

Dendritic cells: controllers of adaptive immunity

Miriam Merad



Dendritic cells (DCs) are a heterogeneous population of rare haematopoietic cells that co-evolved with the formation of the adaptive immune system. Distributed throughout the body, but most abundant in lymphoid organs and at interface tissues, DCs are constantly sampling their environment. Following antigen uptake, they migrate to draining lymph nodes to present tissue-derived antigens and initiate adaptive immunity. DCs tailor adaptive immune

responses to match environmental cues, thereby serving as a bridge between the innate and adaptive immune systems. As such, they have key roles in both initiating immune responses to pathogens and maintaining tissue tolerance¹. Remarkable progress has been made in unravelling the intricacies of DC biology and targeting these cells for therapy is now a realistic goal¹. This Poster summarizes key DC functions, focusing on mouse DC subsets.

War and peace

In the steady state, DCs have crucial roles in maintaining tolerance, not only to self antigen, but also to harmless environmental antigens and commensal organisms. However, DCs also continuously survey the tissue for signs of 'danger' (which they perceive using various pattern-recognition receptors (PRRs)) and they initiate protective adaptive immune responses following tissue damage and infection. The panels below illustrate the role of DCs in promoting a protective immune response in the skin and in maintaining tolerance in the intestine. It is important to state that DCs can promote effector or tolerogenic immune responses in all tissues and the decision to initiate 'war' or 'peace' is determined by numerous factors, including the inflammatory status of the particular tissue.

Skin (left panel)

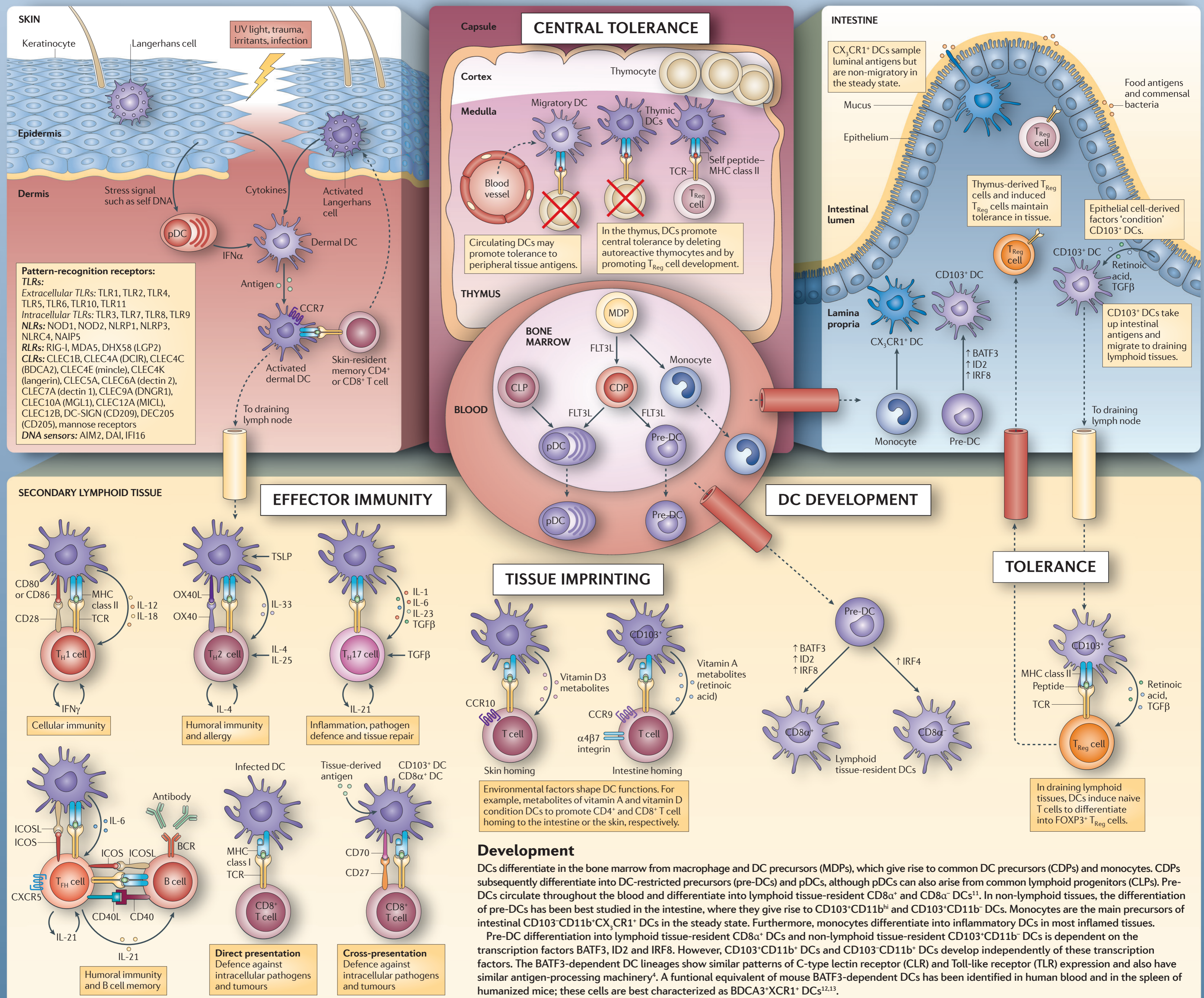
In the skin, DCs form a continuous cellular network and use PRRs to survey the tissue for foreign antigens that breach the barrier with the external environment². DCs in the epidermis (Langerhans cells) are developmentally and functionally distinct from dermal DCs, which include the CD103⁺ and CD11b⁺ DC subsets. Skin-derived DCs constitutively migrate to draining lymph nodes; this process is further increased in response to inflammatory signals.

