Nayak *et al.*: *Intrinsic Activity*, 2023; **11**(Suppl.1):A2.24
doi:10.25006/IA.11.S1-A2.24
published online: 22 September 2023

INTRINSIC ACTIVITY

27th Scientific Symposium of the Austrian Pharmacological Society

Vienna, 29–30 September 2023

MEETING ABSTRACT

A2.24

The role of JAK-STAT signaling in neutrophilic airway inflammation

Barsha Baisakhi NAYAK[1], Iris RED[1], Julia TEPPAN[1], Juliana SCHWANZER[1], Ilse LANZ[1], Melanie KIENZL[1], Philipp DOUSCHAN[2,3], Ákos HEINEMANN[1], Eva BÖHM[1,*]

[1]*Division of Pharmacology, Otto Loewi Research Center for Vascular Biology, Immunology and Inflammation, Medical University of Graz, Austria;* [2]*Ludwig Boltzmann Institute for Lung Vascular Research, Graz, Austria;* [3]*Division of Pulmonology, Department of Internal Medicine, Medical University of Graz, Austria*

Background: Neutrophilic inflammation is a common feature of chronic inflammatory respiratory diseases and is associated with corticosteroid resistance. The IL-23–T_h17 axis is a key contributor to airway neutrophilia. IL-23 from antigen-presenting cells (APCs) binds to its receptors (on naïve T cells), associated with TYK2 and JAK2 leading to T_h17 polarization. IL-17, a T_h17 cytokine, binds to its receptors on structural and immune cells, which results in neutrophil activation. Despite clinical reports suggesting the changes in the IL-23 level in the serum of patients with neutrophilic inflammation, the direct effects of the cytokines are unclear. We aim to study the potential role of JAKs and cytokines involved in the IL-23–T_h17 axis.
Methods: For *in vitro* studies, functional assays like migration, reactive oxygen species (ROS), CD11b were performed on neutrophils. Neutrophils were pretreated with IL-17, IL-23 and vehicle (plus buffer) and stimulated with C5A to study ROS production and CD11b expression. Migration assays were performed with IL-17A and IL-23 as stimulants as well as pretreatments. Whole blood stainings were performed to study TYK2 and JAK2 expression in the various immune cell populations in the whole blood of healthy non-allergic and allergic donors using flow cytometry. For *in vivo* studies, mice were intranasally injected with IL-23 for 3 days and the infiltration of the immune cell population in bronchoalveolar lavage (BAL) and blood was measured using flow cytometry.
Results: IL-17 and IL-23 pretreatments increased ROS. IL-17A increased the migration of neutrophils and enhanced IL-8-stimulated chemotaxis. IL-17A pretreatment significantly increased CD11b in neutrophils. Non-allergic donors showed significantly higher expression of TYK2 and JAK2 compared to allergic donors. In the *in vivo* studies, we observed increased neutrophil count in the BAL fluid with the intranasal treatment of IL-23.
Discussion: Our results indicate that IL-17 and IL-23 might be potential players in neutrophilic lung inflammation, affecting neutrophil migration and ROS production. TYK2 and JAK2 are differentially expressed in immune cell populations from allergic donors compared to healthy controls. From our preliminary data, we conclude that IL-17 and IL-23 directly affect neutrophil functions. In further experiments we plan to evaluate the neutrophil function and JAK-STAT expressions in samples from patients with COPD and non-allergic asthma.
Keywords: neutrophilic inflammation – corticoid-steroid resistance – JAK-STAT signaling

*Corresponding author e-mail: *eva.sturm@medunigraz.at*