

**O02 NOD2 REGULATES THE HOST RESPONSE TOWARD MICROFLORA BY MODULATING T-CELL FUNCTION AND EPITHELIAL PERMEABILITY IN MOUSE PEYER'S PATCHES.**

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NOD2 mutations are associated with susceptibility to Crohn's and Graft-Versus-Host Disease, two Human disorders related with dysfunctions of Peyer's patches (PP). We have shown that PP from Nod2 invalidated mice (KO) exhibit an elevated permeability and bacterial translocation rate associated with an increase number of CD4 T-cell and IFN $\gamma$  level. Thus, we have investigated the role of ileal microflora, CD4 T-cell, IFN $\gamma$  and Myosin light chain kinase (MLCK) in the alteration of PP homeostasis. In independent experiments, KO mice and the wild type controls were treated by i) oral antibiotics, or ii) intraperitoneal injection of anti-CD4 or iii) anti-IFN $\gamma$  antibodies or iv) ML-7 (MLCK inhibitor). The impact of these treatments on PP permeability and bacterial translocation was tested by Ussing-chamber experiments. T-cell composition and cytokine levels were analysed by flow cytometry and ELISA methods. In KO mice, permeability and bacterial translocation are increased in PP. We show that both anti-CD4 and anti-IFN $\gamma$  antibodies abrogate this phenotype, thus demonstrating that immune T cell influence the epithelial function. ML-7 treatment normalise the values of CD4 T-cell, IFN $\gamma$  and TNF $\alpha$ . This reciprocal crosstalk is under the control of the gut microflora as shown by the normalisation of all parameters after antibiotic treatment. Nod2 modulates the cross-talk between CD4 T-cell and the epithelium recovering PP. It down-regulates the pro-inflammatory effect driven by the ileal microflora.