Abstract Title: Dopaminergic amacrine and interplexiform cells exhibit glutamatergic signatures.

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Purpose: To investigate the small molecule signatures, physiologic responses and signaling mechanisms of vertebrate dopaminergic amacrine (AC) and interplexiform (IPC) cells.

Methods: Intrinsic small molecule signals were assayed along with in vivo and in vitro AGB permeation into retinal cells via computational molecular phenotyping (Marc and Jones 2002 J Neurosci 22: 413) in rabbit, mouse and goldfish retinas. Datasets were visualized as rgb and theme maps of classified cell types, thus reporting the identities and excitation states of all neuronal populations. We specifically visualized dopaminergic neurons via tyrosine hydroxylase (TH) signals, to unambiguously determine their small molecule phenotypes and mechanisms of responsivity.

Results: Mammalian TH+ ACs have been proposed to be GABAergic, yet we show that they all contain little or no GABA, low levels of glycine, and high levels of glutamate. In this sense, they share the same molecular phenotype as goldfish IPCs. Rabbit TH+ ACs show moderately high levels of induced AGB permeation, indicating ionotropic glutamate receptor-mediated channel activation. This is consistent with evidence of low frequency OFF-center cone bipolar cell inputs to mammalian TH+ cells. In contrast, teleost TH+ IPCs show no endogenous AGB permeation, consistent with prior pharmacologic evidence that they are entirely under inhibitory control. TH+ ACs and IPCs resemble displaced ganglion cells, but express a molecular phenotype closer to bipolar cells (high glutamate + high taurine).

Conclusions: It is presumed that, but for the teleost dopaminergic IPC, all vertebrate amacrine cells are GABAergic or glycineergic (Marc et al., 1995; Kalloniatis et al., 1996), and that the mammalian TH+ AC is a dual GABA/dopamine cell (Contini and Raviola, 2003). We find that TH+ ACs and IPCs possess a definitive glutamatergic signature resembling the vertical channels of the retina. All vertebrate dopaminergic retinal neurons are strongly activated by release-from-inhibition and may function in part by increasing tonic excitatory drive via synaptic glutamate release.

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