Medical University of Graz

Endotyping of Chronic Rhinosinusitis according to nasal mucus proteomic profile

Summary

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Supervisors:	PD Dr. Peter Valentin Tomazic Dr. Valentina Biasin
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:

Chronic Rhinosinusitis (CRS) is an inflammatory disease of the nose and paranasal sinuses and may affect the upper airways in severe cases. In the EPOS guidelines (1) CRS is diagnosed by at least two of the following major symptoms present for at least 12 weeks: nasal congestion, nasal discharge, pain or facial pressure or impaired sense of smell. There are two major types of CRS: presence of nasal polyps (CRSwNP)or no nasal polyps (CRSsNP). However, clinical classification by those two phenotypes does not reflect the variety of CRS endotypes which are related to different cytokine profiles, and often lead to conservative and surgical failures and to recurrence.

Hypothesis and Objectives:

Our recent data provide evidence that nasal mucus harbours potential protein biomarkers that potentially influence allergic diseases particularly in terms of immune mechanisms and epithelial barrier function. On a functional level, these mucus proteins confer reduced defence (in allergics) or protective mechanisms against allergens (in healthy controls) as analysed by proteomics and denoted by biological processes.

In this study we will test the hypothesis that **proteomic profiling help to endotype CRS and individualise disease management.** In contrast to current studies that mainly focus on epithelial (and subepithelial) cytokines we will address nasal mucus proteins since it is known that key players in CRS such as eosinophils reside significantly more abundantly in nasal mucus (through epithelial transgression) than in epithelium itself. Using cluster analysis of nasal mucus proteins in CRS we will stratify various disease endotypes and shed light on why severity or therapeutic outcomes differ significantly between these groups despite phenotypical similarities. In addition, bronchial lavage fluid may be analysed to elucidate BAL proteome in order to further classify the most severe forms of CRSwNP known as sinubronchial syndrome.

Methodology:

The PhD student will learn how to perform proteomic analyses i.e. protein quantification through high-pressure liquid chromatography and subsequently mass spectrometric analysis **(Year 1).** For cytokine analysis the PhD student will apply targeted MS (parallel reaction monitoring – PRM), and immunoassays (cytoflex) **(Year 2-3)**. CRS subgroup classification (1: CRSwNP minor eosinophils [Eos] in mucus, 2: CRSwNP moderate Eos, 3: CRSwNP high number of Eos, 4: CRSsNP and 5: controls) will be conducted under supervision according to symptoms, nasal endoscopy, pathology and CT scan analysis. The PI will obtain mucus by nasal suction as well. Further sample processing and preparation will be done by the PhD student. Apart from the experimental part the student will learn how to annotate proteins, search protein databases and interpret mass spectra, and perform complex statistical analyses of the data. Correlation analysis with clinical data will be performed **(Year 4)**.

References:

1. Fokkens WJ, Lund VJ, Hopkins C, et al.Rhinology. European Position Paper on Rhinosinusitis and Nasal Polyps 2020. Feb 20;58(Suppl S29):1-464

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