Letters to the Editor
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Role of dendritic cells in specific atherosclerosis types

We have read with great interest the recent article on dendritic cells (DCs) in atherosclerosis by Bobryshev \(^1\) that reviewed the current status of the problem and its clinical relevance. We believe that the author correctly pointed out the role of DCs in the non-diseased vascular wall and in pre-atherosclerotic stages. In addition, he gave a brilliant summary of recent DC findings in manifest vascular lesions, predominantly based on animal work, mainly resulting from the lack of systematically analysed human plaque tissue. However, the author failed to acknowledge that DCs were also found in symptomatic human in-stent restenosis (ISR) \(^2\) as well as in neointima formation after rat carotid balloon injury. \(^3\) First, the latter longitudinal animal data demonstrated DCs adhering along the internal elastic lamina and forming incipient neointima, strongly colocalized with intense Bcl-2 and HSP47 expression as determinants of cell survival and subsequent matrix formation. These and other findings \(^4\) strengthen the concept of co-ordinated anti-apoptotic signals specifically bound to DCs that preserve cellular integrity until neointimal tissue consolidation occurs, thereby promoting neointima formation. \(^5\) Secondly, we showed that the frequency of DCs in tissue probes retrieved from patients with clinical ISR was seven-fold higher when compared with that found in probes from de novo lesions. In addition, the same ISR probes were characterized by low frequency of pathogen burden, inflammation and apoptosis, and absence of proliferation. \(^6\)

Therefore, beyond acknowledging the presence of DCs in hypercellular neointima, we would like to state that it is still too early to develop the conclusion that DCs promote plaque destabilization. \(^7\) We feel that the mere presence of these cells in plaque regions prone to rupture does not exclusively imply that DCs contribute to impaired plaque integrity, but also suggests that these cells are involved in (neo)intimal repair processes.

With respect to DCs and therapeutic intervention in atherosclerosis, in particular, DCs that are implicated in early neointima formation and that exclusively populated the neointimal site \(^8\) seem attractive as carriers for targeted therapies such as DC-mediated gene transfer or other modalities. Of note, recent work of our group revealed neointimal DCs to represent the predominant cell type exhibiting FKBP-12 binding sites for rapamycin early post-vascular injury. \(^9\) Therefore, we propose that the marked prevention of restenosis by use of sirolimus-eluting stents, as widely shown, is primarily mediated by effects on neo-intimal DCs. Likewise, rapamycin specifically induced apoptosis in monocyte and CD34-derived DCs but not in monocytes and macrophages. \(^7\)

References


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Role of dendritic cells in specific atherosclerosis types: reply

In the article entitled ‘Dendritic cells in atherosclerosis: current status of the problem and clinical relevance’, I have reviewed the current knowledge relating to the role of dendritic cells (DCs) in atherosclerosis. The studies of the involvement of DCs in other vascular diseases, such as aortic aneurysm \(^1\) and vasculitis, \(^2\),\(^3\) as well as the studies of DCs in venous pathologies have not been highlighted in the review. The acknowledgement of the studies of DCs in aortocoronary saphenous vein bypass grafts, vascular synthetic grafts, \(^4\) in-stent restenosis (ISR), \(^5\) and in arteries after balloon injury \(^6\) has been beyond the scope of the review.

Over the last decades, the properties of DCs were intensely studied and much knowledge has been gained about the role of DCs in various diseases and health conditions where the immune system is involved. In contrast, studies investigating a possible contribution of DCs in health conditions where the immune system is not involved or is minimally involved are scanty. In this respect, the works of Bauriedel and co-workers \(^5\),\(^6\) are of special interest and importance. Bauriedel et al. \(^5\), have shown that, in early stages of neointima formation, DCs may provide coordinated anti-apoptotic signals that are essential for the maintenance of cellular integrity of the arterial wall, while neointimal tissue consolidation occurs. Bauriedel and co-workers \(^5\) have also identified DCs in human ISR atherectomy tissue samples, and it has been shown that the frequency of DCs in tissue samples obtained from patients with clinical ISR was markedly higher than those in tissue samples representing de novo lesions. \(^5\)

The study of DCs in vascular pathologies is in its infancy. Experimental studies have shown that there is a link between arterial immune inflammation and hypercholesterolaemia, mediated by DCs, and that