Enhancing Reliability of the Laser-Induced Choroidal Neovascularization Mouse Model: Insights From a New Study

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The laser-induced choroidal neovascularization (CNV) mouse model is widely used in neovascular age-related macular degeneration (AMD) research. Developed originally in primates, this model was later adapted to rodents and has been successful in predicting the therapeutic value of anti-VEGF therapies, now approved for treating wet AMD. Yet the reliability of this model in producing consistent CNV lesions is debatable, complicated by many factors: differences in laser parameters and operators, rodent age, sex, background, and lesion analytic methods, as well as variations in inclusion and exclusion criteria—all of which together may impact CNV development or accurate measurement of CNV lesions.

The paper by Poor and colleagues summarizes a massive number of carefully controlled and analyzed laser-induced CNV studies with large numbers of repeated experiments in mice. First, Poor et al. attempted to replicate several previous reports of interventions suggesting suppression of laser-induced CNV development—inhibition of complement pathway (C3 and C5) and small interfering RNA (siRNA) treatment (21mer), as well as anti-VEGF treatments. Except for anti-VEGF treatments, which consistently suppressed CNV, Poor et al. were unable to reproducibly repeat the effects of other examined factors. This study also thoroughly analyzed the influence of genetic background of mice on CNV development and found major variations using mice from different vendors. Based on these results, Poor et al. propose a set of recommendations for both appropriate experimental design and preset lesion inclusion/exclusion criteria to enhance reproducibility and avoid potential pitfalls of the laser-induced CNV model. This study will be a sound reference for many AMD researchers utilizing this model and is likely to improve the reliability of reported results. It is critical to note that there are fundamental pathophysiological differences in this acute thermal-induced VEGF-dependent injury model versus chronic aging in AMD. Thus caution is needed in interpreting the results from non-VEGF-related interventions in laser-induced CNV with respect to relevance to human AMD.

References


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