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Content

NOVEL ARYL HYDROCARBON RECEPTOR MODULATOR PROMOTES IMMUNOSUPRESSIVE IMMUNE RESPONSE BY STIMULATING T REGULATORY CELLS IN THE GUT

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Introduction: The aryl hydrocarbon receptor (AhR) is a ligand-activated transcription factor which is highly expressed in mucosal tissues - by epithelial cells and immune cells such as Th17 $CD4^+$ and T regulatory cells (Treg). Besides its function of clearing environmental pollutants from the body, it was also revealed that AhR has immunoregulatory effects, thus becoming a potential therapeutic target for modulating the immune response. For that purpose we tested a novel synthetic AhR modulator under the code name C43.
Methods: CYP1A1 (downstream effector of AhR) activation was tested by the EROD assay. Sort-purified $CD4^+$ cells from mesenteric lymph nodes (MLN) were treated with C43 for 24 h. Zebrafish embryos were used to test the toxicity of C43. Male C57BL/6 mice orally received C43 (10 mg/kg) for 5 consecutive days, after which MLN were harvested. Phenotype and function of the cells were analyzed by flow cytometry.
Results: C43 showed mild AhR agonistic activity. After treating the sort-purified $CD4^+$ cells with C43, there was a shift in the Th17/Treg ratio in favour of the latter. C43 showed no signs of toxicity when tested on zebrafish embryos. MLN cells from mice that received C43 revealed a shift in the Th1/Treg ratio in favour of Tregs, with a documented rise of the portion of Tregs that expressed CYP1A1 in comparison with the control group of mice.
Conclusion: C43 can modulate the immune response through the intestine by promoting the immunosuppressive Treg population.

Key words: AhR; immunomodulation; gut immunity; Treg; CYP1A1

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