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Dectin-1 deficiency does not affect atherosclerosis development in mice

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ABSTRACT

Objective: Recent data suggest the involvement of dectin-1 in atherosclerosis through regulation of local reactive oxygen species production. The aim of the current study was to assess the effect of dectin-1 deficiency on atherosclerotic plaque development.
Methods: Using immunohistochemistry dectin-1 expression was observed on foamy macrophages in atherosclerotic lesions in mice. Following lethal irradiation LDLR$^{-/-}$ mice were reconstituted with bone marrow from either wild type or dectin-1$^{-/-}$ mice. After recovery, mice were fed a high fat diet for 9 weeks and atherosclerotic lesions were analyzed.
Results and conclusion: Overall, we found no significant differences in plaque size or severity between the groups. Also no differences were observed in granulocyte or macrophage composition of the plaques or in the ability to produce reactive oxygen species by macrophages from both groups. Dectin-1 is dispensable for the development of atherosclerotic lesions in mice.

1. Introduction

Atherosclerosis is a chronic inflammatory disease of the vessel wall [1]. Hyperlipidemia triggers an inflammatory response leading to the recruitment of circulating monocytes, which subsequently differentiate into macrophages. These macrophages scavenge modified lipids and mediate local production of cytokines, chemokines and reactive oxygen species (ROS) resulting in foam cell formation and increasing vascular inflammation [2]. Macrophages express a range of surface pattern recognition receptors that serve as sensors for exogenous pathogen-associated molecular patterns and endogenous damage-associated molecular patterns [3]. Dectin-1 is a well-characterized receptor for β-glucans on macrophages and it plays a critical role in the host defense against fungi [4]. Recently, the intracellular filament protein vimentin was reported to function as an endogenous ligand for dectin-1 [5]. *In vitro* studies showed that binding of vimentin, which is released from macrophages upon inflammatory stimulation [6], can trigger the production of ROS [5] and this might further promote the atherogenic process. The presence of vimentin in human atherosclerotic lesions in close proximity to dectin-1 positive macrophages was also demonstrated, suggesting a possible involvement of the vimentin-dectin-1 axis in the pathogenesis of atherosclerosis [5].

Here, we have directly addressed the involvement of dectin-1 in the development of atherosclerosis. While our findings confirm a distinctive expression of dectin-1 on macrophages in mouse atherosclerotic lesions, we do not find any detectable effect of dectin-1-deficiency on atherosclerotic plaque formation in mice.

2. Material and methods

Bone-marrow transplantation of wild type (wt) and dectin-1$^{-/-}$

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cells into LDLR$^{-/-}$ mice (all on C57Bl/6 background) were performed and the development of atherosclerosis was evaluated. Details of all experimental procedures can be found in online-only supplementary data.

3. Experimental results

3.1. Macrophages in mouse atherosclerotic lesions express dectin-1

Atherosclerotic lesions in LDLR$^{-/-}$ mice, at different stages of development, were stained for dectin-1 to study its expression pattern during lesion formation. As shown in Fig. 1, mouse atherosclerotic lesions show high expression of dectin-1 colocalizing with the macrophage specific marker MOMA-2. Dectin-1 positive macrophages were identified at all stages of lesion development. Particularly in early lesions, dectin-1 showed a complete overlap with MOMA-2 (Fig. 1A–C), whereas in more advanced lesions not all MOMA-2 positive macrophages appeared to show expression of dectin-1 (Fig. 1D–E). These findings are in line with previous reports demonstrating dectin-1 on subsets of macrophages in human atherosclerotic lesions [5,7].

