GP2 is selectively expressed by small intestinal CD103⁺CD11b⁺ cDC

Müller-Luda, Katarzyna; Ahmadi, Fatemeh; Ohno, Hiroshi; Kotarsky, Knut; Agace, William Winston

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expressed by M-cells and to act as a receptor for type 1 anchored protein previously shown to be selectively drive the generation of small intestinal homing T cells. Here we demonstrate that Glycoprotein 2 (GP2), a GPI-anchored protein previously shown 1) to be selectively expressed by small intestinal CD103+CD11b+ cDC was independent of lymphocytes and MyD88 signaling, administration of broad spectrum antibiotics increased the proportion of GP2+ CD103+CD11b+ cDC in the small intestine. Moreover, GP2 expressing cDC in the small intestine were dramatically reduced in the setting of intestinal inflammation. We have previously shown that mice with an IRF4 deletion in CD11c+ cells (Cd11c-cre.Irf4 Δ/Δ mice) have reduced numbers of small intestinal CD103+CD11b+ cDC (2). Interestingly, we found that GP2+ CD103+CD11b+ cDC were dramatically reduced in these mice. Finally, to address the in vivo role of GP2 expression by cDC, we have generated mice with a selective deletion of GP2 in CD103+CD11b+ cDC (huLangerin-cre.gp2 Δ/Δ mice). Results from these ongoing studies will be presented.

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GP2 is selectively expressed by small intestinal CD103+CD11b+ cDC

Katarzyna Müller-Luda1, Fatemeh Ahmadi1, Hiroshi Ohno2,3, Knut Kotarsky1 & William W. Agace1,4

1Immunology Section, Lund University, Lund, Sweden, 2Division of Immunobiology, Graduate School of Supramolecular Biology, Yokohama City University, Yokohama, Kanagawa, Japan, 3Laboratory for Intestinal Ecosystem, RIKEN Center for Integrative Medical Sciences, Kanagawa, Japan, and 4Section for Immunology and Vaccinology, National Veterinary Institute, Technical University of Denmark, Copenhagen, Denmark

The functionality of tissue cDC is regulated, at least in part, by the signals these cells receive within their local environment. For example, we and others, have demonstrated that murine small intestinal but not colonic cDC are imprinted with an ability to generate the Vitamin A metabolite, retinoic acid, and thus an enhanced capacity to drive the generation of small intestinal homing T cells. Here we demonstrate that Glycoprotein 2 (GP2), a GPI-anchored protein previously shown to be selectively expressed by M-cells and to act as a receptor for type 1 fimbriated bacteria (1), is expressed by a large proportion of IRF4-dependent cDC in the small intestine but not in other tissues. While surface expression of GP2 by small intestinal CD103+CD11b+ cDC was independent of lymphocytes and MyD88 signaling, administration of broad spectrum antibiotics increased the proportion of GP2+ CD103+CD11b+ cDC in the small intestine. Moreover, GP2 expressing cDC in the small intestine were dramatically reduced in the setting of intestinal inflammation. We have previously shown that mice with an IRF4 deletion in CD11c+ cells (Cd11c-cre.Irf4 Δ/Δ mice) have reduced numbers of small intestinal CD103+CD11b+ cDC (2). Interestingly, we found that GP2+ CD103+CD11b+ cDC were dramatically reduced in these mice. Finally, to address the in vivo role of GP2 expression by cDC, we have generated mice with a selective deletion of GP2 in CD103+CD11b+ cDC (huLangerin-cre.gp2 Δ/Δ mice). Results from these ongoing studies will be presented.

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A novel saponin adjuvant G3 modulates cytokine responses in equine PBMC

Hellman Stina, Hjertner Bernt, Morein Bror & Fossum Caroline

Department of Biomedical Sciences and Veterinary Public Health, Swedish University of Agricultural Sciences, SLU, Uppsala, Sweden

The applicability of a new saponin adjuvant formulation (G3) was tested in cultures of equine peripheral blood mononuclear cells (eqPBMCs). When immunizing mice with a split influenza vaccine the inclusion of this adjuvant could enhance the antibody response, as well as induce CD8+CD3+ T-cells and a broad protection against influenza challenge when a diterpene was incorporated in the G3 formula (van de Sandt et al., Vaccine. 2014 32:23.). Therefore, the present study aimed to evaluate cytokine responses to G3 alone or in combination with other immunostimulatory compounds. EqPBMC exposed to G3 for 18 h displayed an increased expression of the genes encoding IL-12p40 and IFN-γ (Th1), IL-23p19 (Th17), as well as IL-8 and IL-1β (pro-inflammatory). This G3-induced cytokine expression profile could be modified by co-culturing eqPBMC with G3 and known agonists to TLR5 (Flagellin) or TLR2/1 (Pam3CSK4). The combination of G3 with Pam3CSK4 increased the IFN-γ response compared to that induced by G3 or Pam3CSK4 alone. A similar increase in gene expression of IL-8 was indicated when G3 was combined with Flagellin. In contrast, the presence of G3 reduced the expression of the...