Abstract 2487  B434  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: microneuromes. The goals of our work are to visualize the fine structure, circuitry and functional attributes of microneuromes.

Methods: Models used include the human rhodopsin-GFP knock-in mouse (J Wilson, Baylor Coll 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 1-4µm-guanadionbutanol (AGB) permeation activated by kainate or NMDA, followed by CMP. Some mice were used for in vivo AGB mapping of endogenous activity with 5mM AGB in the eyecup for 45 min. Reconstructions of microneuromes were achieved by a combination of CMP and large-scale image tiling, reconstruction and process tracking of serial high-resolution electron microscope imagery of microneuromes.

Results: Reconstructions of microneuromes reveal bipolar, amacrine and ganglion cells. Though dominated by conventional GABAergic synapses, bipolar, amacrine and ganglion cells form abundant synaptic ribbon contacts with all classes of profiles in microneuromes. Microneuromes are partitioned into distinct structural zones: (1) Müller process ensheathment; (2) orderly fascicles of en passant processes that make few or no contacts; (3) tangles of processes forming numerous synaptic connections. Two reconstructed microneuromes demonstrate either direct contact with retinal ganglion cell axons and bipolar ribbons in them. In vivo excitation mapping with kainate or NMDA activation in vitro demonstrates that microneuromes express functional ionotropic glutamate receptors. In vivo excitation mapping shows that microneuromes have intrinsic excitatory events, even in the absence of photoreceptor drive.

Conclusions: Microneuromes are complex structures with intrinsic neural derived processes from cells that express functional ionotropic glutamate receptors. Microneurom formation is potentially triggered by contact with the RPE. As some processes in microneuroms 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 microneuroms 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.