nine of them produced an additional 92 kDa species. Experimental animal studies have demonstrated that production of both species of gelatinase correlates with increased metastatic potential.[10] Further studies will be required to assess the impact of these findings.

Both human and animal studies into other tumours would suggest that the production of metastases is a very inefficient process and that, although literally millions of cells may be shed by a tumour into the circulation daily, very few cells have the necessary prerequisites to survive and develop.[11] It is probable that uveal melanomas are equally inefficient in producing metastases; indeed their unusual pattern of dissemination strongly supports this. Beware the patient with a glass eye and a large liver: this axiom, known to many, serves to remind us of the curious propensity for uveal melanomas to metastasise to the liver. The majority of patients with metastatic uveal melanoma either present with, or subsequently develop, liver deposits.[12,13] Why uveal melanoma cells are hepatophilic is unknown. It cannot merely be a function of simple anatomical accessibility. Circulating tumour cells, once they have left the confines of the eye, must traverse the lungs before reaching the liver, and yet, despite this, pulmonary metastases are relatively uncommon. Presumably the liver provides the necessary environmental conditions for circulating tumour cells to flourish and replicate. The factors which facilitate the tumour's ability to colonise the liver remain elusive.

At present, we have almost no insight into those crucial events which initiate the development of uveal melanomas and the factors which promote their ultimate dissemination. The acquisition of this knowledge will provide us with more accurate indices of survival and a greater prospect of cure.

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Macrophages in the pathobiology of epiretinal membranes: multifunctional cells for a multistage process

Epiretinal membranes are proliferations at the vitreoretinal junction and frequently cause traction retinal detachment by virtue of scar-like contraction. Contractile epiretinal membranes typically arise as a complication of proliferative diabetic retinopathy (PDR) or rhegmatogenous retinal detachment. Post-detachment membranes form part of the spectrum of proliferative vitreoretinopathy (PVR). PVR membranes essentially are avascular and have a fibrocellular histological appearance, whereas PDR membranes characteristically are fibrovascular in composition. Nevertheless, both fibrovascular and fibrocellular membranes contain a variety of non-vascular cell types including retinal glia (astrocytes and Müller cells), retinal pigment epithelial cells, and inflammatory cells.

Inflammatory cells have long been recognised as a component of epiretinal membranes.[1] However, epiretinal inflammatory cells have received relatively little attention while much research effort has concentrated on the contribution of non-inflammatory cells like retinal pigment epithelial cells. Indeed, there is evidence that dedifferentiated retinal pigment epithelial cells contribute to some of the macrophage-like cells present in epiretinal membranes.[2] However, PDR and PVR membranes also contain cells with the locomotory characteristics of the mononuclear phagocyte system (MPS),[3] and MPS macrophages may be detected in PVR membranes using immunohistochemical methods.[4]

The introduction of immunohistochemical and tissue culture techniques into the study of epiretinal membranes has marked a shift in the emphasis of research towards the functions, rather than the origins, of cells in the membranes. It is believed that macrophages are involved in both the initiation and the subsequent development of epiretinal membranes. Thus macrophage injections into the vitreous can provoke experimental epiretinal membrane formation.[5] Moreover, epiretinal membrane formation is a multistage process which is likened to wound repair mechanisms elsewhere in the body, a process which is critically dependent upon the multiple activities of macrophages.[6] Apart from their phagocytic functions, macrophages in repair processes are capable of producing a range of enzymes which degrade tissue components.[6] Other macrophage products involved in wound healing include chemotactic agents (for example, the fibronectins), mitogens (such as peptides of the fibroblast growth factor family), and factors which promote extracellular matrix synthesis (for example, peptides of the transforming growth factor ß family).

Variations in macrophage behaviour are reflected by alterations within a group of antigens expressed by the cells. Two such macrophage activity related antigens are recognised by the monoclonal antibodies 27E10 and RM3/1 respectively.[7,8] The antigen detected by 27E10 is displayed by macrophages during the early, inflammatory stages of healing wounds but not during the late, fibrosing phases. By contrast, RM3/1 is expressed by macrophages during the late rather than the early phases of wound repair. Although the precise functional significance of the antigens identified by 27E10

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and RM3/1 is yet to be resolved, the implication is that 27E10+ macrophages are involved in the events of early wound repair (when active cell recruitment and proliferation is taking place in response to locally produced motogens and mitogens) while RM3/1+ macrophages are involved in late stage events (a phase when collagen production and remodelling are occurring).[7 8]

In this issue, Esser and colleagues report the findings of their study concerning 27E10+ and RM3/1+ macrophage subsets in epiretinal membranes. Idiopathic epimacular membranes and membranes from patients with PVR following conventional detachment procedures were devoid of 27E10+ macrophages and only a few of these membranes contained occasional RM3/1+ macrophages. By contrast, both types of macrophage were observed in most PDR membranes as well as in some post-traumatic (surgical or accidental) PVR membranes of less than 9 months' clinical duration. The results of Esser and coworkers suggest that post-traumatic PVR and PDR epiretinal membranes have a more protracted course than do non-traumatic PVR and idiopathic macular pucker membranes. Furthermore, the findings of the investigation intimate that there is no clear delimitation between early, inflammatory phase events and late stage fibrosis in the formation of many epiretinal membranes.

Esser and colleagues conclude that epiretinal proliferation may be inhibited by the early use of steroids. Indeed, there is hope that other therapeutic agents will be revealed as we expand our understanding of the pathobiology of PVR and PDR.

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