

Thymic studies

Investigations into the effects of childhood thymectomy, and characterization of thymic B cells and Hassall's corpuscles

Akademisk avhandling

Som för avläggande av medicine doktorexamen vid Sahlgrenska akademien, Göteborgs universitet kommer att offentligens försvaras i föreläsningssalen våning 3, Guldhedsgatan 10A, Göteborg
Tisdagen den 14e maj, klockan 13.00

av Christina Lundqvist

Fakultetsopponent:

Professor Ludger Klein

Ludwig-Maximilians-Universität, Tyskland

Avhandlingen baseras på följande delarbeten

- I. Gudmundsdóttir J*, Lundqvist C*, Ijspeert H, van der Slik E, Óskarsdóttir S, Lindgren S, Lundberg V, Berglund M, Lingman-Framme J, Telemo E, van der Burg M, Ekwall O. **T-cell receptor sequencing reveals decreased diversity 18 years after early thymectomy.** *J Allergy Clin Immunol.* 2017 Dec;140(6):1743-1746.e7. doi: 10.1016/j.jaci.2017.08.002. Epub 2017 Sep 1. * These authors contributed equally to this work.
- II. Lundqvist C*, Camponeschi A*, Visentini M, Telemo E, Ekwall O[‡], Mårtensson IL[‡]. **Switched CD21-/low B cells with an antigen-presenting phenotype in the infant thymus.** *J Allergy Clin Immunol.* 2018 Nov 30. pii: S0091-6749(18)31721-4. doi: 10.1016/j.jaci.2018.11.019. * These authors contributed equally to this work. [‡] These authors contributed equally to this work.
- III. Lundqvist C, Lindgren S, Cheuk S, Lundberg V, Berglund M, Thörn K, Telemo E, Ekwall O. **Characterization of Hassall's corpuscles in the human thymus.** *Manuscript*

**SAHLGRENSKA AKADEMIN
INSTITUTIONEN FÖR MEDICIN**



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Abstract

This thesis focuses on the human thymus, a primary lymphoid organ responsible for the maturation of T cells. Progenitors arrive from the bone marrow and start to randomly assemble their T cell receptor (TCR) followed by a thorough selection process in which the TCR is tested for functionality and autoreactivity. In the selection process, also T regulatory cells that can maintain tolerance by acting immunosuppressive are generated from subset of the autoreactive T cells. Only around 3% of the progenitors that enter the thymus leave as mature T cells. The thymus is most active during childhood. Starting at puberty the thymus gradually involutes, but even though only a fraction of its original capacity eventually remains it is functional throughout life.

In **paper I** we investigated the effect of early thymectomy on the diversity of the TCR in the peripheral T cell pool. We followed up on thymectomized children 18 years after thymectomy by analyzing peripheral blood samples. Thymectomized children showed reduced diversity of the T cell receptor repertoire in the periphery compared with controls.

Paper II focuses on thymic B cells, a small population that while consisting of less than 1% of the total cell count in the thymus, covers a relatively large area of the medulla. The thymic B cells displayed a mature phenotype and expressed high levels of co-receptors for T cell communication and the transcription factor AIRE, which would imply a role in the T cell selection process.

Paper III aims to characterize the Hassall's Corpuscles. Analyses showed an increasing similarity with skin epidermis the more differentiated and closer to the Hassall core the cells were located. The center, devoid of nuclei, also contained bacterial defense proteins, further emphasizing similarity to the skin. The mTEC differentiation is thought to be influenced by the expression of the *AIRE* gene. Comparisons between Down syndrome thymus (three copies of *AIRE*) and control thymus showed larger corpuscles in the former, perhaps due to a higher turn-over and differentiation of mTECs than in control tissue. In mouse models in which the *Aire* gene is knocked out, the corpuscle-like structures in the thymus were fewer and smaller, and the skin was thinner.

Keywords: thymus, thymectomy, TCR, B cells, APC, Hassall's corpuscles, AIRE

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