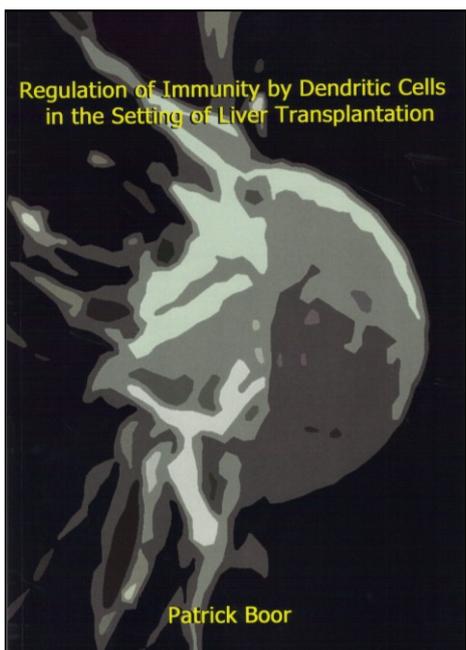




Nederlandse
Vereniging voor
Hepatology



Samenvatting proefschrift Patrick Boor

‘Regulation of immunity by dendritic cells in the setting of liver transplantation’

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The liver itself possesses tolerogenic properties, far more than other solid organs. This is necessary because the liver is exposed to harmless food antigens and microbial products from the small intestine. These agents do not pose a threat, and must therefore be ignored by the immune system. The first part of my thesis describes studies on the possible involvement of various types of myeloid dendritic cells (MDC) in liver lymph nodes in the maintenance of liver tolerance. It was investigated whether hepatic MDC undergo an alternative maturation program leading to the presence of tolerogenic effector MDC in the hepatic lymph nodes. Immunophenotypical and functional characteristics of human hepatic lymph node MDC were compared with those of skin/muscle draining inguinal lymph node MDC, splenic and liver perfusate MDC. The second part of my thesis focuses on the effect of immunosuppressive drugs on plasmacytoid dendritic cells. Prednisolone induces apoptosis in plasmacytoid dendritic cells and rapamycin affect their ability to stimulate T-cells. To prevent rejection of their graft, the majority of liver transplant recipients need life-long treatment with immunosuppressive drugs. These agents have adverse effects, such as nephrotoxicity, hypertension, and increased risk for infections and the development of cancer. Induction of specific transplant tolerance is, therefore, a major goal in transplantation research. We showed that plasmacytoid dendritic cells can induce the generation of a peculiar subset of CD8⁺ regulatory T cells that are able to inhibit allo-reactive memory T-cell responses in a donor-specific fashion. This knowledge could in the future be utilized to develop a novel immune-therapy aiming to induce donor-specific Treg in liver transplant recipients, or to treat liver transplant recipients with autologous Treg that are expanded *ex vivo* using donor-derived plasmacytoid dendritic cells. ◀

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