Successful optic nerve regeneration in the senescent zebrafish despite age-related decline of cell intrinsic and extrinsic response processes

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Dysfunction of the central nervous system (CNS) in neurodegenerative diseases or after brain lesions seriously affects life quality of a growing number of elderly, since the adult CNS lacks the capacity to replace or repair damaged neurons. Despite intensive research efforts, full functional recovery after CNS disease and/or injury remains challenging, especially in an aging environment. As such, there is a rising need for an aging model in which the impact of aging on successful regeneration can be studied. Here, we introduce the senescent zebrafish retinotectal system as a valuable model to elucidate the cellular and molecular processes underlying age-related decline in axonal regeneration capacities. We found both intrinsic and extrinsic response processes to be altered in aged fish. Indeed, expression levels of growth-associated genes are reduced in naive and crushed retinas, and the injury-associated increase in innate immune cell density appears delayed, suggesting retinal inflammaging in old fish. Strikingly, however, despite a clear deceleration in regeneration onset and early axon outgrowth leading to an overall slowing of optic nerve regeneration, reinnervation of the optic tectum and recovery of visual function occurs successfully in the aged zebrafish retinotectal system.

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