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Investigations of FIBCD1: Immunohistochemical localization and immunomodulatory role upon helminth antigen stimulation in colon epithelium

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presentation to CD8⁺ T cells. Specific deletion of WASp in DCs using CD11c-Cre bred to a loxP-flanked WASp allele led to marked expansion of CD8⁺ T cells at the expense of CD4⁺ T cells. WASp-deficient DCs induced increased cross-presentation to CD8⁺ T cells by activating Rac2 that maintains a near neutral pH of phagosomes. To address if WASp directly reduces cross-presentation in DCs, we placed back WASp in bone marrow-derived DCs using Amara transfection. WASp-deficient DCs transfected with wild-type WASp restored acidification capacity resulting in decreased proliferation of CD8⁺ T cells. To identify if actin polymerization by WASp is needed to dampen cross-presentation, we expressed WASp lacking the actin-binding VCA domain in WASp-deficient DCs. The WASp Δ VCA increased acidification and reduced proliferation of CD8⁺ T cells, suggesting that the VCA domain of WASp is dispensable for reducing cross-presentation. Together, our data reveals an intricate balance between activation of WASp and Rac2 signaling pathways in DCs.

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Investigations of FIBCD1: Immunohistochemical localization and immunomodulatory role upon helminth antigen stimulation in colon epithelium

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Introduction: Fibrinogen C domain-containing 1 (FIBCD1) is a homotetrameric type II transmembrane protein, expressed at epithelial surfaces. FIBCD1 has a wide ligand spectrum, including chitin found in various pathogens such as helminths and fungi. Current understanding points towards a role as a pattern recognition receptor in the innate immune response.

Aim: In the present study, we investigate the localization of FIBCD1 in 49 different healthy human tissues by immunohistochemistry. Further, we investigate the *in vitro* effects of excretory-secretory (ES) antigens from pig whipworm (*Trichuris suis*) on FIBCD1-transfected colon epithelial cells, and identify protein fractions in the ES-antigen that binds to FIBCD1.

Results: Immunohistochemical staining shows that FIBCD1 is present at mucosal surfaces throughout the human body, with high intensity in the airways and gastrointestinal and urogenital tract. Transfection of the human colon epithelial cell line HCT116 with FIBCD1 did not result in any major genotypic differences upon stimulation with ES antigens, as determined by quantitative PCR of various pro- and anti-inflammatory genes. FIBCD1 recognizes and binds to whipworm eggshell and ES antigens. Analysis of the *T. suis* ES-antigen by size chromatography reveals predominant sizes of proteins ranging from 10 kDa to 200 kDa.

Conclusion: FIBCD1 is present at mucosal surfaces throughout the human body, which may underline its function as a pattern recognition receptor in the innate immune system. FIBCD1 binds to ES antigens. Stimulation with ES antigens does not appear to be influenced by FIBCD1 transfection *in vitro*. FIBCD1 may play a role in whipworm infections *in vivo*.

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Deleted in Malignant Brain Tumours 1 affects intestinal regeneration during doxorubicin toxicity

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Gastrointestinal toxicity is a major dose-limiting adverse effect of chemotherapeutic treatment. The intestinal barrier and the adaptive immune system are compromised during treatment. Deleted in Malignant Brain Tumours 1 (DMBT1) is a secreted scavenger protein with effects on innate immunity and epithelial differentiation. We investigated the effect of Dmbt1 deletion on intestinal toxicity and inflammation after chemotherapeutic treatment in mice. C57BL/6 mice deficient in DMBT1 (KO) and wild-type (WT) littermates were treated with intraperitoneal injections of doxorubicin and terminated on day 3 (D3) or 7 (D7) after treatment. Intestinal inflammation and gastrointestinal toxicity was investigated through daily weighing, serum citrulline levels, histological evaluation and quantitative real-time PCR analysis of Dmbt1, Tnf, Il1b and Il6 gene expression.

Doxorubicin treatment induced wasting and gastrointestinal inflammation. Citrulline levels were lower in doxorubicin treated mice D3 compared to saline controls