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Leibniz-Institut für Altersforschung
Fritz-Lipmann-Institut e.V. (FLI)

# New resource for aging research: Genome of turquoise killifish publicly available as clone library

**The turquoise killifish (*N. furzeri*) has a lifespan between 3 and 10 months and is the shortest-lived vertebrate species that can be bred in captivity. Over recent years researchers at the Leibniz Institute for Age Research (FLI) in Jena established *N. furzeri* as a new vertebrate model for studying biomedical aspects of aging. FLI researchers together with colleagues from the Clemson University Genomics and Computational Laboratory (USA) have now made the genome of *N. furzeri* available in the form of a bacterial clone library comprised of 130,000 defined DNA fragments. The FLI group has sequenced the ends of 63,000 DNA-fragments to facilitate their exact positioning in the fish genome.**

Roundworm, yeast and fly are amongst the most important and probably also the most familiar model organisms currently used to study biological aspects of aging. However, in recent years new model systems with either long or short life spans have entered the scene. An interesting new short-lived model is the African turquoise killifish (*Nothobranchius furzeri*), a fish species, which for many years has also been most popular amongst aquarium hobbyists worldwide. *N. furzeri* completes the course of a lifetime within as few as three months, being a plain fish of few millimeters (mm) at birth and turning into a beautifully colored adult fish of 30 to 50 mm in its reproductive phase but showing typical signs of aging, like reduced activity, coloration and fertility before eventually dying from a natural death.

## *N. furzeri* – a new vertebrate model in age research

*N. furzeri* live in the Southeast of Africa, and have adapted to the natural habitat where water is only present during the short rainy season. Depending on locality, their life span varies between 3 (short-lived populations, rainy season ca. 3 months) and 10 months (longer-lived populations, rainy period at least 8 months). Also in optimal laboratory conditions, that is, unlimited availability of water and food, life span of the fish is similarly

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short as it would be in the wild. This strongly suggests that the information determining the extremely short life expectancy of *N. furzeri* is deposited and fixed in its genome (genome, all chromosomes containing all inheritable information).

Over recent years, the African turquoise killifish was established as a new vertebrate model organism at the Leibniz Institute for Age Research – Fritz Lipmann Institute (FLI) in Jena and since has been in the focus of several research projects. “Even though breeding the fish in the laboratory has been challenging, it is definitely worth the effort”, says Dr. Matthias Platzer who heads the Genome Analysis Group at the FLI. Starting in 2007, genome-wide sequence analyses were performed in his group resulting in the initial characterization of the *N. furzeri* genome. The size of it is 1.9 billion base pairs which is 2/3 the size of the human genome and bigger than that of other established fish model organisms (e.g., zebrafish and stickleback). “Because the human genome is closer related to the *N. furzeri* genome than to the genomes of roundworm or fly (which are two established short-lived models in aging research), we expect that we can translate findings from *N. furzeri* more faithfully to humans than is possible for worm or fly”, points out Dr. Platzer.

Researchers at the FLI have also tried to identify those regions in the *N. furzeri* genome where the information about the short life expectancy is encoded. In 2012 they have first identified four chromosomal regions which harbor determinants of the *N. furzeri* life span, based on classical crossing experiments of short- and longer-lived strains.

**A genomic library of *N. furzeri***

In a joint effort between the FLI and the Clemson University Genomics and Computational Lab (GCL, Clemson, South Carolina, USA) the genome of the short-lived *N. furzeri* has now been made available to the scientific community in the form of a genomic library. “A genomic library is essentially an ordered catalogue of DNA fragments to systematically dissect the genome and underlying genes”, says Dr. Christopher Saski, Director of the GCL. DNA of *N. furzeri* was randomly fragmented into pieces of 150,000 base pairs on average that were inserted into bacterial artificial chromosomes (BACs). This allows for each DNA fragment of the fish genome to be maintained inside bacteria, be amplified and eventually analyzed in detail. The *N. furzeri* genomic library comprises 129.035 BACs, which together represent over 10 times the total size of the fish genome, and thus each

region in the fish genome is represented by 10 different BACs on average. By sequencing the ends of the fish genomic inserts of 62.788 BAC clones the FLI group has determined exactly which part of the fish genome is carried by these clones. These DNA sequences have been deposited in DNA databases in Europe, USA and Japan and since January 2015 have been accessible to the scientific community. Both GCL and FLI maintain a copy of the genomic library and are open for clone requests.

