ImmunoTools *special* Award 2014

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The impact of helminth infection on Diabetes mellitus in Ethiopia

Introduction and aim of research. Recently, it has been demonstrated that the immunomodulatory properties of parasitic worms affect the course and severity of a number of inflammatory diseases. For example, infection with several different worm species is strongly associated with reduced clinical signs of several inflammatory diseases, including diabetes mellitus (DM) and multiple sclerosis (MS). Interestingly, in mice models for DM or MS, exposure of the animals to the human worm-parasite *Schistosoma mansoni* was shown to reduce the severity of the clinical symptoms, indicating that this parasite can induce protection to these diseases. My research is focused on Diabetes mellitus, the most prevalent non communicable disease World wide. Although different risk factors are associated with the development of DM, its occurrence is increasing at an alarming rate, even in countries such as Ethiopia which were relatively free of many autoimmune diseases for a long time.

My major hypothesis is that chronic *S. mansoni* infection lowers the risk for development of DM type I or II. This may be “visible” by a lower prevalence of pre diabetic markers and a healthier serum lipid profile in infected individuals, as compared to control groups. I hypothesize that helminths induce immunological, systemic effects via modulation of innate immune mechanisms. Understanding the immunological changes during helminth infections, may lead to the discovery of clues towards new preventive medicines for those who are at risk to develop the disease. Currently I am performing epidemiological studies of the relation of risk to DM, and infection to the helminth *S. mansoni,* in Ethiopia in areas where parasitosis is endemic. In addition, I will perform immunological studies in Amsterdam with sera collected from the same Ethiopian patients. I will also perform in vitro experiments using blood cells from Amsterdam blood donors, which are triggered with different *S.*

mansoni antigens, to evaluate how interaction with *S. mansoni* antigens modulate their phenotypes.

Study approach and Methods. Plasma samples were collected from Ethiopian individuals which are infected by *S. mansoni*, and which have or have not enhanced risk to develop DM. Cytokine profiles are determined in these sera by ELISA. Human monocytes and monocyte-derived macrophages from healthy donors are stimulated with or without *S. mansoni* antigens and resulting phenotypes are determined by flow cytometery, and secreted cytokine levels are measured using ELISA

Monocyte and macrophage phenotypes will be assessed by flow cytometry using different markers including: CD14 and CD16 (lowered CD16 is associated with development of cardiovascular diseases), CD40 (immune activation marker), HLA-DR, and Annexin V to assess cell viability. Inflammatory and anti inflammatory cytokine production will be assessed using ELISA test kits for IL-6, IL-8, IL-4, IL-12-total and -p40. Moreover, to evaluate the potential of *S. mansoni* antigens to interfere with activation of macrophages, we stimulate monocytes with GM-CSF to obtain classically activated macrophages, and with IL-4 to obtain alternatively activated macrophages.

ImmunoTools *special* AWARD for **Mistire Wolde Gebre** includes 25 reagents

FITC - conjugated anti-human HLA-DR Control-IgG2a,

PE - conjugated anti-human CD14, Control IgG1, Annexin V,

APC - conjugated anti-human CD16, CD40, Control-IgG1, Control-IgG2a, Control-IgG2b, Annexin V,

human IL-4 ELISA-set for 96 wells, human IL-6 ELISA-set for 96 wells, human IL-8 ELISA-set for 96 wells, human IL-12p40 (total) ELISA-set for 96 wells, human IL-12p40 (diffential) ELISA-set for 96 wells, (each 3 reagents),

recombinant human cytokines: rh GM-CSF, rh IL-4 DETAILS more AWARDS