Structure and Function of Microneuromas in Retinal Remodeling

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Purpose: Retinal remodeling triggered by retinal degenerations can lead to formation of new synaptic neuropil: microneuromas. The goals of our work are to visualize the fine structure, circuitry and functional attributes of microneuromas.

Methods: Models used include the human rhodopsin-GFP knock-in mouse (J Wilson, Baylor Col Med), an RGS9 truncation transgenic mouse (Jason C-K Chen, Virginia Commonwealth Univ) and the rd1 mouse. Postnatal day 100-450 mice were euthanized, eyes enucleated and fixed for visualization by computational molecular phenotyping (CMP; Jones et al., J Comp Neurol 2006;464: 1-16) or incubated for in vitro excitation mapping (Marc, J Comp Neurol 1996; 407:47-64) using 1-amino-4-guanidobutane (AGB) permeation activated by kainate or NMDA, followed by CMP. Some mice were used for in vivo AGB mapping of endogenous activity with 5 mM AGB in the eyecup for 45 min. Reconstructions of microneuromas were achieved by a combination of CMP and large-scale image tiling, interpolation and process tracking of serial high-resolution electron microscope imagery of microneuromas. The red cells in [C] are GABAergic amacrine cells. The blue tinted cell is a bipolar cell and the yellow tinted cell is a Müller cell. Both conventional [A] and ribbon synapses [B, D, E] are abundant and display all common synaptic arrangements.

Results: Reconstructions of microneuromas reveal bipolar, amacrine and ganglion cells. Though dominated by conventional GABAergic synapses, bipolar cells form abundant synaptic ribbon contacts with all classes of profiles in microneuromas. Microneuromas are partitioned into distinct structural zones: (1) Müller process ensheathment; (2) orderly bipolar, amacrine and ganglion cells. Though degenerations can lead to formation of new synaptic neuropil: microneuromas. The goals of our work are to visualize the fine structure, circuitry and functional attributes of microneuromas.

Conclusions: Microneuromas are complex structures with intrinsic neural derived processes from cells that express functional ionotropic glutamate receptors. Microneuroma formation is potentially triggered by contact with the RPE. As some processes in microneuromas derive from retinal ganglion cells, ectopic signaling complications attempts to restore visual signaling with transplants or prosthetic devices.

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Further reconstruction of microneuromas is underway with novel code incorporating algorithms to deal with the nonlinear distortions inherent in electron microscopy. This will allow the complete reconstruction of neural structures with automated image mosaicking and slice to slice registration of terabyte sized datasets.