Medical University of Graz

Polyunsaturated fatty acids and allergic lung inflammation

Summary

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Supervisors:	PD Dr. Gunther Marsche Dr. Katharina Jandl
Availability:	This position is available.
Offered by:	Medical University of Graz
Application deadline:	Applications are accepted between March 24, 2021 00:00 and May 05, 2021 23:59 (Europe/Zurich)

Description

Background

Airway eosinophilia is present in 50 to 60 % of asthmatics. Eosinophils are regarded as key factors for asthma exacerbation (1) and lung connective tissue remodeling (2). However, there have been recent discoveries illuminating important homeostatic functions of eosinophils in the local environment (3). Therefore, novel treatment strategies aimed at attenuating the overactivation of eosinophils rather than their complete eradication may be beneficial.

Hypothesis and objectives

Dietary n-3 polyunsaturated fatty acids (PUFAs) possess potent immunomodulatory properties (4), and are precursors of pro-resolving lipid mediators such as resolvins. In adults diagnosed with asthma, eicosapentaenoic acid blood levels were associated with a lower risk of non-specific bronchial hyperresponsiveness (5), suggesting a regulatory activity in asthma development. However, direct effects of PUFAs on eosinophil recruitment and activation remain not well understood. In this project, the student will investigate effects of major PUFAs on human primary blood eosinophil effector responses and in models of *in vivo* chemotaxis and ovalbumin-induced allergic lung inflammation.

Methodology

Techniques that the student will acquire include flow cytometry to determine the expression of receptors and adhesion molecules, cell adhesion assays under flow, Western blot, multiplex ELISA to measure cytokine release, immunofluorescence microscopy, assays to detect reactive oxygen species, phagocytosis, degranulation and eosinophil-endothelial adhesion under flow. Endothelial barrier function will be investigated by electrical impedance measurements. The student will learn how to isolate leukocytes from peripheral blood and to isolate lung endothelial cells. Functional responses of eosinophils and endothelial cells will be investigated in assays of shape change, integrin up-regulation, chemotaxis and Ca2+ signaling. *In vivo* effects of PUFAs on chemotaxis of eosinophils will be assessed in IL-5 Tg mice. Ovalbumin-induced lung inflammation will be examined in Balb/c mice.

References

1. Haldar P, Brightling CE, Hargadon B, et al. Mepolizumab and exacerbations of refractory eosinophilic asthma. *N Engl J Med*. 2009;360(10):973-984.
2. Hirota N, Martin JG. Mechanisms of Airway Remodeling. *Chest*. 2013;144(3):1026-1032.
3. Weller PF, Spencer LA. Functions of tissue-resident eosinophils. *Nat Rev Immunol*. September 2017.
4. Hutchinson AN, Tingö L, Brummer RJ. The potential effects of probiotics and ω-3 fatty acids on chronic low-grade inflammation. Nutrients 2020, 12, 1–15.

5. Adams, S., Lopata, A., Smuts, C., Baatjies, R., Jeebhay, M. (2018). Relationship between Serum Omega-3 Fatty Acid and Asthma Endpoints. Int. J. Environ. Res. Public Health 2018, 16 (1),