Atherosclerotic vascular disease remains the number one cause of death and morbidity in the Western world. It is now well established that atherosclerosis is a chronic inflammatory disease of the vessel wall. Besides macrophages, also other immune cells, namely dendritic cells (DCs) and T cells, can be found within atherosclerotic lesions and contribute to atherogenesis.1,2

Abstract—Atherosclerotic vascular disease is driven by chronic inflammation involving both innate and adaptive immune responses. Dendritic cells (DCs) are found in healthy arteries and accumulate in atherosclerotic lesions and engage in diverse pathogenic and protective mechanisms during atherogenesis. DCs contribute to early foam cell formation, regulate lipid metabolism, and control pro- and antiatherosclerotic T-cell responses by multifarious mechanisms. We, here, review the roles of DCs and plasmacytoid DCs in experimental models of atherosclerosis and the approaches to target DCs in therapeutic vaccination strategies. We, furthermore, discuss the evidence of the potential function of DCs in human atherosclerosis, and dissect the efforts to harness DC subsets as biomarkers of disease. Finally, we discuss necessary future steps that will help to understand the specific contribution of bona fide DCs in atherosclerosis to move toward novel therapeutic approaches. (Arterioscler Thromb Vasc Biol. 2015;35:763-770. DOI: 10.1161/ATVBAHA.114.303566.)

Key Words: atherosclerosis • dendritic cells • humans • immune system • inflammation • leukocytes • mice

In general, DCs have functionally been ascribed to play the main role in initiating antigen-specific adaptive immune responses and maintaining tolerance to self-antigens, whereas macrophages excel in phagocytotic processes. The distinction between DCs and macrophages, however, is much debated, in particular because of their partially overlapping phenotypes and functions. In previous studies, mostly promiscuous surface markers were used to discriminate these populations, and DCs were often defined as CD11c+ major histocompatibility complex (MHCII)+ and macrophages as CD11c− F4/80high cells. CD11c, however, can be expressed by activated monocytes/macrophages under inflammatory conditions, as well as by other lineages.3

In atherosclerosis, efforts have been made to functionally discriminate DCs and macrophages. For instance, Choi et al4 demonstrated aortic CD11c+ MHCII+ DCs to display strong immune stimulatory capacities, whereas CD11c− MHCII− macrophages showed high phagocytotic activity. Similarly, Koltsova et al5 noted aortic CD11c+ cells to be pivotal for T-cell activation, whereas lipid uptake was observed by CD11c− CD11b+ cells referred to as macrophages. Because of the paucity of studies clearly discriminating DCs and macrophages (see below) and their functional plasticity, the interpretation of these findings and published literature and a clear attribution to the cell type in atherosclerosis may, therefore, often be difficult.

Given these limitations, this review provides an overview about the role of cells ascribed to be DCs in atherosclerosis in mice and humans (Figure), stating the markers used to identify these, and discusses necessary future steps that will help to understand the specific contribution of bona fide DCs in atherosclerosis to move toward novel therapeutic approaches.

