

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

Baumgart M, Groth M, Priebe S, Savino A, Testa G, Dix A, Ripa R, Spallotta F, Gaetano C, Ori M, Terzibasi Tozzini E, Guthke R, Platzer M, Cellerino A (2014) RNA-seq of the aging brain in the short-lived fish *N. furzeri* - conserved pathways and novel genes associated with neurogenesis. *Aging Cell* 13(6), 965-974.

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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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Identifier

doi: 10.1111/accel.12257

PMID: 25059688