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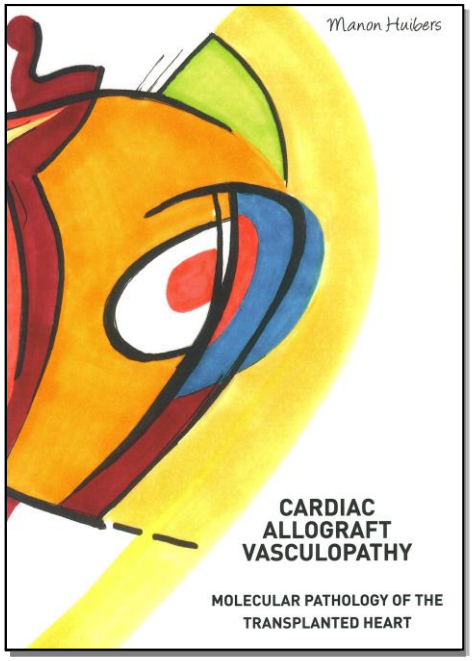

Samenvatting proefschrift Manon Huibers

"Cardiac allograft vasculopathy"

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Universiteit Utrecht

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Cardiac Allograft Vasculopathy (CAV) is a disease which has a high prevalence in Heart transplant (HTx) patients. It is characterized by concentric thickening of the wall of the coronary artery of the transplanted heart. The pathogenesis of CAV is complex; various cell types from both the host and the donor play a role. Activation of immunological components affects the vasculature of the allograft. Although in the past a lot of knowledge is gained about the processes that underlie the pathogenesis of CAV, there are still gaps in our knowledge. By clarifying the exact roles of all these different components, a solution for CAV may come in reach. We have the unique opportunity to study allograft vasculopathy in hearts after transplantation, collected at autopsy in our Pathology department.
The aim of this thesis was (1) to study the pathogenesis of Cardiac Allograft Vasculopathy on a morphological, cellular, and molecular level. Furthermore (2) the purpose of this thesis was to study the role of ectopic lymphoid structures surrounding CAV arteries. Understanding the role of these structures could provide therapeutic options. Ultimately, we aimed (3) to identify a molecular target and test the ability of this therapy in a well-established humanized mouse model for CAV.
Cardiac Allograft Vasculopathy after heart transplantation is characterized by an immunological response leading to vascular fibrosis. Besides intima expansion, this thesis showed that ectopic lymphoid structures (ELS) surrounding CAV arteries should not be underestimated in the pathogenesis of chronic rejection. New insights in molecular pathways (e.g. microRNA regulation) could be applied on CAV and may give new options for diagnosis, prognosis, and therapeutic applications.
In the future therapeutic options should be more directed to the histological stage of CAV. Early immunological activation may need other approaches that late fibrotic lesions. T cells, proliferations, smooth muscle cells.