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MONOCYTE-DERIVED MACROPHAGES ARE NECESSARY FOR BETA-ADRENERGIC RECEPTOR-DRIVEN CHOROIDAL NEOVASCULARIZATION

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Purpose: We previously demonstrated that beta-adrenergic receptor (beta-AR) blockade inhibits laser-induced choroidal neovascularization (CNV) by 50-80% and reduces interleukin-6 (IL-6) levels by 40%. IL-6 is a pro-inflammatory cytokine, which is known to be produced by macrophages. Additionally, both monocyte-derived macrophages and IL-6 are necessary for CNV. Therefore, we hypothesized that monocyte-derived macrophages are the primary producers of IL-6 downstream of the beta-AR, and are necessary for beta-AR-dependent CNV. **Methods:** Female C57BL/6J or C57BL/6J-CCR2^{-/-} mice underwent laser-induced CNV at 10-12 weeks of age. Female mice received daily intraperitoneal injections of either vehicle (PBS), propranolol (20 mg/kg), CCR2 inhibitor INCB-3284 (1 mg/kg) and vehicle, or INCB-3284 and propranolol for 14 days. On Day 14, fluorescein angiography (FA) was performed, eyes were harvested, and immunofluorescence (IF) was performed to measure CNV area. Data were analyzed using Student's unpaired t-test. **Results:** In female C57BL/6J mice, propranolol reduced laser-induced CNV by 60% using FA (N=4 per group, p=0.01) and 47% using IF (N=4 per group, p=0.09). In C57BL/6J-CCR2^{-/-} mice, propranolol inhibited laser-induced CNV by 36% (N=3-4 per group, p=0.34) and 28% (N=3-4 per group, p=0.63), using FA and IF respectively. In female C57BL/6J mice treated with INCB-3284, propranolol had zero effect upon CNV area (N=7 per group, p=0.99). **Conclusions:** In the absence of CCR2 signaling, which inhibits monocyte recruitment to areas of inflammation, propranolol had reduced or no effect upon CNV area. Although these results are preliminary and increased sample size is required, our data suggest that monocyte-derived macrophages are necessary for beta-AR dependent CNV. **Financial Disclosures:** "Funding for this research was supported by the Global Ophthalmology Awards Program (GOAP), a Bayer-sponsored initiative committed to supporting ophthalmic research across the world".