Proceedings of the British Pharmacological Society at http://www.pA2online.org/abstracts/Vol10Issue2abst011P.pdf

Alarin as a novel regulator of polymorphonuclear neutrophils

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Primary afferent nerve fibers control cutaneous blood flow and vascular permeability by releasing neuropeptides that in turn can evoke inflammation. These vascular reactions and the additional recruitment and activation of leukocytes are the key features of neurogenic inflammation. Alarin, a recently discovered bioactive neuropeptide of the galanin-peptide family, has been shown to inhibit neurogenic inflammation in the skin. Therefore, we aimed to elucidate if this peptide is also involved in the recruitment and physiology of polymorphonuclear leukocytes/neutrophils (PMNs).

In PMNs, isolated from healthy individuals, alarin exposure increases the release of myeloperoxidase, which is a marker of degranulation of azurophil/ primary granules that occurs during PMN activation. In addition, we found that alarin boosts lactoferrin and metalloproteinase 9 (MMP 9) activity, indicating that it can mobilize specific secondary (lactoferrin) and gelatinase granules, which are secreted during cell activation. FACS analysis revealed that on human PMNs and the PMN-like cell line HL-60, alarin also enhances the expression of the beta-2-integrin CD11b, a marker of secondary and azurophil granules, that are activated during cellular activation and adhesion. In accordance with these findings, we were able to demonstrate that treatment with alarin (10 µM) results in significant changes in PMN adherence.

Taken together, we have identified and characterized alarin as another regulator for human PMN activity, implying possible functions in acute inflammatory responses.

Funding: Austrian Research Promotion Agency (FFG, 822782/THERAPEP)