Defining DCs

Recently, efforts have been undertaken to unequivocally define DCs and differentiate these from macrophages, taking the ontogeny, phenotype and transcriptional profile into account.6-10 On the basis of these considerations, DCs in mice were proposed to be classified as a separate lineage of mononuclear phagocytes that arises from progenitors that are distinct from precursors of monocytes/macrophages. In the bone marrow common monocyte-DC precursors (MDPs) either give rise to monocyte progenitors restricted to monocytes and their descendants or commit toward DC precursors. Common DC precursors differentiate into plasmacytoid DCs (pDCs) in bone marrow, or can give rise to pre-DCs, which exit the bone marrow, circulate in blood and subsequently develop into classical DCs (cDCs). It should be noted that the exact
branching points of cDCs, pDCs and monocytes, and the existence of MDPs or common DC precursors as precursors for cDCs and pDCs, however, have recently been challenged. On the basis of distinct developmental pathways, cDCs are further segregated into cDCs type 1 (cDC1s), encompassing CD8α+ DCs in lymphoid and CD103+ DCs in nonlymphoid tissue, and CD11b+ cDC2s. Analyses of the entire transcriptome revealed a core cDC gene signature absent from monocytes/macrophages and pDCs that include the genes Zbtb46 and Ccr7, CD8α+/CD103+ cDCs were furthermore revealed to express toll like receptor (Tlr) 3 and Xcr1, and to require the transcription factors BATF3, IRF8, Id2 for their development, whereas the differentiation of CD11b+ cDCs is controlled by RELB, RBPJ and IRF4. The transcription factor E2-2/Tcf4 is an essential regulator of pDC development. Both cDCs and pDCs depend on the growth factor fms-like tyrosine kinase 3 ligand (Flt3L), and Flt3L-dependence can serve as a surrogate marker for common DC precursor origin. In contrast, macrophage colony-stimulating factor 1 receptorα monocytes that circulate in blood and enter tissues under inflammatory conditions, give rise to macrophages and monocyte-derived DCs. It is currently unclear if monocyte-derived DCs and macrophages constitute two distinct lineages, or if they are instead highly plastic cells that acquire different functional modules in response to microenvironmental cues (Table 1).

In humans, pDCs and 2 types of cDCs (previously referred to as myeloid DCs), namely CD1c+ and CD141+ DCs are discriminated, which are considered homologs of CD11b+ and CD8α+CD103+ DCs in mice, respectively. These DC subsets circulate as precursors or in an immature state in blood (Table 2) and originate from hematopoietic stem cells in the bone marrow via either granulocyte macrophage progenitors or multilineage progenitors. Human homologs of murine DC precursors remain unidentified.

 Localization of DCs in Atherosclerotic Lesions and the Adventitia

In mice, CD11c+ DCs are frequently located in the aortic intima in areas predisposed to atherosclerosis. Moreover, CD11c+ MHCII+ DCs accumulate in atherosclerotic lesions, including Flt3/Flt3L-dependent CD103+ and CD11b+CD172a+ cDCs, and a large fraction of monocyte-derived CD11b+ DCs that are macrophage colony-stimulating factor–dependent or express CD64.

Similar to mice, DCs can be detected in the arterial intima of healthy young individuals, and increased numbers of DCs are found in atherosclerotic lesions using unspecific markers, such as S100, CD1a, or fascin. However, a detailed analysis of the different DC subsets is still lacking. DCs are mainly found in the plaque shoulder and rupture-prone regions, as well as in marginal parts of the plaque core. The majority of DCs in advanced plaques seems to be activated, as revealed by the expression of costimulatory molecules (eg, CD83 and CD86) and cytokines, and to cluster with T cells. Notably, significantly higher numbers of DCs and blood DC antigen (BDCA)-1+ cDCs reside in carotid plaques with characteristics of vulnerable versus stable lesions, and in symptomatic compared with asymptomatic patients. These data indicate that DCs may locally modulate inflammatory responses and precipitate plaque vulnerability.

In addition, pDC antigen (PDCA)-1+ (bone marrow stromal cell antigen 2 [BST2+]) pDCs can be found in the nondiseased vessel wall and within atherosclerotic lesions in apolipoprotein E–deficient (Apoe−/−) and low-density lipoprotein receptor-deficient (Ldlr−/−) mice, albeit at low numbers. In human tissue, CD123+ pDC numbers were increased in unstable compared with stable lesions, mainly localizing to the shoulder region of plaques, where they cluster with cDCs, and increased transcripts of pDC markers can be evidenced.
DCs can furthermore be detected in the adventitia and in tertiary lymphoid organs (TLOs) that form in the adventitia of aged \textit{Apoe}−/− mice primarily in the proximal abdominal aorta. TLOs are organized into distinct compartments, including T- and B-cell areas, and harbor cDCs, pDCs, and monocyte-derived DCs. These TLOs may participate in primary immune responses in advanced atherosclerosis. Of note, TLO-like adventitial aggregates are also reported in patients with atherosclerotic abdominal aneurysms, which may indicate a relevance of TLO formation also in humans. The mechanisms of their formation and function, as well as their location in humans are unknown and deserve attention in future studies.