Following skin injury, DCs become activated, modulating their chemokine receptor profile to facilitate their migration and positioning in the draining lymph node, and upregulating their expression of MHC and co-stimulatory molecules and cytokines³. Activated DCs promote the differentiation of naive antigen-specific T cells into effector T cell subsets³, and distinct DC populations can be associated with different types of T cell response. For example, migratory CD103⁺ DCs and lymphoid tissue-resident CD8 α ⁺ DCs show a superior ability to cross-present tissue-derived antigens and prime CD8⁺ T cells⁴. Depending on the nature of the immune challenge, DCs promote the differentiation of distinct effector CD4⁺ T helper (T_H) cell populations and drive the development of T follicular helper (T_{FH}) cells, which promote B cell antibody responses.

During inflammation, two additional subsets of DCs accumulate in the skin: monocyte-derived DCs and plasmacytoid DCs (pDCs). Upon activation, pDCs secrete large amounts of IFN α and initiate T cell responses against microorganisms⁵. Monocyte-derived DCs can also participate in tissue immunity by initiating innate and adaptive immune responses against pathogens⁶.

Intestine (right panel)

Intestinal DCs must maintain tolerance to food antigens and commensal bacteria, but are also crucial for protective immunity against invading pathogens. In the lamina propria, CD103⁺ CX₃CR1⁺ CD11b⁺ DCs sample luminal antigens by projecting dendrites through the epithelial cell layer⁷. CD103⁺ CD11b⁺ DCs migrate to the draining lymph nodes in a CCR7-dependent manner and present intestinal antigens to T cells; these DCs are potent producers of retinoic acid and promote the peripheral differentiation of regulatory T (T_{Reg}) cells, which help maintain gut integrity⁸⁻¹⁰. Retinoic acid-producing DCs also 'imprint' T cells with gut-homing molecules, such as α 4 β 7 integrin.



BioLegend (www.biolegend.com)

BioLegend brings decades of reagent development expertise to your research, delivering the highest quality antibodies and cutting-edge reagents at the best value. With our tireless dedication to customer satisfaction, we strive to execute strict quality procedures at all levels, from purification to packaging to customer support, at our San Diego, CA facility. Our product areas include:

- cell immunophenotyping
- cytokines and chemokines
- adhesion molecules
- cancer research
- cell cycle analysis
- apoptosis
- T regulatory cells
- stem cells
- innate immunity
- MSDCs
- T helper subsets

All of BioLegend's reagents are supported by superior customer service and come with a 100% quality guarantee. Through an aggressive product development program, including technology licensing, collaborations, and internal hybridoma development, BioLegend produces reagents for use in a variety of applications, including:

- flow cytometry
- ELISA
- immunoprecipitation
- Western blotting
- immunofluorescence microscopy
- immunohistochemistry
- in vitro and in vivo functional assays

BioLegend offers the broadest selection of fluorochrome conjugates for multi-color flow cytometry. Introducing Brilliant Violet™, a novel family of exceptionally bright fluorochromes for the violet laser – an extensive antibody conjugate selection is available. BioLegend offers a wide array of custom assays and services, including development of multicolor flow cytometry panels to meet our customers' specific needs. BioLegend was selected by the Harvard Immunology Program as the preferred vendor for antibodies and reagents, based on our exceptional quality and pricing. Our commitment to the research community is also reflected in generous sponsorships of societies and meetings world-wide, our monthly travel award for young investigators, and our flexibility, fast turnaround, and bulk discounting. With iPhone/iPad apps, web tools, and hundreds of new reagents each year, we look forward to providing more innovative tools to make your research legendary.

Abbreviations

AIM2, absent in melanoma 2; BATF3, basic leucine zipper transcriptional factor ATF-like 3; BCR, B cell receptor; BDCA, blood DC antigen; CCR, CC-chemokine receptor; CLEC, C-type lectin; CTL, cytotoxic T lymphocyte; CXCR5, CX3C-chemokine receptor 5; CX₃CR1, CX₃C-chemokine receptor 1; DAI, DNA-dependent activator of IFN-regulatory factor; DCIR, DC immunoreceptor; DC-SIGN, DC-specific ICAM3-grabbing non-integrin; DHX58, DEAH box protein 58; FLT3L, FMS-related tyrosine kinase 3 ligand; FOXP3, forkhead box P3; ICOS, inducible T cell co-stimulator; ICOSL, ICOS ligand; ID2, inhibitor of DNA binding 2; IFI16, interferon- γ inducible protein 16; IFN, interferon; IL, interleukin; IRF, interferon regulatory factor; MDA5, melanoma differentiation-associated gene 5; NAIIP5, NLR apoptosis-inhibitory protein 5; NLR, NOD-like receptor; NLR, NOD-, LRR- and CARD-containing; NLRP, NOD-, LRR- and pyrin domain-containing; NOD, nucleotide-binding oligomerization domain;

RIG-I, retinoic acid-inducible gene 1; RLR, RIG-I-like receptor; TCR, T cell receptor; TGF β , transforming growth factor- β ; TSLP, thymic stromal lymphopoietin; XCR1, XC-chemokine receptor 1.

Affiliations

Miriam Merad is at the Mount Sinai School of Medicine, 1425 Madison Avenue, New York 10044, USA. email: miriam.merad@mssm.edu

The author declares no competing financial interests.

Edited by Yvonne Bordon and Olive Leavy; copyedited by Isabel Woodman; designed by Simon Bradbrook. © 2011 Nature Publishing Group. All rights reserved.

http://www.nature.com/nri/posters/dendriticcells
References available online.