Generation and transcriptional programming of intestinal dendritic cells: essential role of retinoic acid - DTU Orbit (08/11/2017)

Generation and transcriptional programming of intestinal dendritic cells: essential role of retinoic acid

he vitamin A metabolite retinoic acid (RA) regulates adaptive immunity in the intestines, with well-characterized effects on IgA responses, Treg induction, and gut trafficking of T- and B-effector cells. It also controls the generation of conventional dendritic cell (cDC) precursors in the bone marrow and regulates cDC subset representation, but its roles in the specialization of intestinal cDC subsets are understudied. Here we show that RA acts cell intrinsically in developing gut-tropic pre-mucosal dendritic cell (pre-μDC) to effect the differentiation and drive the specialization of intestinal CD103+CD11b- (cDC1) and of CD103+CD11b+ (cDC2). Systemic deficiency or DC-restricted antagonism of RA signaling resulted in altered phenotypes of intestinal cDC1 and cDC2, and reduced numbers of cDC2. Effects of dietary deficiency were most apparent in the proximal small intestine and were rapidly reversed by reintroducing vitamin A. In cultures of pre-μDC with Flt3L and granulocyte-macrophage colony-stimulating factor (GM-CSF), RA induced cDC with characteristic phenotypes of intestinal cDC1 and cDC2 by controlling subset-defining cell surface receptors, regulating subset-specific transcriptional programs, and suppressing proinflammatory nuclear factor-κB-dependent gene expression. Thus, RA is required for transcriptional programming and maturation of intestinal cDC, and with GM-CSF and Flt3L provides a minimal environment for in vitro generation of intestinal cDC1- and cDC2-like cDC from specialized precursors.

General information

State: Published
Organisations: National Veterinary Institute, Section for Virology
Authors: Zeng, R. (Ekstern), Bscheider, M. (Ekstern), Lahl, K. (Intern), Lee, M. (Ekstern), Butcher, E. C. (Ekstern)
Pages: 183-193
Publication date: 2016
Main Research Area: Technical/natural sciences

Publication information

Journal: Mucosal Immunology
Volume: 9
ISSN (Print): 1933-0219
Ratings:
Web of Science (2017): Indexed Yes
Scopus rating (2016): CiteScore 6.36 SJR 4.368 SNIP 1.531
Web of Science (2016): Indexed yes
Scopus rating (2015): SJR 4.407 SNIP 1.447 CiteScore 6.53
Web of Science (2015): Indexed yes
Scopus rating (2014): SJR 4.542 SNIP 1.695 CiteScore 6.82
Scopus rating (2013): SJR 4.003 SNIP 1.625 CiteScore 6.75
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
Scopus rating (2012): SJR 3.908 SNIP 1.641 CiteScore 6.69
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
Scopus rating (2011): SJR 4.482 SNIP 1.453 CiteScore 6.66
ISI indexed (2011): ISI indexed yes
Scopus rating (2010): SJR 4.551 SNIP 1.495
Scopus rating (2009): SJR 2.684 SNIP 0.862
Original language: English
DOIs:
10.1038/mi.2015.50
Source: FindIt
Source-ID: 2279594799
Publication: Research - peer-review › Journal article – Annual report year: 2015