Given recent advances in defining bone fide DCs, an in-depth characterization of the ontogeny of vascular and adventitial DCs in healthy and atherosclerotic arteries is now warranted. For example, fate mapping studies will bring clarity to the origin of vascular DCs versus macrophages, such as the one exploiting DNGR-1 expression to trace cDC precursors. Subsequently, their transcriptional profiling could help identifying genes specifically regulated during disease development. This knowledge is requisite for further characterizing the phenotype and function of distinct DC subsets in atherosclerosis.

**Trafficking of DCs**

In mice, the 3 major DC precursors in blood include Flt3+ pre-DCs and pDCs, and macrophage colony-stimulating factor+ monocytes. The loss of CD103+ and of some CD11b+ cDCs in the nonatherosclerotic aorta in Flt3/Flt3I-deficient mice indicates that monocyte-derived DCs and bone fide cDCs are already present prior disease development. Whereas blood monocytes systemically increase, it is unclear whether circulating DCs or their precursors are altered in hyperlipidemia. Importantly, however, DC numbers rapidly expand during atherosclerotic lesion growth, and a reduction in CD103+ cDCs and monocyte-derived DCs is evidenced in atherosclerotic arteries of mice lacking Flt3 and macrophage colony-stimulating factor, respectively. A decrease in CD11c+ DC numbers in \textit{Cx3cr1}−/− mice may relate to diminished DC or monocyte recruitment. These data suggest that DCs or their precursors are recruited during disease development.

Elucidating the DC subsets/precursors in blood and other organs during atherogenesis may contribute to resolve the question of the origin of vascular DCs and could facilitate the identification of factors that regulate circulating and plaque DC numbers. Blocking the recruitment of specific DC subsets/precursors may be tested as therapeutic approaches to limit lesion size and local inflammation. Notably, CD11c+ MHCII+ DCs can also proliferate in early lesions. The contribution of DC (precursor) recruitment versus local proliferation remains to be defined.

**Circulating DCs: Biomarkers of Disease?**

In humans, several contradictory studies have addressed whether circulating DC numbers correlate with disease severity and thus may serve as biomarkers of disease. Shi et al
have identified numbers of total Lineage (Lineage−) human leukocyte antigen (HLA)-DR+ DCs, CD11c+ cDCs but not CD123+ pDCs to be increased in patients with coronary artery disease (CAD) compared with controls. In contrast, Yilmaz et al20 and Wen et al,24 reported decreased circulating BDCA-1+ cDC but not BDCA-2+ or CD123+ pDC precursors in patients with unstable CAD. Van Vré et al 25 and Yilmaz et al 26 observed reduced BDCA-1+ cDCs and BDCA-2+ pDC numbers in patients with CAD, which were identified as independent predictors of the presence of or subsequent therapeutic procedures in stable CAD.26 Moreover, total DC, BDCA-1+ or CD11c+ cDC and BDCA-2+ pDC numbers in patients with CAD, which were identified as independent predictors of the presence of or subsequent therapeutic procedures in stable CAD.36 However, total DC, BDCA-1+ or CD11c+ cDC and BDCA-2+ or CD123+ pDC numbers were shown to be decreased in patients with CAD irrespective of disease severity.27

The mechanisms responsible for the decline in blood DCs in atherosclerosis may include an enhanced recruitment to lymphoid organs or sites of inflammation, as suggested by their accumulation in vulnerable lesions,20 an increased DC turnover, or a decreased production or release from bone marrow.46 Interestingly, decreased numbers of blood Lineage−HLA-DR−CD11c+ cDCs and CD123+ pDCs in CAD correlated with decreased plasma FLT3L, suggesting that reduced DC counts in CAD may, in part, be because of an impaired DC differentiation from progenitors.38

Although these studies have failed to unequivocally identify certain DC subsets as biomarkers of disease, the majority of studies observed a decline in DC numbers in CAD. With a finer delineation of circulating DC subsets/precursors, including CD141+ cDCs, their abundance may prove to be useful as potential biomarkers of disease.

