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ACTIVATION OF THE ARYL HYDROCARBON RECEPTOR IN VIVO PRIMES HUMAN T CELLS FOR INTERLEUKIN 22 PRODUCTION AND INHIBITS TH17 CELLS

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10.1136/ard.2010.129668y

Ligands of the aryl hydrocarbon receptor (AHR), a transcription factor mediating dioxin effects, favour Th17 cell differentiation and exacerbate autoimmunity in mice. The authors investigated how AHR ligands affect human T cell polarisation. The high affinity and stable AHR ligand dioxin as well as the natural AHR ligand FICZ induced the downstream AHR-target CYP1A1 and, without affecting interferon- γ (IFN γ), they enhanced interleukin 22 (IL22), simultaneously decreasing IL17A production by CD4 T cells. The specific AHR inhibitor CH-223191 abolished these effects. Furthermore, blockade of IL23 and IL1, important for Th17 expansion, profoundly decreased IL17A but not IL22 production. AHR agonists reduced the expression of the Th17 master transcription factor RORC/ROR γ T without affecting T-bet, GATA-3 and Foxp3. They also decreased the expression of the IL23 receptor. Importantly, AHR ligation did not only decrease the number of Th17 cells but also primed naive CD4 T cells to produce IL22 without IL17 and IFN γ . Furthermore, IL22 single producers did not express CD161, which discriminated them from the CD161-positive Th17 cells. Finally, the authors observed that lymphocytes from an individual exposed to high levels of dioxin presenting with inflammatory skin lesions were high producers of IL22 but not of IL17A. These data, which include a seminal clinical observation, provide compelling evidence that AHR activation participates in shaping human CD4 T cell polarisation, favouring the emergence of a distinct subset of IL22-producing cells involved in skin immunopathology that are independent of the Th17 lineage.