

Systems immunological analysis of lymph node structure and function in viral infection

Burkhard Ludewig, Qian Chai, Christian Perez Shibayama, Cristina Gil Cruz, Mario Novkovic

Peripheral lymph nodes (PLNs) perform three central functions as a structural interface between the innate and adaptive immune systems: first, sentinel PLNs retain microbial-derived antigen (Ag) from the periphery arriving via afferent lymphatic vessels, therefore preventing the further spread into adjacent tissue. Second, macrophages and dendritic cells (DCs), which phagocytose microbial-derived Ag from peripheral sites, present Ag to passing lymphocytes within sentinel PLNs. During inflammation, PLNs typically undergo substantial morphological changes in size, blood and lymph vascularization, cell number and subset composition, and cytokine levels. As a consequence, the numbers of blood and lymphatic endothelial cells, as well as stromal cells of the T cell zone and of B cell follicles increase to accommodate the rising influx of lymphocytes and influence the outcome of immune responses. Third, the lymphoid microenvironment and the T cell – DC interactions regulate the activation or tolerance induction of Ag-specific lymphocytes, as well as the further survival and differentiation of these cells. Here, we propose to use novel stromal mutant mouse models, dynamic in vivo imaging of cellular interactions by two-photon microscopy (2PM) and cutting-edge mesoscopic imaging methods (Optical projection tomography, OPT and selective plane illumination microscopy, SPIM) created during the first Sinergia funding period (2009-2012) to address the role for stromal cells during adaptive and innate immune responses. Importantly, we will apply a comprehensive systems biology approach for mathematical modelling of high-resolution imaging data and functional analysis of PLN structure and its immunological relevance.

keywords

Lymph Node, Viral Infection, stromal cells

project partner

Prof. Burkhard Ludewig, Institut für Immunbiologie, Kantonsspital St. Gallen

Dr. James Sharpe, Systems Analysis of Development Laboratory Centre for genomic Regulation, Barcelona

type of project

fundamental research

status

completed

start of project

2012

**end of project
project manager**

2016
Dr. Jens Volker Stein