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A_3AR Modulations in Response to Chronic Treatment with CF101: Data from Experimental Inflammatory Animal Models

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Background: A_3 adenosine receptor (A_3AR) is over-expressed in inflammatory cells whereas normal cells show low or no receptor expression. CF101, a highly selective agonist at the A_3AR, acts as an anti-inflammatory agent via the de-regulation of the NF-κB signaling pathway. The aim of the present study is to look at A_3AR fate upon chronic treatment with CF101 in different experimental animal models.

Methods The following experimental inflammatory animal models were used: Myelin Basic Protein induced Experimental Auto-immune Encephalomyelitis, Dextran Sulfate Sodium induced colitis, Mono Iodoacetate induced osteoarthritis, Collagen induced Arthritis and adjuvant induced arthritis (AIA). CF101 (10 or 100 μg/kg) was administered orally upon onset of disease two/three times per day. Disease severity was evaluated utilizing clinical score. A_3AR, NF-κB and GATA1 expression levels were tested by Western blot analysis in protein extracts derived from inflammatory tissues and peripheral blood mononuclear cells (PBMCs).

Results A_3AR and NF-κB expression levels were directly correlated to disease severity. In all experimental animal models, A_3AR expression levels were down-regulated in the inflammatory cells shortly after CF101 administration. CF101 exerted an anti-inflammatory effect manifested by a significant decreased clinical score. In the AIA model, A_3AR and GATA1 expression levels in PBMCs were decreased 2 hours but were up-regulated 12 hours after treatment with CF101, demonstrating that receptor is recovered.

Conclusions CF101 is a potent disease modifying drug in various inflammatory animal models. A_3AR is down-regulated shortly after agonist treatment followed by receptor recovery, suggesting the receptor as an anti-inflammatory target for chronic treatment.