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MEETING ABSTRACT

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Galanin is a potent modulator of cytokine/chemokine expression of human macrophages

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Background: The regulatory peptide galanin (GAL) is broadly distributed in the central/peripheral nervous system but also in non-neuronal tissues. GAL exerts its diverse physiological functions via three G protein-coupled receptors (GAL_{1-3}-R). Regulatory peptides are important players in the cross-communication between the nervous and the immune system and are in focus as therapeutics for diverse inflammatory diseases. Various studies on immune cells and inflammatory animal models revealed either a pro- or an anti-inflammatory role of GAL, suggesting a complex regulation of GAL signaling at the tissue and cellular level. However, the microenvironment of tissues upon an immune challenge is dynamic and depends on the type of stimulus and duration, and might be important for the specific actions of GAL during inflammation. Thus, we aimed to elucidate the role of GAL in macrophages.

Methods: CD14+ monocytes were isolated from human buffy coats and differentiated for 6 days with GM-CSF (M0-GM-Mφ) or M-CSF (M0-M-Mφ), without or with GAL co-treatment. Differentiated cells were treated with GAL alone for 20 hours or they were polarized with IFNγ+LPS, IL-4, or IL-10 to generate M1-GM-Mφ-, M2a-M-Mφ-, or M2c-M-Mφ-type macrophages, respectively. Polarization was also performed with and without GAL co-treatment. Relative mRNA expression levels of inflammatory cytokine and chemokines, and the GAL system were analyzed by qPCR. Protein levels of cytokines and chemokines, and GAL in cell culture supernatants were analyzed by ELISA.

Results: Macrophage subtypes exhibited varied GAL secretion and a distinct balance of GAL_1-R and GAL_2-R expression. GAL itself affected the cytokine/chemokine expression profile of macrophages differently, depending on differentiation and polarization and mainly modulated the expression of chemokines (CCL2, CCL3, CCL5 and CXCL8) and anti-inflammatory cytokines (TGF-β, IL-10 and IL-1Ra) especially in type-1 macrophages. Cytokine/chemokine expression of IFNγ+LPS-polarized macrophages were upregulated, whereas cytokine/chemokine expression levels of unpolarized macrophages were downregulated upon GAL treatment after 20 hours.

Discussion: These results demonstrate that galanin can regulate macrophage chemokine and cytokine secretion. However, a more detailed analysis of the effect of galanin on chemokine secretion of macrophages will be reported.

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