MEETING ABSTRACTS

CHOLINERGIC MECHANISMS AT THE CORE OF SKELETAL AND RETINAL HISTOGENESIS

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Recently we could establish major cholinergic impact on vertebrate *in vivo* and *in vitro* skeletogenesis (1,2). Cholinergic mechanisms are also at the core of formation of the vertebrate retina. Retinal histogenesis of a so-called inner plexiform layer (IPL) was disturbed in an AChE KO mouse (3). Characterized best by their ChAT expression, the only cholinergic cells in all vertebrate retinae are so-called *starburst amacrine cells* (SACs), which send processes into synaptic IPL sublaminae. We documented that SACs are derived from a larger pool of postmitotic AChE^{+} cells. A developmental comparison of ChAT[+] and AChE^{+} cells revealed a close spatial localization of both proteins first within individual cells (nuclear ChAT, vs. extranuclear AChE), and later between adjacent cells, e.g., ACh-secreting and -degrading cells have the same cell lineage origin, and later remain in close apposition (4). Using our 3D stem cell organoid approach (retinal spheroids), we could show that ChAT^{+} cells were first to initiate IPL formation by establishing two synaptic sublaminae. Unexpectedly, the earliest ChAT^{+} cells co-expressed markers of Müller glial precursors (MCPs), indicating that a direct SAC precursor i) gives rise to neurons and glial cells, and ii) that these premature cholinergic cells drive earliest processes of network formation in vertebrate retinae, e.g. could function as *IPL founder cells* (5, cf. also 6,7). These findings could have profound relevance for a basic understanding of neuronal network formation.

References

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