Editorial for special issue: rat models of ROP

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A continuing worldwide epidemic of retinopathy of prematurity (ROP) and consequent increase in the number of children with visual impairment strongly motivate further ROP research. The retinal mechanisms leading to the visual impairments that are common in patients with ROP remain incompletely understood despite spectacular advances in the clinical management of acute ROP and brilliant vascular biology. What are the retinal pathways that result in formation of abnormal retinal lamina, elevated scotopic thresholds, low acuity, abnormal eye growth, and high refractive errors? The usual readership of *Documenta Ophthalmologica*, the members of the International Society for Clinical Electrophysiology of Vision (ISCEV), has the expertise to investigate these issues.

For this special issue of *Documenta Ophthalmologica*, we sought contributions from established laboratories that might ultimately encourage application of ISCEV talents to ROP research. In this issue, the nine review papers crystallize each laboratory's perspective and also offer new data. The first four papers use the so called 50/10 model that was originated by Professor John Penn; this is the most

widely used rat model of ROP. The ROP models are created in young animals by controlled exposure to an ambient oxygen level higher than, or alternating higher and lower than, air. In the rat model, the retinal disease is properly designated oxygen-induced retinopathy, OIR. At the time of the inducing exposure, both the neural retina and its vasculature are immature as is the case in infants with ROP. Although the hallmark of ROP is abnormal retinal vasculature, a growing body of evidence supports a critical role for the neural retina in the ROP disease process. Professor Bruce Berkowitz' contribution makes clear that it is a pan-retinal disease.

Animal models of ROP have the huge advantage of being created by controlled oxygen exposures that produce the disease in all animals. Studies of molecular mechanisms and signaling pathways, anatomic features, and experimental treatments can be carried out with relative efficiency (Barnett et al.; Hartnett; Kermorvant-Duchemin et al.) In infants and young children with ROP, rigorous studies of retinal mechanisms and therapeutic interventions, while necessary, are demanding and slow going. It is already known that the rat eye can model some of the key features of human ROP, including neovascularization (Barnett et al.; Hartnett; Akula et al., Fletcher et al.), stunted eye growth (Akula et al.), and retinal dysfunction (Dorfman et al.) and is just large enough to permit fundamental studies of oxygen consumption, such as those of Cringle and Yu herein. Among inbred rat strains, variations in expression of pro-

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angiogenic factor genes, ocular pigmentation, and susceptibility to the retinopathy (Wijngaarden et al.) provide a fresh perspective on ROP risk factors.

An understanding of the neurovascular cross-talk has been critical to understanding disease in other developing neural tissues. Thus, in the developing retina, neurovascular relationships, or perhaps more exactly, as the paper of Fletcher and colleagues shows, the conversation among developing glia,

neurons, and blood vessels must go amiss and result in the ROP abnormalities. A combination of modern biology and investigation of retinal and visual function, wherein lies the expertise of ISCEV members, will surely lead to new understanding of the ROP disease processes and translate into much needed novel therapeutic approaches to this disease that begins in the immature retina of preterm infants and may lead to lifelong visual impairment.