a CD4$^+$ T-cell response by *Giardia*-stimulated MoDCs was confirmed in an autologous lymphocyte proliferation assay, using MoDCs and PBMCs from calves artificially infected with *G. duodenalis* cysts.
Our data show that *G. duodenalis* trophozoites induce a functional maturation of bovine MoDCs. Functionally active MoDCs, lacking the expression of co-stimulatory molecules are known as semi-mature DC. Although semi-mature DC can cause T-cell tolerance, MoDCs stimulated with *G. duodenalis* showed a significantly increased mRNA transcription level of IL-15, which can explain the activation and proliferation of the T-cell populations despite the lack of co-stimulatory molecules present on the cell surface. Proliferating CD4$^+$ T-cells will be further characterised to investigate whether a regulatory T-cell response is induced by *Giardia*-stimulated MoDCs.

Acknowledgements:
G.H. Grit is funded by a PhD grant from IWT-Vlaanderen.
S. Van Coppernolle is funded by the EU FP7 project (Paravac)
B. Devriendt is funded by a post-doc grant of Ghent University