### Emigration of DCs

The ability to migrate to secondary (or tertiary) lymphatic tissue is considered a functional characteristic of DCs. Although it is unclear where T-cell sensitization occurs, DCs may emigrate from the vessel wall after antigen uptake and home to lymphatic tissue. Indeed, CD11c+ cells seem to be able to leave atherosclerotic plaques in a chemokine-dependent manner. When the aortic arch of Apoe−/− mice with established atherosclerotic lesions was transplanted into wild-type recipients, blockade of the CCR7 ligands CCL19 and CCL21 inhibited plaque regression and preserved CD11c+ cell content, 39 suggesting that CCR7 mediates the egress of DCs during lesion regression. In other different models of lesion regression, however, deficiency of CCR7 did not affect myeloid cell content, and lead to increased lesion formation in Apoe−/− but reduced plaque development in Ldlr−/− mice, findings that may also relate to altered T-cell trafficking.40 Whether DC emigration plays a role during atherogenesis remains to be defined, but may be impaired by a reduced migratory ability of DCs under conditions of hyperlipidemia.41

### DCs Take Up Lipids and Control Cholesterol Homeostasis

In the arterial intima, lipid accumulations can be found within vascular CD11c+ DCs in Ldr−/− mice after only few days of hypercholesterolemia, where they adopt a foam cell–like appearance that may constitute the earliest stages of plaque formation.42 Several studies furthermore point toward a role of DCs in cholesterol metabolism. In mice overexpressing antiapoptotic...
hBcl-2 under the control of the CD11c promoter, the extended lifespan of DCs not only enhanced T-cell activation but also lead to hypocholesterolemia with a decrease in very low-density lipoprotein and LDL levels, resulting in a net unaltered lesion formation. In the reverse approach, depletion of DCs in CD11c-DTR Apoe<sup>−/−</sup> mice induced an elevation in plasma cholesterol levels. The mechanisms that underlie these effects remain to be addressed. Gautier et al. speculated that DCs may contribute to an enhanced lipoprotein uptake and clearance from the circulation. Whether this primarily occurs within lesions, or also in other organs, for example, in spleen, has not been addressed. Of note, diphertheria toxin-treated CD11b-DTR Apoe<sup>−/−</sup> mice with a depletion of monocytes/macrophages, neutrophils, and CD11b<sup>+</sup> DCs did not show any changes in cholesterol levels, which may be because of confounding effects of other cell populations or indicate that mostly CD11b<sup>+</sup> DCs control cholesterol metabolism. The loss of CD103<sup>+</sup> cDCs in atherosclerotic Flt3<sup>−/−</sup>Ldlr<sup>−/−</sup> mice, however, did similarly not affect lipid levels.

Lipid uptake may be mediated by scavenger receptors of modified LDL (eg, CD36) and be controlled by ABCA1/ABCG1-mediated cholesterol efflux pathways, reverse cholesterol transport, activity of peroxisome proliferator-activated receptor-γ, or liver X receptors, as recently reviewed in macrophages; in addition, fluid-phase endocytosis of native or modified LDL by DCs may contribute to lipid uptake.

In future studies, these hypotheses will have to be experimentally tested. Especially in humans, a correlation between lipid levels and circulating or plaque DC numbers remains to be investigated. In addition, it will be interesting to characterize DC numbers and phenotype both in lesions and the circulation with regard to the expression of mediators that could control cholesterol metabolism in mice and humans. Enhancing the lipid-lowering potential of DCs could be an interesting approach to limit hypercholesterolemia and atherosclerosis.

