Retinal Remodeling Triggered by Light Damage in the Albino Rat

Purpose: Our goal was to assess the nature, scope and chronology of remodeling in the neural retina in non-genetic retinal degeneration triggered by light damage (LD) in the albino rat, in comparison with over fifteen different genetic models (Jones et al. 2003, J Comp Neurol; in press). Our hypothesis is that all retinas evince incipient plasticity upon deafferentation, regardless of the mode of photoreceptor loss.

Methods: Over 90 albino Sprague-Dawley rat retinas were analyzed by computational molecular phenotyping (Jones and Marc, 2002, J Neurosci 22:413-427) after light exposures (Organisciak et al., 1998, IOVS 39:1107-1116) of varied durations, pre-adaptation states, circadian phases, and survival times. Post-euthanasia, enucleated eyes were rapidly fixed in glutaraldehyde, resin-embedded and thin sections serially probed for key retinal metabolites and markers (e.g. amino acids, glutathione and rhodopsin).

Results: Within 14 days of even a brief, 3 hr LD treatment, focal photoreceptor loss was accompanied by irregular 2-4 fold increases in RPE glutamine and rod aspartate levels, perhaps presaging cell death. The onset of Müller cell (MC) remodeling (formation of a fibrotic glial seal in regions of extensive rod/cone cell death) is accompanied by a dramatic >10-fold increase in MC glutamine. This occurs only in MCs engaged in seal formation; MCs a mere 0.1 mm away are normal. The neural retina remains stable until about 120-240 days post-LD, when both neuronal migration on hypertrophic MC columns and synaptic remodeling are initiated. Synaptic remodeling is evidenced by neurorpli arising from new neurites in the remnant distal retina containing GABAergic, glycineric, and glutamatergic synapses in novel circuits. Distal migration of MC nuclei, MC hypertrophy and disorganization of the inner nuclear layer, including cell loss, match remodeling processes in advanced genetic forms of retinal degeneration, including human retinitis pigamentosa. By 240 days post-LD there is extensive emigration of MCs and neurons into the remnant choroid, similar to that described by Sullivan et al. (IOVS 44, 2003) for the aged ambient-LD rat.

Conclusions: All insults that kill photoreceptors represent sensory deafferentations that trigger retinal remodeling akin to CNS plasticities, including neuronal loss, growth of new neurites, formation of new synapses, and reorganization of the neuronal and glial somatic positions. LD is a fast, effective trigger of large-scale remodeling (perhaps due to the high temporal coherence of the insult) and will enable study of circuitry defects emergent from remodeling.

Commercial Relationship: BW Jones, None; CB Watt, None; DK Vaughan, None; DT Organisciak, None; RE Marc, Signature Immunologics F, E.