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Nothobranchius furzeri: A new model organism of alpha-synucleinopathy

Nothobranchius furzeri are short-lived fish from Zimbabwe and Mozambique (Africa) that inhabit ephemeral water bodies. Their captive lifespan is 12 to 40 weeks. Previous experiments have demonstrated lifespan extension by ambient temperature reduction, dietary restriction, resveratrol-treatment, hermetic small molecule inhibition of mitochondrial complex I, and, as presented here, NT-020-treatment. NT-020 is a proprietary mixture that has been demonstrated to stimulate stem cell proliferation and retard neurodegeneration in rats and humans. Western blotting of Nothobranchius brain extracts using the SNL-4 antibody showed an accumulation of monomeric and oligomeric ¸alpha-synculein (asyn) protein. Neurodegeneration was confirmed with the observation of GFAP accumulation in the brain. Histological analysis revealed formic acid resistant SNL-4 immunoreactivity in the olfactory bulb, pallium, nuclei associated with the locus coeruleus and other nuclei in the midbrain, optic tectum and periventricular nucleus of the posterior tuberculum as well as the retina. The human equivalents of these central nervous system regions are associated with Parkinson's Disease pathology. Analysis of extracted PARK7 protein (DJ-1) demonstrated increased redox sensitivity and propensity to aggregate. Inspection of the gene, which is associated with a lifespan-determining locus in Nothobranchius, revealed four PARK7 alleles as well as several interesting point mutations. Mutations within two critical DJ-1 regions associated with dimer formation may underlie the observed protein accumulation and consequent variation of lifespan phenotypes. N. furzeri could prove a valuable model organism for idiopathic age-associated¸ alpha-synucleinopathy based on its age-associated changes in asyn protein content, accumulation in certain Parkinson's Disease associated brain regions together with the possible role of PARK7 mutations in effecting lifespan.

Biography

Tyrone Genade completed his PhD and Post-doctoral studies at the University of Cape Town, South Africa, in the Department of Human Biology. His research subject is neurodegeneration and aging of the short-lived Nothobranchius killifish. He currently teaches Anatomy, Physiology and Zoology at Northwestern College (Orange City, Iowa). He is Executive Editor of Killi-Data News: A quaterly review of killifish research.

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