**DCs as Antigen Presenting Cells That Control T-Cell Activation and Phenotype**

As discussed, DCs may emigrate from the vessel wall to home to lymphatic tissue, or interact with T cells in the adventitia. It may also be conceivable that circulating antigens can directly be ingested by DCs in the spleen or lymph node and that DCs at these sites contribute to T-cell priming. The presence of oligoclonally expanded T cells and CD4<sup>+</sup> T cells reactive to disease-related antigens in human lesions indicates that priming of T cells or re-encounter of antigen may (also) occur locally at sites of inflammation in human atherosclerosis.

**Classical DCs**

In principle, vascular DCs bear the capacity to interact with T cells. In model systems, CD11c<sup>+</sup> MHCI<sup>+</sup> DCs take up injected antigen from the bloodstream, and after sorting are capable of inducing antigen-specific MHCI or MHCI<sup>II</sup>-restricted T-cell proliferation in vitro. Furthermore, aortic DCs promote tumor necrosis factor-α and interferon (IFN)γ production in exogenously added antigen-specific T cells from Apoe<sup>−/−</sup> mice ex vivo, suggesting that DCs can cause local T-cell activation and proinflammatory cytokine production.

Several lines of evidence indicate that DC–T cell interactions causally contribute to atherogenesis. For instance, Ldlr<sup>−/−</sup> mice lacking the invariant chain of MHCI<sup>II</sup> are protected from atherogenesis, caused by reduced T-cell activation in atheroma. Evidence for DC-intrinsic effector functions in atherosclerosis was, furthermore, obtained by disrupting TGF-β type II receptor-signaling in CD11c<sup>+</sup> cells in Apoe<sup>−/−</sup> mice, which lead to increased atherosclerotic lesion formation and an expansion of activated effector/memory T cells, indicating that TGF-β–signaling in DCs dampens proatherosclerotic T-cell responses in atherosclerosis. Several studies have further linked DCs with Treg responses in atherosclerosis. Whereas a subset of CCL17-expressing CD11b<sup>+</sup>CD11c<sup>+</sup>MHCI<sup>II</sup> DCs constrains Treg-maintenance and, thereby, drives atherosclerosis, Flt3-dependent CD103<sup>+</sup> CD11c<sup>+</sup>MHCI<sup>II</sup> cDCs promote Treg responses, based on findings showing that Flt3-deficiency reduced aortic CD103<sup>+</sup> cDC content, diminished systemic and local Treg numbers and increased atherosclerosis. Moreover, the absence of the key TLR adaptor MyD88 in CD11c<sup>+</sup> DCs led to a loss in Tregs, which trumped decreased proatherogenic effector T-cell activation, and entailed an increased atherosclerotic lesion formation, indicating that Treg-mediated suppression of atherosclerosis requires MyD88 signaling in DCs. Thus, specialized DC subsets exert pro- and anti-inflammatory functions in T-cell activation. Interestingly, reduced peripheral Treg numbers in patients with CAD may be in line with an expansion of CCL17<sup>+</sup> DCs in atherosclerosis and increased CCL17 serum levels in CAD, or point toward a loss of tolerogenic DC subsets/functions in advanced atherosclerosis.

CCL17-expressing DCs also contribute to the accumulation of T cells in atherosclerotic lesions. Moreover, adoptively transferred Ccr7<sup>−/−</sup> T cells showed a reduced migration into the inflamed aorta; given the expression of CCR7 ligands CCL19/CCL21 by plaque DCs, DCs may also recruit or retain T cells in the inflamed vessel wall.

In future studies, it will be important to further investigate the role of specific DC subsets and the effector molecules involved in modulating T-cell responses in atherosclerosis. Identifying genes expressed in certain DC subsets, for example, transcription factors differentially regulating DC subset development, may facilitate their specific targeting. For instance, harnessing the cDC-specific transcription factor Zbtb46 may help to define the contribution of cDCs (versus monocytes/macrophages or pDCs) to adaptive immunity and atherosclerosis.

