Glucocorticoids: **GUARDIANS** of the inflammatory processes

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The resolution of inflammation is an active, coordinated and tightly controlled process where glucocorticoids (GCs) play a major role. GCs are well known therapeutics to repress inflammation and are widely prescribed drugs to combat inflammatory disease like rheumatoid arthritis, allergies and acute lung injury. GCs are guardians of the inflammatory processes and promote the resolution of inflammation. After binding of GCs to the ubiquitously expressed glucocorticoid receptor (GR), the ligand bound GR translocate from the cytoplasm into the nucleus. In the nucleus, the GR act as a transcription factor and can either mediate it´s function by repressing pro-inflammatory gene expression as a GR monomer or inducing genes mainly responsible for side effects as a GR dimer. The beneficial anti-inflammatory effects thought to be mainly mediated through the GR monomer are accompanied by severe adverse effects (diabetes, liver steatosis, osteoporosis, muscle atrophy) thought to be mainly mediated by the GR dimer. However, this hypothesis could not be confirmed in mice lacking the GR dimerization and was reassessed.

It is of utmost importance to understand the GR action and the function of the GR in e.g. macrophages to develop specific GR ligands and treat diseases with cell-type specific applications to foster the resolution of inflammatory processes without severe side effects.

In my talk I will discuss the role of the GR monomer and dimer, as well as the function of the GR in macrophages in lipopolysaccharide mediated inflammatory models (systemic inflammation and acute lung inflammation). Surprisingly, I found that a synergy of pro- and anti-inflammatory signals in macrophages is necessary for the resolution of inflammation. Furthermore, not only GCs, also catecholamines play an important role during the inflammatory process and work in synergy with GCs to mediate anti-inflammatory effects. From all our *in vitro* and *in vivo* findings with different inflammatory models and in conditional knockout mice, we are able to suggest new therapeutic options to enhance the resolution of inflammation and thereby support the endogenous resolution phase with less severe side effects.