

Macrophages Inhibit Neovascularization in a Murine Model of Age-related Macular Degeneration (AMD)

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PURPOSE

CNV is the process by which abnormal blood vessels develop underneath the retina and lead to blindness in over 90% of patients with AMD. Although the precise etiology of CNV in AMD remains unknown, the macrophage component of the inflammatory response has been thought to be important in this process. We have directly examined the role of macrophages in a murine model of CNV.

METHODS

Mouse Strains C57/Bl6 (B6), B6-IL-10^{-/-}, B6-gld, and B6-lpr mice were purchased from Jackson laboratories, Bar Harbor, ME. All mouse experiments contained 3-5 mice and were repeated at least 3 times with similar results. All work is carried out in accordance with Association for Research in vision and Ophthalmology (ARVO) guidelines for the Use of Animals in Ophthalmic and Vision Research. Laser-induced murine model of CNV was induced by rupture of the RPE and underlying Bruch's membrane with a krypton laser in 5-7 week old mice.

RESULTS

IL-10^{-/-} mice, which have increased inflammation in response to diverse stimuli, have significantly reduced CNV with increased macrophage infiltrates compared to wildtype. Prevention of macrophage entry into the eye promoted neovascularization while direct injection of macrophages significantly inhibited CNV. Inhibition by macrophages was mediated by the TNFfamily death molecule Fas-ligand (CD95-Ligand).

CONCLUSION

These data suggest that normal macrophage function can be critical in controlling pathologic neovascularization in the eye and might prevent blindness from AMD.