Abstract

Tolerance to “self” is the fundamental property of the immune system and its breakdown can lead to autoimmune diseases. In order to eliminate self-reactive T-cells during their development in thymus (central tolerance), Aire promotes the expression of peripheral self-antigens in medullary thymic epithelial cells (mTECs). Recently, Aire was suggested to fulfil a similar function in rare lymph node and spleen cells (peripheral tolerance). However, the detection, characterization and function of these extrathymic Aire-expressing cells is still obscure. The main objective of presented thesis was to investigate if Aire positive cells are also present in other lymphoid as well as non-lymphoid tissues. Using two independent mouse transgenic models we identified the Aire-reporter expressing cells in several lymphoid tissues such as Peyer´s patches, spleen and bone marrow as well as in one non-lymphoid organ, the lungs. We show here that based on the expression of B220, EpCAM and CD11c markers these heterogenic cells consist of at least five phenotypically distinct subpopulations, and with the exception of those from lungs, all of them are strictly of hematopoietic origin. This study also demonstrates that Aire on protein level is predominantly expressed by one of these subpopulations with CD45⁺MHCII⁺B220⁻CD11c⁻EPCAM⁻ phenotype and thus the study provides detail phenotypic characterisation of Aire-protein expressing cells in the immune periphery. We have also demonstrated that peripheral Aire-expressing cells possess the capacity to produce the set of TRAs which largely overlaps with that of mTECs. This study thus brings a new perspective to Aire-regulated peripheral immune tolerance and contributes to better understanding of cellular and molecular events that prevent autoimmunity.

Key words:

Aire, Aire-expressing cells, autoimmunity, immune tolerance