Göteborg, 2022

A Study of Eosinophils – From the Human Thymus to Eosinophilic Esophagitis

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademin, Göteborgs universitet kommer att offentligen försvaras i föreläsningssalen, Klinisk Mikrobiologi, Guldhedsgatan 10A, Göteborg, fredagen den 1 april 2022, klockan 09:00

av
Sofie Albinsson Högberg

Fakultetsopponent:
Professor Florence Roufosse
Université Libre de Bruxelles, Belgien

Avhandlingen baseras på följande delarbeten

I. Lingblom C, Albinsson S, Johansson L, Larsson H, Wennerås C. **Patient-Reported Outcomes and Blood-Based Parameters Identify Response to Treatment in Eosinophilic Esophagitis.** Dig Dis Sci. 2021 May;66(5):1556-1564.

II. Albinsson S, Tuomi L, Wennerås C, Larsson H. **Patient-Reported Dysphagia in Adults with Eosinophilic Esophagitis: Translation and Validation of the Swedish Eosinophilic Esophagitis Activity Index.** Dysphagia. 2021 Mar 8.

III. Albinsson S, Lingblom C, Johansson L, Larsson H, Wennerås C. **Eosinophils release galectin-10 and co-localize with T cells in eosinophilic esophagitis** (submitted manuscript).

IV. Albinsson S*, Lingblom C*, Lundqvist C, Telemo E, Ekwall O, Wennerås C. **Eosinophils interact with thymocytes and proliferate in the human thymus.** Eur J Immunol. 2021 Jun; 51(6):1539-1541.
*The authors contributed equally

V. Albinsson S*, Lingblom C*, Lundqvist C, Hennings V, Telemo E, Ekwall O, Wennerås C. **Phenotypic and functional studies of eosinophils in the human thymus** (in manuscript).
*The authors contributed equally

SAHLGRENSKA AKADEMIN
INSTITUTIONEN FÖR BIOMEDICIN

GÖTEBORGS UNIVERSITET

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A Study of Eosinophils – From the Human Thymus to Eosinophilic Esophagitis

Sofie Albinsson Högberg

Avdelningen för Infektionssjukdomar, Institutionen för Biomedicin, Sahlgrenska akademin, Göteborgs universitet, Sverige, 2022

Abstract

Eosinophils are cells of the innate immune system. They primarily reside within tissues and are most numerous in the gastrointestinal tract but are absent from the healthy esophagus. During the inflammatory disease eosinophilic esophagitis, eosinophils infiltrate the esophagus but their function is unknown. Eosinophils also reside within the human thymus, although their function within this organ dedicated to T cell development is unclear. This thesis is a study of eosinophils resident within the human thymus and of the disease eosinophilic esophagitis. The aim was to increase knowledge on the eosinophil granulocyte and to improve healthcare of patients afflicted with eosinophilic esophagitis. In paper I, molecular patterns of eosinophils in the blood of patients with eosinophilic esophagitis were combined with patient-reported outcomes to yield a multivariate model capable of separating patients who had responded to topical corticosteroid treatment from patients who did not respond to treatment. The use of such multivariate models based on less invasive methods than endoscopic procedures to evaluate success of therapy could improve patient care and patients' quality of life. Paper II was also focused on the advancement of patient care. The first Swedish instrument specifically developed for assessment of symptom severity of eosinophilic esophagitis was translated and validated in order to improve clinical assessment of the disease among Swedish adults. In paper III, esophageal eosinophils found in biopsies from patients with eosinophilic esophagitis were studied using fluorescent immunohistochemistry. These analyses revealed associations between eosinophils and CD4+ T cells, the presence of CD16+ "suppressive" eosinophils, and massive release of extracellular galectin-10 within the esophageal mucosa. Tissue resident eosinophils were further studied in human thymus of thymectomized children in papers IV and V. In paper IV, eosinophils were studied using fluorescent immunohistochemistry to investigate their maturity, distribution, and cellular interactions within the thymus. Immature and proliferating eosinophils were found, as well as mature cells, and the primary location of thymic eosinophils was in the corticomedullary junction. In paper V, thymic eosinophils were phenotypically characterized using cytometry by time-of-flight and their interactions with thymocytes were studied by co-culture experiments of fluorescence-activated cell sorted thymic eosinophils and thymocytes of the double-positive (CD4+CD8+), CD4 single-positive, and CD8 single-positive stages. The thymic eosinophils displayed a distinct phenotype compared to blood eosinophils and the thymic eosinophils were capable of directing thymocytes toward the CD4 single-positive phenotype. In this thesis, T cell suppression is presented as a possible function of eosinophils in eosinophilic esophagitis and thymic eosinophils are shown to be specialized cells that can affect the thymocyte development process.

Keywords: eosinophil, eosinophilic esophagitis, galectin-10, human, patient-reported outcome, T cell, thymocyte, thymus

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