UNIVERSITY OF HOHENHEIM

Special Seminar

Wednesday, 14th of December 2022, 2 p.m.

Lecture hall G-A11

Regulation of Group 2 Innate Lymphoid Cells (ILC2s)

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Abstract

Group 2 innate lymphoid cells (ILC2s) comprise a remarkably potent source of cytokines and have been shown to be central in instructing and sustaining human type 2 immunopathologies including allergic lung inflammation and asthma. ILC2s directly sense alarmins such as interleukin (IL)-33 following allergen or microbial challenge, driving ILC2 proliferation and type 2 cytokine production. However, the precise molecular signatures of IL-33-mediated ILC2 activation remain unknown. Using an RNA-sequencing approach we revealed that IL-33 stimulation rapidly induces the expression of diacylglycerol acyltransferase 2 (DGAT2), an enzyme known catalyze triacylglycerol synthesis and lipid storage in lipid droplets. In addition, we observed that IL-33-mediated ILC2 activation leads to elevated fatty acid uptake and storage that requires activity of fatty acid binding protein 5 (FABP5) and fatty acid transporter protein 2 (FATP2). Importantly, lipidomic analysis revealed a selective role of DGAT2 in fatty acid metabolism in ILC2. Moreover, in a preclinical mouse model of allergic airway inflammation, we demonstrate that DGAT2 inhibition decreases ILC2 proliferation, lung inflammation and airway hyperreactivity. These observations highlight the crucial role of DGAT2 in ILC2 biology and ILC2-mediated lung inflammation and suggest that DGAT2 inhibitors should be considered for the treatment of type 2 immunopathologies.

Host

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