VASCULAR PATTERNING AS A DETERMINANT OF IMMUNOLOGICAL COMPETENCE IN VISCERAL LYMPHOID TISSUES

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The capacity of mammalian organisms to mount efficient adaptive immune responses requires the establishment of highly ordered tissue architecture in peripheral lymphoid organs, ensuring continuous leukocyte influx and subsequent segregation. As a crucial component, local vasculature plays a key role in the tissue-specific recirculation of leukocytes. The patterning and differentiation of specialized vessels are closely linked to the embryonic development of peripheral lymphoid organs; however, details of endothelial commitment, morphogenic signals and communication pathways between hemopoietic cells, stromal cells and endothelial cells, and their impact in inflammatory processes are still largely unexplored. Recently Nkx2-3 homeodomain-containing transcription factor has emerged as a major regulator for splenic and intestinal lymphoid vascular commitment and a susceptibility trait associated with chronic inflammatory bowel diseases. Work in our laboratory has established that Nkx2-3 plays an important role in the local decision between lymphatic/blood endothelium within the spleen as well as commitment towards the high endothelial lineage within Peyer's patches. Here we report that, in addition to defining local vasculature, altered Nkx2-3 expression also influences intestinal IgA secretion and in the spleen the capacity for germinal center formation and plasma cell proliferation in a process that may involve red pulp megakaryocytes. Collectively, these observations indicate that the vascular commitment influenced by Nkx2-3 has far-reaching consequences beyond the structural evolution of peripheral lymphoid organs.

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