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Immune modulation by schistosomes: mechanisms of regulatory B cell induction and inhibition of allergic asthma

Obieglo, K.

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Stellingen behorende bij het proefschrift

IMMUNE MODULATION BY SCHISTOSOMES: mechanisms of regulatory B cell induction and inhibition of allergic asthma

1. In addition to lymphoid organs such as the spleen, B cells with regulatory properties can also be found in peripheral tissues at the site of inflammation, such as the lungs of allergic and schistosome-infected mice (this thesis).
2. The *S. mansoni* egg antigen IPSE/alpha-1 induces IL-10-producing regulatory B cells by a direct interaction with both murine splenic marginal zone B cells and human peripheral B cells (this thesis).
3. Splenic marginal zone and follicular B cells undergo partially distinct transcriptional changes in response to chronic *S. mansoni* infection, with preferential involvement of innate inflammatory signals in the activation of marginal zone B cells (this thesis).
4. Allergic asthma can not only be ameliorated by chronic *S. mansoni* infection, but also by the preventive treatment with isolated eggs or with the egg glycoprotein omega-1 (this thesis).
5. The mechanisms by which helminths including *S. mansoni* ameliorate allergic asthma are not limited to the induction of regulatory T and B cells, but also include the interference with innate immune mechanisms such as inhibiting epithelial cell cytokine production, altering type 2 innate lymphoid cell function, or inducing regulatory features in myeloid cells (this thesis and McSorley et al., *Parasite Immunol.* 2018 Jul 25:e12574).
6. The identification of antibody-secreting plasma cells with regulatory properties suggests that B cells at different stages of development and differentiation can acquire a regulatory phenotype (Shen et al., *Nature.* 2014 Mar 20;507(7492):366-370; Lino et al., *Immunity.* 2018 Jul 17;49(1):120-133.e9).
7. Now that the initial excitement about the application of controlled helminth therapy has diminished as a consequence of recent negative clinical trial outcomes, the identification of single helminth-derived molecules has become more important for the development of novel helminth-based treatment strategies (Maizels et al., *Immunity.* 2018 Nov 20;49(5):801-818).
8. The term 'hygiene hypothesis' is misleading and should be replaced by 'old friends hypothesis', which better covers our current understanding of how immune functions are undermined in industrialized societies by a profound depletion of micro- and macrobionts from the ecosystem of the human body (Bloomfield et al., *Perspect Public Health.* 2016 Jul;136(4):213-24; Bilbo et al., *Med Hypotheses.* 2011 Oct;77(4):494-504).
9. If I had eight hours to chop down a tree, I'd spend six hours sharpening my ax (Abraham Lincoln, 1809-1865). *Preparation is an integral part of conducting scientific experiments.*
10. Climb mountains not so the world can see you, but so you can see the world (David McCullough Jr., 2012). *Science should be more about gaining (and sharing) knowledge, and less about gaining recognition.*
11. Knowledge isn't all that counts. We will be judged by our children and grandchildren, not by what we know, but by what we do with what we know (Daniel M. Davis, *The beautiful cure*, Penguin Random House UK, 2018). *Science should be conducted with the benefit for society as ultimate goal.*