New gold compound shows immunosuppressive functions and leads to an amelioration of skin inflammation
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Aryl hydrocarbon receptor (AhR) mediates biological responses in a ligand-dependent way. Upon ligand binding the receptor translocates into the nucleus and acts as a transcription factor. We could show that a newly generated gold metal compound (3) binds to the AhR 100-fold stronger compared to the AhR ligand 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). To investigate the in vitro immunosuppressive function of MC3, murine CD4+ T cells were isolated and treated with 3. Treatment with MC3 showed an upregulation of C/EBPα and TGFβ1 in comparison to mock solution using real time PCR. In addition, flow cytometry analysis showed a 2-3 fold higher expression of the co-stimulatory molecule CD80 and CD86 and a 1.5 fold higher expression of the cytokine IL-10. Furthermore, the increased Treg frequency could be reversed by using an AhR antagonist or TGFβ inhibitors in vitro. The effect of MC3 was additionally investigated using an autoimmune-mouse model. Scurfy mice lack Treg control and show activation of autoimmune disease. When treated with MC3, scurfy mice showed a reduced skin thickness and a reduced infiltration of Th1- and Th2-cells. Furthermore, MC3 treatment reduced the disease score and the disease activity index (DAI). In conclusion, MC3 is a promising new compound with potential therapeutic effects in the treatment of autoimmune diseases.

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