3.2. Mice lacking dectin-1 show normal atherosclerosis development

In order to investigate the functional role of dectin-1 in atherosclerosis we next reconstituted LDLR$^{-/-}$ mice with bone marrow from wild-type or dectin-1 deficient mice [8] and studied

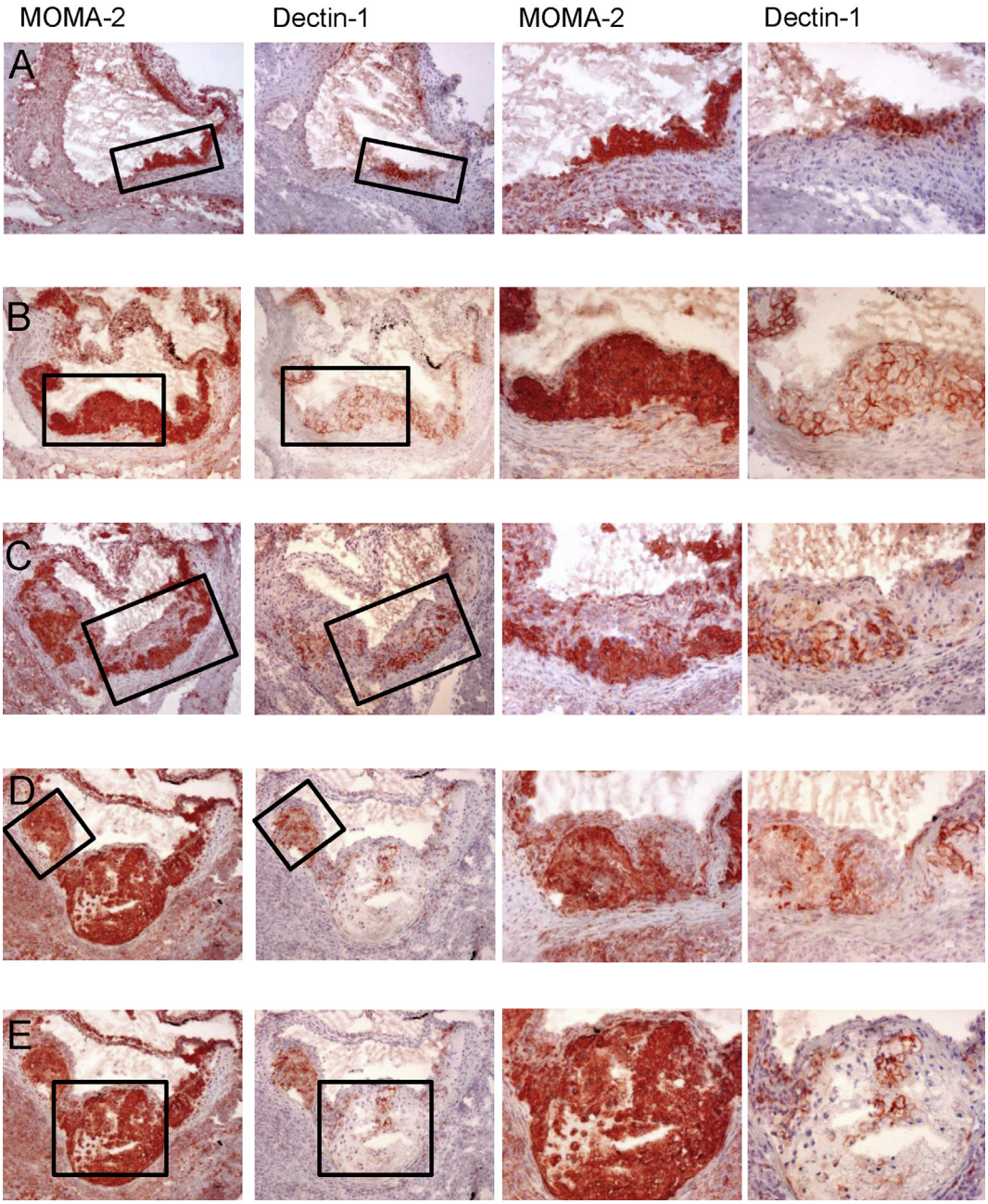

Fig. 1. Plaque macrophages in mice express dectin-1 at all stages of development. Mouse atherosclerotic lesions were stained for macrophages using MOMA-2 as a macrophage marker and with α-dectin-1 antibody at different stages of development: A = early lesion; B = moderate lesion; C = advanced lesion (stable phenotype); D and E = advanced lesion (unstable phenotype) with a small necrotic core (D) and a large necrotic core (E). First two images in each row show 10× magnification, second two images show 20× magnification.