Adhesion Molecules on High Endothelial Venules of Pancreatic Lymph Nodes from Humans with Type 1 Diabetes

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Purpose: In the nonobese diabetic (NOD) mouse model of type 1 diabetes, naive autoreactive T cells migrate through high endothelial venules (HEVs) into pancreatic lymph nodes (PanLNs), where the T cells are primed by β cell antigens. Progeny of the primed T cells migrate from blood vessels into pancreas, leading to development of islet inflammation, β cell destruction and overt diabetes. We have shown that the mucosal addressin cell adhesion molecule-1 (MAdCAM-1) is strongly expressed on HEVs of PanLNs from young NOD mice and plays a major role in migration of naive autoreactive T cells into PanLNs. In contrast, the peripheral node addressin (PNAd) shows various levels of expression on HEVs of PanLNs from young NOD mice and plays a minor role in migration of naive autoreactive T cells into PanLNs. The HEV adhesion molecules that mediate the migration of T cells from the bloodstream into PanLNs of humans are not known.

Methods: We used immunohistology staining to determine which adhesion molecules are expressed on HEVs of PanLNs from humans with type 1 diabetes.

Summary of Results: We found that most PanLN HEVs in humans, as in NOD mice, had:
1) strong expression of MAdCAM-1; and
2) variable expression of PNAd, with some HEVs showing strong diffuse staining and others showing weak and/or focal staining.

Conclusions: These results suggest that the HEV adhesion molecules that mediate T cell migration into PanLNs in the initiation stage of the autoimmune response in NOD mice might also mediate T cell migration into human PanLNs. This supports the use of NOD mice in translational research on the lymphocyte migration pathways that are involved in the development of human type 1 diabetes.