To link experimental observations to clinical manifestations of atherosclerosis, functions and associated DC effector molecules should be explored in human DCs from atherosclerotic plaques and blood, and correlated to disease severity. Targeting DC subsets or their mediators that drive atherosclerosis or enhance atheroprotective Treg responses could be of potential interest for translational therapeutic strategies.
**Plasmacytoid DCs**

Several studies have addressed the role of pDCs in atherosclerosis. pDC-depletion using an antibody against BST2 (120G8) aggravated atherosclerotic lesion development in carotid arteries after collar placement and in aortic roots in diet-fed *Ldlr*−/− mice, attributed to a loss of IDO (indoleamine 2,3-dioxygenase)-dependent restraint in T-cell proliferation.18 Contrary, pDC-depletion with a different antibody against BST2 (anti–PDCA-1) decreased diet-induced lesion formation in 2 independent studies in the aortic root and aorta in *ApoE*−/− mice.16,17 Self-DNA (eg, released from dying cells or in neutrophil extracellular traps) and an increased expression of the antimicrobial peptide Cramp/LL37 in atherosclerotic lesions was shown to stimulate breakdown of tolerance to self-DNA and promote IFN-α production by pDCs, aggravating early atherosclerosis and antidouble-stranded DNA antibody formation in *ApoE*−/− mice.32 In addition to releasing type I interferons, pDCs however, also exert typical cDC functions. pDCs can present antigen via MHCII and stimulate T-cell activation, which is increased on oxidized LDL exposure,16 and an increased antigen presentation was observed in aortic PDCA-1+ pDCs in atherosclerotic *ApoE*−/− mice,17 suggesting that pDC-driven immunity is enhanced in atherosclerosis.

Notably, a recent study has now elegantly shown that genetically modified mice with a selective deficiency in pDCs (CD11c-restricted deletion of the transcription factor E2-2/ Tcf4) or an abrogation of MHCII-restricted antigen presentation by pDCs were protected from atherosclerotic lesion formation with a reduction in proatherogenic Th1 T cells.19 Although pDCs may thus promote disease development by triggering IFN-α production, these studies provide compelling evidence for a critical role of MHCII-restricted antigen presentation by pDCs in driving proatherogenic T-cell responses in atherosclerosis.

In humans, CD123+ pDCs and their index cytokine IFN-α were suggested to function as inflammatory amplifiers. Secretion of IFN-α, triggered by stimulation of plaque tissue with CpGs in vitro, correlated with the expression of proinflammatory mediators (tumor necrosis factor-α, IFN-γ, and matrix metalloproteinase-9), upregulation of TLR4 on cDCs, and tumor necrosis factor–related apoptosis inducing ligand by CD4+ T cells, resulting in killing of vascular smooth muscle cells.30,31 Notably, isolated immune complexes containing DNA-fragments can stimulate IFN-α secretion by pDCs in vitro.16,52 Given findings that elevated antinuclear antibody titers are associated with a decreased carotid elasticity and can be found in patients with symptomatic compared with asymptomatic carotid artery stenosis,16,52 antinuclear antibodies may contribute to the pathogenic effect in atherosclerosis by activating pDCs.

It will now be interesting to further address the recruitment of pDCs and role of specific mediators in pDCs in atherosclerosis. Mouse models using strategies to investigate these factors, for example, in a CD11c and E2-2/Tcf4-restricted fashion, could be developed to further expand preclinical knowledge about this cell population in atherosclerosis. A possible function of pDCs in antigen presentation and T-cell stimulation in human atherosclerosis remains to be investigated.

The mechanisms of antigen uptake and activation, as well as the role of cytokines released by pDCs will be of importance to bring together existing data in humans and mice, and to move toward approaches to interfere with these processes for atheroprotection.