“If a certain gene or region of the *N. furzeri* genome needs to be studied in detail, we can easily provide the desired BAC clone(s) from our genomic library”, explains Dr. Kathrin Reichwald, project leader at FLI.

„The genomic library is an invaluable resource for researchers world-wide, because it allows performing genetic studies in *N. furzeri* without having to breed and maintain the fish, points out Dr. Reichwald. Currently, 45 research groups work on projects related to *N. furzeri* - mainly in Italy, Germany and the US. “By exploiting our genomic library as a common resource, the interest in this new and fascinating model will grow and likely nourish the field of aging research”, the researchers agree – especially since very recently a toolkit has been published by colleagues from Stanford University (USA) in the well-known scientific journal “CELL” in which it is described how *N. furzeri* genes can be effectively manipulated (www.ncbi.nlm.nih.gov/pubmed/25684364).

**Publication**

The *Nothobranchius furzeri GRZ BAC library* is accessible via GCL (SC, USA) at www.genome.clemson.edu/online_orders?page=serviceBrowse&service=bacrc. DNA sequences generated at FLI (Jena, Germany) have accession numbers KG817100 to KG925981 and are deposited at the „European Bioinformatics Institute“ (EBI/ENA: www.ebi.ac.uk/ena/data/view/KG817100), at the „DNA Databank of Japan“ (DDBJ: getentry.ddbj.nig.ac.jp/getentry/na/KG817100?filetype=html) and at „National Center for Biotechnology Information“ (NCBI: www.ncbi.nlm.nih.gov/nucgss/KG817100).

## Background information

The **Leibniz Institute for Age Research - Fritz Lipmann Institute (FLI)** is the first German research organization dedicated to biomedical aging research since 2004. More than 330 members from over 30 nations explore the molecular mechanisms underlying aging processes and age-associated diseases. For more information, please visit *www.fli-leibniz.de*.

**Clemson University Genomics and Computational Lab (GCL)** in Clemson, South Carolina is well-known and offers genomics and computational biology as sophisticated solutions to competitively address complex problems in agriculture, human health, and environmental systems. The GCL focuses on the discovery and functional analysis of important genes, networks, and genomic regions from plants, animals, fungi, microbes. Further information can be found here: *www.genome.clemson.edu*.

The **Leibniz Association** connects 89 independent research institutions that range in focus from the natural, engineering and environmental sciences via economics, spatial and social sciences to the humanities. Leibniz institutes address issues of social, economic and ecological relevance. They conduct knowledge-driven and applied basic research, maintain scientific infrastructure and provide research-based services. The Leibniz Association identifies focus areas for knowledge transfer to policy-makers, academia, business and the public. Leibniz institutions collaborate intensively with universities - in the form of "WissenschaftsCampi" (thematic partnerships between university and non-university research institutes), for example - as well as with industry and other partners at home and abroad. They are subject to an independent evaluation procedure that is unparalleled in its transparency. Due to the importance of the institutions for the country as a whole, they are funded jointly by the Federation and the Länder, employing some 17,200 individuals, including 8,200 researchers. The entire budget of all the institutes is approximately 1.5 billion EUR. For more information, please visit *www.leibniz-gemeinschaft.de/en*.

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**Figure 1**

A male African turquoise killifish (*Nothobranchius furzeri*, short-lived strain GRZ).

[Picture taken by: Nils Hartmann / FLI]