CHARACTERIZATION OF ISOLATED LYMPHOID AGGREGATIONS IN THE MUCOSA OF THE SMALL INTESTINE

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ABSTRACT

Novel lymphoid structures which may be sites of T-cell differentiation have been identified in rat and mouse small intestine. These structures have been designated as lymphocyte-filled villi (LFV). They are present in conventional and in mutant mice (nude, scid mice, RAG-1, LTα, LTβ, TNF α and TNF/LT knockout mice). Similar structures have been identified in the small intestine from Syrian hamsters.

The main population of lymphocytes in LFV in mice, expressed the CD45 and Thy-1 antigens. The majority of them did not stain with antibodies against either T cell (CD4, CD8, CD3, α/βTCR, γ/δTCR), B cell (B220 and anti-Ig) or natural killer (NK1.1) markers. They were located in the centers and bases of LFV and they expressed the IL-2Rα and the antigens TSA-1, Sca-2, HSA and Pgp-1. They were sensitive to hydrocortisone and a significant proportion of them were actively dividing cells.

A subset of $CD4^+$ cells was identified in the center of LFV. The lack of CD3 expression implies that they were not mature $CD4^+$ T cells. These $CD4^+$ cells were $Sca\text{-}2^+$, $TSA\text{-}1^+$ and $IL\text{-}2R^+$ and they may be early committed T cell progenitors.

Large non-lymphoid cells with irregular morphology were identified in LFV. They bear the surface markers CD11c and MHC class II molecules and they are believed to be dendritic cells. They were present in subepithelial region and also between the lymphocytes.

This thesis explored the hypothesis that structures similar to lymphocyte-filled villi in rats and mice are present in the human small intestine. Resection specimens of apparently normal human small intestine have been examined histologically and by immuno-histochemistry. Structures that resemble rodent LFV were identified in all of the specimens. The LFV contained MHC class II-positive dendritic cells, a majority of memory T cells, a variable B cell component and no evidence of immature lymphocytes

that expressed either c-kit or CD1a. The absence of HEV in these structures suggests that they are not sites of lymphocyte recirculation. LFV in adult humans do not appear to be sites of primary T cell development.

Two other isolated lymphoid aggregations (isolated lymphoid follicles and submucosal lymphoid aggregations) were also identified in these specimens. They have been shown to be components of a single structure. The complete structure contains a B cell follicle, T cells with mainly memory (CD45RO-positive) phenotype, high endothelial venules and no detectable population of immature lymphocytes. These structures appear to be related to Peyer's patches.

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