RNA-seq of the aging brain in the short-lived fish *N. furzeri* - conserved pathways and novel genes associated with neurogenesis.

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Details

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Abstract

The brains of teleost fish show extensive adult neurogenesis and neuronal regeneration. The patterns of gene regulation during fish brain aging are unknown. The short-lived teleost fish Nothobranchius furzeri shows markers of brain aging including reduced learning performances, gliosis, and reduced adult neurogenesis. We used RNA-seq to quantify genome-wide transcript regulation and sampled five different time points to characterize whole-genome transcript regulation during brain aging of N. furzeri. Comparison with human datasets revealed conserved up-regulation of ribosome, lysosome, and complement activation and conserved down-regulation of synapse, mitochondrion, proteasome, and spliceosome. Down-regulated genes differ in their temporal profiles: neurogenesis and extracellular matrix genes showed rapid decay, synaptic and axonal genes a progressive decay. A substantial proportion of differentially expressed genes (~40%) showed inversion of their temporal profiles in the last time point: spliceosome and

proteasome showed initial down-regulation and stress-response genes initial up-regulation. Extensive regulation was detected for chromatin remodelers of the DNMT and CBX families as well as members of the polycomb complex and was mirrored by an up-regulation of the H3K27me3 epigenetic mark. Network analysis showed extensive coregulation of cell cycle/DNA synthesis genes with the uncharacterized zinc-finger protein ZNF367 as central hub. In situ hybridization showed that ZNF367 is expressed in neuronal stem cell niches of both embryonic zebrafish and adult N. furzeri. Other genes down-regulated with age, not previously associated with adult neurogenesis and with similar patterns of expression are AGR2, DNMT3A, KRCP, MEX3A, SCML4, and CBX1. CBX7, on the other hand, was up-regulated with age.

Beteiligte Forschungseinheiten

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