**DC-Based Vaccination Approaches**

Importantly, DC-based vaccination strategies have yielded encouraging results in animal models. For instance, oxidized LDL–pulsed bone marrow–derived DCs have been shown to induce oxidized LDL–specific T cells with a reduced Th1 profile, and to decrease atherosclerotic carotid artery plaque size in *Ldlr*−/− mice.53 Moreover, tolerogenic bone marrow–derived DCs pulsed with the LDL protein ApoB100 in combination with IL-10 reduced effector T-cell proliferation, inhibited IFN-γ production, and increased the generation of Tregs, which was accompanied by a reduction in atherosclerotic lesion size in *Ldlr*−/− mice transgenic for human ApoB100.54 These data indicate that DC-based therapeutic approaches harbor potential for the prevention of atherosclerosis. Although in these studies DCs were injected before the commencement of diet to induce atherosclerosis, further experiments are needed to test DC vaccination in mice with established disease. This is of particular importance as the feasibility of vaccination approaches at later stages of atherosclerosis may be prerequisite for an application in patients.

**Conclusions**

Distinct DC subsets can be found in arterial vessels in healthy mice and humans, and an accumulation of DCs is observed in atherosclerosis. Moreover, an increased abundance of DCs seems to correlate with signs of plaque vulnerability in humans.

Although there is tentative evidence that DCs control lipid uptake, cholesterol metabolism and modulate adaptive immune responses in atherosclerosis, a clear attribution to bona fide DCs and the exact molecular mechanisms engaged are mostly still unclear. Knowledge about the ontogeny of vascular DC subsets and of genes specifically expressed by these will be requisite to experimentally test and provide undisputed evidence of their role in atherosclerosis and of mediators that control recruitment, emigration, lipid uptake, and T-cell responses in mice. The relative scarcity of human tissue, with the exception of blood, has hampered translational efforts of mechanistic findings uncovered in mice. However, blood and human plaque tissue should be used to isolate specific DC subsets for these endeavors. The identification of human homologs of mouse DC subsets and further work in this area will aid to promote translational approaches.

A clear understanding of the functional contribution of DC subsets in atherosclerosis will serve as an essential basis for targeting proatherogenic or tolerogenic cell populations or their mediators as novel therapeutic approaches for treating cardiovascular disease.

**Sources of Funding**

This study was supported by the Deutsche Forschungsgemeinschaft (SFB688 TPA22 and ZE 827/1–2).
Disclosures

None.

References


Atherosclerotic vascular disease and its sequelae, such as coronary artery disease, myocardial infarction, and stroke, remain the leading cause of death and morbidity worldwide. In order for the development of novel therapeutic approaches, a detailed understanding of the key players and their functions in atherosclerosis are prerequisite. Although atherosclerosis is known to be driven by chronic inflammation, little is known about the role of dendritic cells that are found in healthy arteries and accumulate in atherosclerotic lesions in both mice and humans. This review highlights the latest advances in defining dendritic cells and their functions in atherosclerosis. In particular, evidence in mice and humans is combined with a focus on necessary future steps and translational endeavors that should now be tackled to move toward novel therapeutic strategies.
Dendritic Cells in Atherosclerosis: Evidence in Mice and Humans
Alma Zernecke

Arterioscler Thromb Vasc Biol. 2015;35:763-770; originally published online February 12, 2015;
doi: 10.1161/ATVBAHA.114.303566
Arteriosclerosis, Thrombosis, and Vascular Biology is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2015 American Heart Association, Inc. All rights reserved.
Print ISSN: 1079-5642. Online ISSN: 1524-4636

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://atvb.ahajournals.org/content/35/4/763

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Arteriosclerosis, Thrombosis, and Vascular Biology can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Arteriosclerosis, Thrombosis, and Vascular Biology is online at:
http://atvb.ahajournals.org//subscriptions/