Chi-Chao Chan, J Clin Exp Ophthalmol 2014, 5:3
http://dx.doi.org/10.4172/2155-9570.S1.017

OMICS Group Conferences
Accelerating Scientific Discovery

4th International Conference on
Clinical & Experimental Ophthalmology
July 14-16, 2014 DoubleTree by Hilton Baltimore-BWI Airport, USA

Animal models of age-related macular degeneration in different species

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While the best animal model for age-related macular degeneration (AMD) should be the nonhuman primate because it has a macula leutea, the cost, availability, and ethical issues have largely limited its usage. Instead, researchers prefer to use the mouse as it can be genetically manipulated. Although the mouse has no maculae and rarely develops drusen, its neuroretina and retinal pigment epithelium (RPE) can develop lesions simulating certain features of AMD. Such lesions include focal RPE and photoreceptor degeneration as well as increased A2E levels. Different genetically engineered AMD mouse models often provide valuable information into AMD pathogenesis and have become useful tools for screening novel preventive and therapeutic compounds for the disease. While using a mouse model can have great benefit on this preclinical research, appropriate controls are critical to assess experiments. In general, there are group control and self control paradigms for the experimental design. In the group control experiment, the genetically manipulated mice with retinal AMD-like lesions and the wild type control mice without retinal AMD-like lesions are randomized by age, size, and weight. The AMD mice and control mice are further divided to treated and non-treated (or placebo-treated) groups (4 total). At the end of the experiment, the group of treated mice is compared to control group of the same mouse strain to determine the efficacy of treatment. In the self control experiment, the two eyes of the same mouse are treated differently; one eye receives a therapeutic agent and the contralateral eye receives a control agent or placebo. At the end of the experiment, the same mouse's eyes are compared. However, in addition to the lack of macula, the mouse models have other limitations, including small globe size and simple retinal structure, for which some other models have been developed to address. Rat models have the advantage of larger eye size than mouse. Rabbits has a totally dissimilar retinal vasculature compared to human eyes and can be only applied for evaluation of pharmacokinetics and pharmacodynamics. While the pig eye has similar measurements and an area of enriched cone density like humans, more studies are required in this animal to validate its usefulness in AMD studies. In any of these models, findings may not always reflect those in AMD patients. Careful interpretations of animal experiments with clinical and in vitro data will improve our understanding of AMD pathogenesis and our ability to prevent and treat the disease.

Biography

Chi-Chao Chan earned her M.D. from Johns Hopkins University and ophthalmology residency from Stanford University School of Medicine. She has completed two post-doctoral fellowships: ophthalmic pathology at Wilmer Institute, Johns Hopkins and clinical ocular immunology at National Eye Institute, National Institutes of Health. Chan is the Chief of Immunopathology Section, Laboratory of Immunology and Head of Histopathology Core, National Eye Institute, the federal government medical research institute in the US. She has published more than 600 papers in peer-reviewed journals and one textbook. She also serves as an editorial board member for 20 medical journals.

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