Research Highlight

Macrophages Coming of Age: Their Role in Promoting CNV Is Modulated by FasL

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Macrophages have been suspected of having a role in age-related macular degeneration (AMD) since the late '70s and '80s when groups in the United Kingdom and Australia described the localization of cells with the ultrastructural appearance of macrophages either in drusen or penetrating Bruch's membrane in human pathological samples. Despite the subsequent immunophenotypic identification of extensive populations of macrophages in the normal mammalian choroid and evidence of a putative role for inflammation in AMD pathogenesis, we are still unclear about the role of macrophages in the normal and aged choroid. This gap in our knowledge has been partly addressed in a study published in this edition of *IOVS* by Zhao and colleagues.[1] These authors have exploited a range of experimental tools to explore the links between aging changes in the eye and the choroidal neovascular (CNV) response that follows a laser-induced injury to the retina—a model many groups use to mimic the early changes that characterize wet AMD. Zhao et al. have shown that the response to laser injury includes an upregulation of FasL in the eye, most likely due to increased metalloproteinase activity, which is augmented in older mice and appears to attract and activate a more proangiogenic or "M2" type of macrophage population. They demonstrated that neutralizing soluble FasL, which also increases to a greater extent in the blood of older mice following the laser injury, reduced the CNV response in the eye. The subversion of normal macrophage function and skewing of macrophage heterogeneity has been emerging as an important causal factor in a range of diseases such as fibrosis, obesity, and cancer[2]; and this recent study suggests novel opportunities for targeting molecules such as FasL, which appear to regulate macrophage function, in the diseased eye.

References

1. Zhao H, Roychoudhury J, Doggett TA, Apte RS, Ferguson TA. Age-dependent changes in FasL (CD95L) modulate macrophage function in a model of age-related macular degeneration. *Invest Ophthalmol Vis Sci*. 2013;54:5321–5331.
2. Wynn TA, Chawla A, Pollard JW. Macrophage biology in development, homeostasis and disease. *Nature*. 2013;496:445–455.

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