Schwanzer *et al.*: *Intrinsic Activity*, 2023; **11**(Suppl.1):A2.14
doi:10.25006/IA.11.S1-A2.14
published online: 22 September 2023

27th Scientific Symposium of the Austrian Pharmacological Society

Vienna, 29–30 September 2023

MEETING ABSTRACT

A2.14

The role of a basement membrane fragment on neutrophil function

Juliana SCHWANZER[1], Grażyna KWAPISZEWSKA[2,3,4], Ákos HEINEMANN[1], Katharina JANDL[1,2,*]

[1]*Division of Pharmacology, Otto Loewi Research Center, Medical University of Graz, Austria;* [2]*Ludwig Boltzmann Institute for Lung Vascular Research, Graz, Austria;* [3]*Division of Physiology, Otto Loewi Research Center, Medical University of Graz, Austria;* [4]*Institute for Lung Health, Justus Liebig University, Giessen, Germany*

Background: During acute inflammation in the lung, neutrophil granulocytes form the first line of immune defense. Despite their beneficial role, uncontrolled and excessive recruitment and consequently activation may further contribute to tissue damage. Proteolytic degradation of the basement membrane, a specialized compartment of the extracellular matrix, is a common feature in various acute and chronic lung diseases and can lead to the generation of novel, bioactive fragments. These so-called matrikines have functions distinct to their parent molecule and their function on neutrophils is until now mostly unknown.
Methods: We hypothesize that pentastatin (PS)-1, a matrikine derived from type IV collagen α5, modulates neutrophil function by acting as a damage-associated molecular pattern (DAMP), thus contributing to continuous inflammatory response within the lung.
Results: To investigate the effect of PS-1 on neutrophils, functional assays *in vitro* were carried out via flow cytometry such as determination of shape change, chemotaxis and apoptosis assays. To look further into involved pathways, western blot analysis was performed.
Discussion: PS-1-concentrations ranging from 3–50 µg/ml induced neutrophil shape change and migration, indicating activation of the cells upon treatment. At lower concentrations (3–12 µg/ml) of PS-1 an increased pro-survival effect was observed, whereas the highest concentration exerted a toxic effect upon neutrophils. By inhibiting integrin αLβ2, αMβ2, αXβ2 receptors, migration was decreased, suggesting them as cognate receptors. Treatment with PS-1 induced ERK1/2 phosphorylation as determined by western blot analysis. Using a MEK1/2 inhibitor (U0126, 20 µM), reduced migration of neutrophils towards lower concentrations of PS-1 was observed, indicating an involvement of the ERK/MAPK pathway. We could demonstrate that PS-1 leads to neutrophil activation. Future experiments will identify further downstream signaling partners and upstream receptors.
Acknowledgements: K.J. was supported by the Austrian Society for Pulmonology (Wissenschaftsförderung) and the Medical University of Graz (Start fund).
Keywords: neutrophil granulocytes – basement membrane – matrikines – extracellular matrix

*Corresponding author e-mail: *katharina.jandl@medunigraz.at*