Galanin is a potent activator of neutrophils

Sabine Schmidhuber[1], Andreas Lang[1], Jason McDougall[3], Bernhard Brodowicz[1], Roland Lang[2], Barbara Kofler[1]. *[1]Laura Bassi Centre of Expertise-THERAPEP, Research Program for Receptor Biochemistry and Tumor Metabolism , Department of Pediatrics, Paracelsus Medical University, Salzburg, Austria, [2]Department of Dermatology, Paracelsus Medical University, Salzburg, Austria, [3]Department of Physiology and Biophysics, University of Calgary, Calgary, Canada*

Primary afferent nerve fibers control cutaneous blood flow and vascular permeability by releasing neuropeptides, such as galanin, that in turn can evoke inflammation. These vascular reactions and the additional recruitment and activation of leukocytes are the key features of neurogenic inflammation.

Recently, we were able to show that accumulation of polymorphonuclear neutrophils (PMNs), upon induction of different inflammatory stimuli in the skin, is disrupted in galanin knockout mice (Gal-KO). Here we tested the hypothesis that galanin is directly influencing PMN function *in vivo* and *in vitro*.

Co-injection of galanin (10 nmol) along with the inflammatory stimulant carrageenin in the skin of Gal-KO was able to rescue PMN accumulation in the skin to levels comparable to wild type mice. Local administration of galanin to inflamed knee joints caused a dose-dependent increase in PMN rolling velocity and adhesion within the synovial microvasculature in wild-type mice.

In human PMNs, isolated from healthy individuals, galanin exposure dose dependently increased PMN adherence. Furthermore, the surface expression of the beta-2-integrin CD11b, CD66b and CD63, markers of secondary and azurophil granules, respectively, that are activated during cellular activation and adhesion, are significantly upregulated already 10 minutes after galanin treatment.

Galanin (100 nM) was also able to induce the secretion of the matrix metalloproteinase MMP-9, indicating that galanin also mobilizes tertiary granules of PMNs.

These activation of PMNs by galanin is possibly mediated by the galanin receptor subtypes GalR2 and/or GalR3, which are expressed in human PMNs.

Here, we have identified and characterized galanin as another crucial regulator for PMN recruitment, rolling and adhesion, establishing this peptides as another important partaker in inflammatory processes.

Funding: Austrian Science Fund (FWF, P14906); Austrian Research Promotion Agency (FFG, 822782/THERAPEP) and Federation of European Biochemical Societies (Return to Europe-Fellowship).