A new model organism for aging research: The short-lived African killifish

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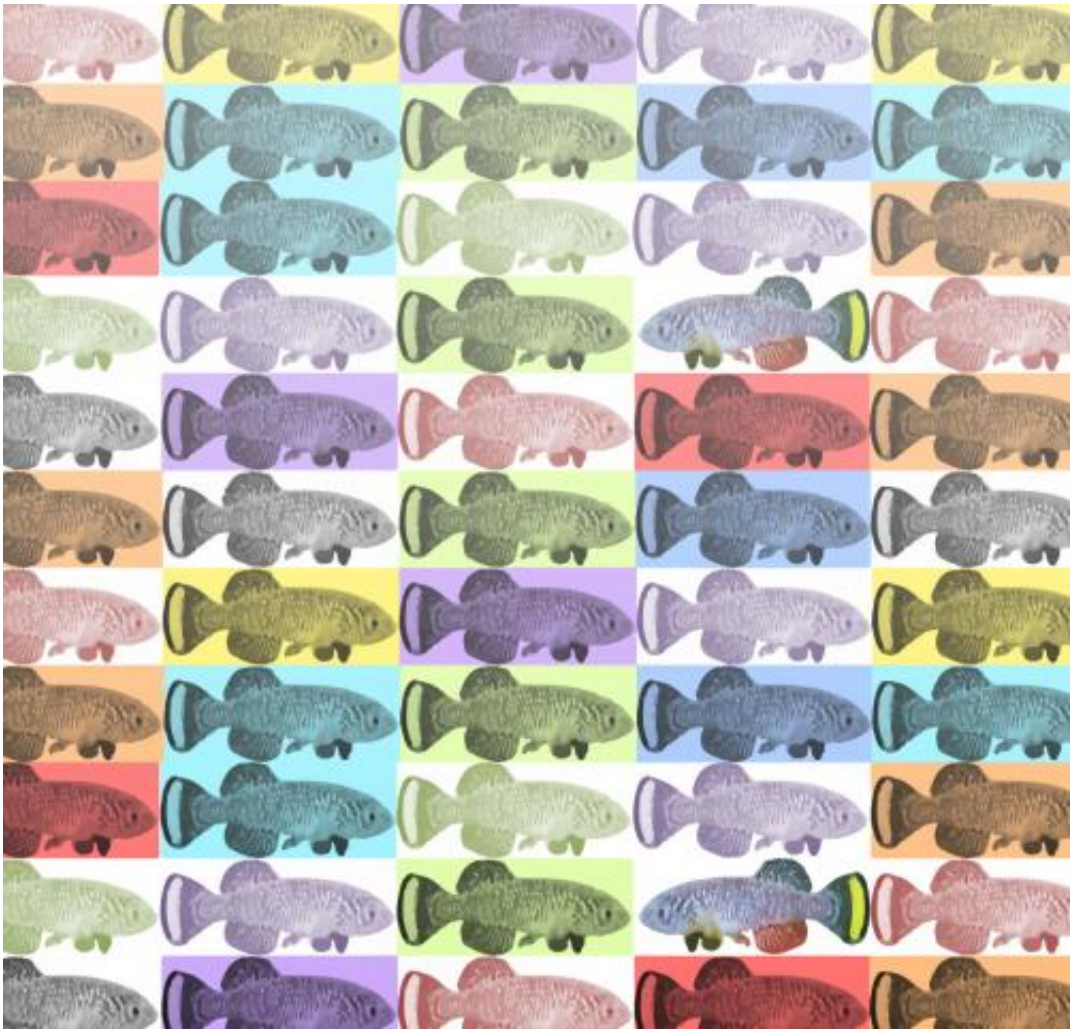

Researchers have developed a genome-editing toolkit to study aging in the naturally short-lived African turquoise killifish. Credit: Itamar Harel

Studying aging and its associated diseases has been challenging because existing vertebrate models (e.g., mice) are relatively long lived, while short-lived invertebrate species (e.g., yeast and worms) lack key features present in humans. Stanford University scientists have found a new middle ground with the development of a genome-editing toolkit to study aging in the naturally short-lived African turquoise killifish. The investigators hope these fish will be a valuable new model for understanding, preventing, and treating the diseases of old age. They present their work in the February 12 issue of *Cell*.

African turquoise killifish live in temporary ponds of water in Zimbabwe and Mozambique that disappear with the dry season. Consequently, unlike their counterparts in more permanent bodies of water, they have evolved a short lifespan of only 4-6 months, making them excellent candidate organisms for studying aging. However, until now, few genetic tools were available for studying them.

Taking advantage of recently developed CRISPR/Cas-based genome editing techniques, the researchers generated the platform needed for the killifish to be used experimentally. "This means knowing the ensemble of its genes and being able to manipulate or mutate them in a variety of ways to better understand aging and diseases of old age," says senior author Dr. Anne Brunet, professor of genetics at Stanford School of Medicine, who has made the genetically engineered fish available to the entire research community.

Some of the killifish mutants have already shown promise for studying aging and disease. "One of our killifish mutants recapitulates, but in a rapid manner, a human disease called Dyskeratosis congenita, which is due to deficits in a complex involved in maintaining the end of chromosomes, or telomeres," says lead author Dr. Itamar Harel, a postdoctoral research fellow in genetics. "These killifish mutants, like their human counterparts, have defects in blood, gut, and display fertility

problems."

Now that the team has generated the tools necessary to rapidly manipulate killifish, the model organism can be used to screen for genes and drugs that slow or reverse aging and age-related diseases.

"Understanding how the genome encodes for complex characteristics like lifespan is one of the biggest challenges of modern biology," Dr. Brunet notes. "This model system and the tools and resources we have created can help tackle this challenge."

Older African turquoise killifish. Credit: Itamar Harel

Younger African turquoise killifish. Credit: Itamar Harel

More information: *Cell*, Brunet et al.: "A platform for rapid exploration of aging and diseases in a naturally short-lived vertebrate", www.cell.com/cell/abstract/S0092-8674(15)00116-6

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