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## **The role of the innate and adaptive immune system on vascular remodeling**

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Stellingen behorend bij het proefschrift getiteld:

**The role of the innate and adaptive immune system on vascular remodeling**

**K.H. Simons, 5 juni 2019**

1. Thrombosis, constrictive remodeling, intimal hyperplasia, and unstable atherosclerotic lesions are the critical mechanisms contributing to vein graft failure, in different phases. *(this thesis)*
2. The introduction of immune checkpoint inhibitors revolutionized cancer treatments and improved cancer survival, however their use may induce cardiovascular toxicity. *(this thesis)*
3. Co-stimulation blockade is a promising therapeutic approach to prevent progression of cardiovascular diseases. *(this thesis)*
4. IRF3 and IRF7 are essential regulators of both neovascularization and vein graft disease but their individual contribution differs in time. *(this thesis)*
5. The reduced VSMC proliferation and intima hyperplasia after adenoviral overexpression of IFN $\beta$  in a porcine balloon injury model underscores the role of the type I interferons in vascular remodeling. *(Stephan, D et al. Mol Med. 1997;3(9):593-9)*
6. Certain cytokines such as IL-12, IL-18, TNF $\alpha$  and IL-33, can induce bystander proliferation and activation of CD8 $^+$  T cells in a T cell receptor independent manner. *(Freeman, B. E. et al. Proceedings of the National Academy of Sciences of the United States of America. 2012;109(25):9971-6)*
7. The maturation of pre-existing collateral arteries by arteriogenesis, together with the angiogenic sprouting of new capillaries, is essential for recovery of the blood flow towards ischemic tissues. Therefore a proper vascular bed of pre-existing arterioles formed by vasculogenesis is essential. *(Semenza, G.L. et al. Journal of cellular biochemistry. 2007;102(4):840-7)*
8. TLR3 is activated by RNA released by necrotic cells. Since necrotic cells are highly present in vein grafts during and after vein graft surgery as a result of the engraftment procedure, vein graft handling, flow disturbances and subsequent arterialization phase cells, careful handling of the engrafted vena saphena magna by the surgeon would increase patency rates and clinical outcome after vein graft surgery. *(Osgood, M. J. et al. Journal of vascular surgery. 2014;60(1):202-11)*
9. Oxygen is overrated, except for peripheral artery disease patients.
10. Sporten voor het werk verhoogt je arbeidsproductiviteit.
11. Kennis is macht. Kennis delen is kracht.
12. We hebben steeds tijd om iets over te doen maar nooit tijd hebben om het meteen goed te doen.

