

Neo-lymphoid aggregates in the adult liver can initiate potent cell-mediated immunity

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Subcutaneous immunization delivers antigen (Ag) to local Ag-presenting cells which subsequently migrate into draining lymph nodes (LNs). There, they initiate the activation and expansion of lymphocytes specific for their cognate Ag. In mammals, the structural environment of secondary lymphoid tissues (SLTs) is considered essential for the initiation of adaptive immunity. Nevertheless, cold-blooded vertebrates can initiate potent systemic immune responses even though they lack conventional SLTs. The emergence of lymph nodes provided mammals with drastically improved affinity maturation of B cells.

We combined the use of different strains of alymphoplastic mice and T-cell migration mutants with an experimental paradigm in which the site of Ag-delivery is distant from the site of priming and inflammation. We demonstrate that in mammals SLTs serve primarily B cell priming and affinity maturation, while the induction of T cell-driven immune responses can occur outside of SLTs. We found that mice lacking conventional SLTs generate productive systemic CD4- as well as CD8-mediated responses, even under conditions in which draining LNs are considered compulsory for the initiation of adaptive immunity.

I will describe an alternative pathway for the induction of cell-mediated immunity (CMI), in which Ag-presenting cells sample Ag and migrate into the liver where they induce neo- lymphoid aggregates. These structures are insufficient to support affinity maturation and class-switching, but provide a novel surrogate environment for the initiation of CMI.

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