The liver has particular immune functions attributed by its unique microenvironment and its liver-resident cell populations. During autoimmunity and viral hepatitis, the liver serves as target for effector responses of immune cells. However, skewing of effector T cell functions through tolerogenic liver-resident antigen-presenting cells and through the immune regulatory hepatic microenvironment. Importantly, the liver also participates in shaping systemic antigen-specific immunity. Local antigen-presenting cell populations, in particular liver sinusoidal endothelial cells (LSECs), cross-present soluble, circulating or hepatocyte-derived antigens to naïve CD8 T cells. Upon priming by cross-presenting LSECs, naïve CD8 T cells develop into a unique population of antigen-experienced memory-like T cell population that can be reactivated in an inflammatory context to protect against infection with viruses or bacteria. Furthermore, upon prolonged inflammatory TNF-dependent signaling, the induction of intrahepatic myeloid cell aggregates for T cell population expansion (iMATEs) is observed in liver tissue. iMATEs are formed by inflammatory monocytes developing into dendritic cells and function to attract recently activated CD8 T cells. Those CD8 T cells located within the cocoon-like iMATE structure show strong proliferation initiated by co-stimulatory signaling. Locally expanded CD8 T cells are key to control acute and chronic viral infections. The mechanistic
understanding of local hepatic T cell priming and local expansion of effector CD8 T cells will help to develop novel therapeutic vaccination strategies.