nine of them produced an additional 92 kDa species. Experimental animal studies have demonstrated that produc-
tion of both species of gelatinase correlates with increased metastatic potential. 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. It is
probable that uveal melanomas are equally inefficient in
producing metastases; indeed their unusual pattern of dis-
semination 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 subse-
quently develop, liver deposits. Why uveal melanoma cells
are hepatoplastic is unknown. It cannot merely be a function
of simple anatomical accessibility. Circulating tumour cells,
when they leave 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 mem-
branes 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 charac-
teristically 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 com-
ponent of epiretinal membranes. However, epiretinal
inflammatory cells have received relatively little attention
while much research effort has concentrated on the contribu-
tion of non-inflammatory cells like retinal pigment epithelial
cells. Indeed, there is evidence that dedifferentiated retinal
pigment epithelial cells contribute to some of the macro-
phage-like cells present in epiretinal membranes. However,
PDR and PVR membranes also contain cells with the
locomotory characteristics of the mononuclear phagocyte
system (MPS), and MPS macrophages may be detected in
PVR membranes using immunohistochemical methods.

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.
Moreover, epiretinal membrane formation is a multistage
process which is likened to wound repair mechanisms
either in the body, or in the uvea which is critically dependent
upon the multiple activities of macrophages. Apart from
their phagocytic functions, macrophages in repair processes
are capable of producing a range of enzymes which degrade
tissue components. 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 extra-
cellular matrix synthesis (for example, peptides of the
transforming growth factor β 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 recog-
nised by the monoclonal antibodies 27E10 and R3M3/1
respectively. The antigen detected by 27E10 is displayed by
macrophages during the early, inflammatory stages of healing
wounds but not during the late, fibroging phases. By contrast,
R3M3/1 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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Macrophages in the pathobiology of epiretinal membranes: multifunctional cells for a multistage process

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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