Medical University of Graz

Phenotypic changes of eosinophil granulocytes in aging

Summary

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Supervisor:	Prof. Dr. Akos Heinemann
Availability:	This position is available.
Offered by:	Medical University of Graz
Application deadline:	Applications are accepted between February 15, 2022 00:00 and March 28, 2022 23:59 (Europe/Zurich)

Description

Background:

Aging is associated with derangements in immune competence, broadly referred to as immunosenescence, whose hallmarks include persistent low-grade inflammation (also known as inflammaging), increased susceptibility to infection or cancer, compromised ability to effectively respond to new antigens, increased likelihood of developing autoimmunity and defective wound healing (1). Eosinophils are mostly known for their cytotoxic effects in parasitic infections and allergic inflammation, such as bronchial asthma. Recently, a novel role of eosinophils in regulating tissues homeostasis and immunomodulation and a new subset coined as ‘regulatory eosinophils’ have been uncovered (2), along with dysregulated eosinophil responses in white adipose tissue as a conserved aging phenotype in humans and mice, and eosinophils from young conferring immunological and physical fitness in aged mice (3).

Hypothesis and Objectives:

In this project, we will address the hypothesis that eosinophils in aging individuals show signs of senescence and are functionally compromised, which reflects their failed metabolic adaptation.

Approaches and methods:

Using advanced methodologies (4) we will address the following questions: i) Do circulating eosinophils isolated from aged blood donors show distinct phenotypic/functional profiles relative to young donors’ cells, particularly regarding their migratory, regulatory and tumor-suppressive capacity? ii) Does plasma from aged individuals show markers of eosinophil dysregulation or dysfunctionality, and altered profiles of eosinophil regulatory molecules? iii) Are metabolic derangements detectable in eosinophils from aged individuals and is there a correlation with their functionality? iv) Is manipulation of altered metabolic pathways in eosinophils a suitable approach to correct their functional impairment?

The student will isolate peripheral blood eosinophils from young and aged donors, will perform a wide range of functional assays (migration, apoptosis, degranulation) and metabolic studies (Seahorse), and establish profiles of secreted cytokines and surface markers. The effects of ‘young’ and ‘aged’ eosinophils on macrophage polarization and cancer cell proliferation and survival will be assessed in co-culture studies. The results of this study will teach us how the functionality and metabolic phenotype of circulating eosinophils are altered in aging and create the possibility that selective targeting of eosinophil metabolism may be of therapeutic benefit in metabolic homeostasis and cancer immunity.

References:

1. Lian J, et al. Immunosenescence: a key player in cancer development. J Hematol Oncol. 2020;13(1):151.

2. Weller PF, et al. Functions of tissue-resident eosinophils. Nat Rev Immunol. 2017;17(12):746-760.

3. Brigger D, et al. Eosinophils regulate adipose tissue inflammation and sustain physical and immunological fitness in old age. Nat Metab. 2020;2(8):688-702.

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4. Theiler A, Heinemann A, et al. Butyrate ameliorates allergic airway inflammation by limiting eosinophil trafficking and survival. J Allergy Clin Immunol. 2019 Sep;144(3):764-776.