12th EFIS-EJI South Eastern European Immunology School (SEEIS2023)

October 20 – 23, 2023
Čiovo-Trogir, Croatia

Program and Abstracts

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14. DEVELOPMENT OF A NOVEL COMPOUND THAT UPREGULATES TREG IN THE GUT BY MODULATING ARYL HYDROCARBON RECEPTOR'S ACTIVITY

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The aryl hydrocarbon receptor (AhR) is a ligand-activated transcription factor that has an important role in regulating the immune system, with high expression in Th17 CD4+ T cells and T regulatory cells (Treg). The expression of AhR is especially important at mucosal surfaces where it is involved in balancing the immune response towards external factors. The aim of our research was to evaluate the effect on the gut immune system of a novel fluorescent indole-containing compound that was designed as a putative AhR ligand (encoded C43). By using the EROD assay, we determined that C43 has mild AhR agonistic activity. Sort-purified mesenteric lymph node (MLN) CD4+ cells were treated with C43 for 24 h and flow cytometry analysis (FCM) showed that the Treg/Th17 ratio shifted in favour of Tregs. Zebrafish embryos were used for the evaluation of potential C43 toxicity. No nephrotoxicity, hepatotoxicity or cardiotoxicity was detected, even at the highest concentrations. Next, C43 was orally administered to healthy male C57BL/6 mice for 5 consecutive days, and later its effects on the gut immune system were recorded by analyzing the MLNs. FCM unveiled a higher proportion of Treg cells that expressed CYP1A1 (downstream effector of AhR) and the ratio of Treg/Th1 shifted towards Tregs. The presence of C43 was also visualized by confocal microscopy in the small intestine lamina propria of treated animals. With such results obtained from healthy animals, C43 presents a promising compound for the treatment of inflammatory diseases that generally involve activation of the gut immune system.
Supported by the Hellenic Foundation for Research and Innovation (HFRI) (PROTECT, project no.: 991) and Ministry of Science, Technological Development and Innovations of the Republic of Serbia No. 451-03-47/2023-01/200007.

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