Research on aging accelerates at UNIL thanks to killifish

Improving the quality of life of the aging population is the goal of the laboratory of Alejandro Ocampo, Assistant Professor in the Department of Biomedical Sciences at UNIL. The group is the first in Switzerland to initiate research on killifish, a small animal that can cut the duration of aging studies six to ten times and offers an alternative to other experimental models. This laboratory can accommodate up to 400 fish.

***Nothobranchius furzeri*, a strain of killifish, is used at the University of Lausanne to better understand the processes of aging. © Ocampo Lab**

In Switzerland, the number of centenarians is constantly increasing and the life expectancy of the population is one of the highest in the world. However, this increase in age constitutes a risk factor for the appearance and worsening of certain pathologies such as cardiovascular disease, cancer, pneumonia, Alzheimer's disease or, even more currently relevant, the Covid-19. Due to its high economic impact, the study of aging and therapies aimed at delaying the development of these age-associated diseases is therefore becoming increasingly important.

The research laboratory of Professor **Alejandro Ocampo**, Department of Biomedical Sciences (DSB), Faculty of Biology and Medicine (FBM) at UNIL, is interested in aging. Since January 2020, the team has started to work with an animal with incredible properties, killifish, a small fish with a short lifespan of about six months. This aquatic vertebrate opens up new horizons

at UNIL for the study of aging, as well as research in the fields of development, neurology, cardiology, and immunology.

A successful example of international cooperation between scientists

It was in a laboratory in Italy, about twenty years ago, that killifish was first used in aging research by Dr. Alessandro Cellerino, who at that time worked at the CNR *(Consiglio Nazionale delle Ricerche)* in Pisa. Following that, Dr. Dario Valenzano, one of his first doctoral students, established this model first at Stanford University and later at the Max Planck Institute in Cologne, where he now houses more than 2000 killifish tanks! There, Professor Ocampo and one of his doctoral students got trained on killifish maintenance. At the start of 2020, the "Ocampo Lab" established the first colony of African turquoise killifish *(Nothobranchius furzeri)* in Switzerland. Despite a difficult spring with the closure of UNIL in response to the alarming health situation, the group managed to keep the colony alive. The killifish facility can now accommodate up to 80 aquatic tanks. Now, this model has become the favorite of the team. “Being the first laboratory in Switzerland to work with killifish is very exciting. I am delighted to use this model, which might revolutionize research in the field of aging” says **Calida Mrabti**, doctoral student at the DSB.

A lifespan that reflects adaptation to its ephemeral environment

To understand why the longevity of this fish is surprisingly short, one has to go back to its natural environment in Mozambique and Zimbabwe. *Nothobranchius furzeri* comes from areas characterized by a short rainy season and a wider dry season. The animal lives in small pools of rainwater that disappear as soon as the dry season arrives. Hence, the killifish has to adapt to this environment in order to survive. The quickness of its life cycle reflects on the alternation between the two seasons. As long as the dry season persists, the fertilized egg stays in a suspended developmental state, called **diapause**. The development of the egg into an embryo will only resume with the onset of rain and the formation of new water ponds, which are necessary for its growth, sexual maturation, reproduction, and life.

A fish almost as quick to use as a fly

Reduce the time of experiments is the dream of every researcher. Scientists use many organisms for their research, ranging from less complex invertebrates, such as yeast, worms, and flies, to more complex vertebrates, like fish and mice. The lifespan of the killifish is six to eight times shorter than the mouse and ten times shorter than the zebrafish. However, it is barely twice as long as that of a fly.

Thanks to this aquatic animal, the results of aging studies can be obtained more quickly. “It is amazing to see how rapid killifish develops and gets old,” says **Nibrasul Haque**, doctoral student at the DSB. “I look forward to make important discoveries about the process of aging using this model.” From a technological point of view, this fish can be genetically modified (CRISPR-Cas9 method) for research purposes in just three months, compared to six months for mice. Time means money! Therefore, the expenses required to maintain and care for the animal during an experiment are also reduced.

A fish that is biologically close to humans

“The killifish has the advantage of being almost as quick to use as an invertebrate, while still being representative of what is happening in mammals and humans,” explains Professor Ocampo. Indeed, the killifish presents many biological functions (digestive, muscular, immune, nervous, etc.) common to mammals, as well as the capacity of cell regeneration, a closed blood circulation, and a functional heart. As they get old, the killifish also develop many of the characteristics of human aging, including among others, depigmentation, loss of regenerative capacity and muscle mass, dysfunction of mitochondria (the energy powerhouses of our cells), development of cancers, and beta-amyloid deposition (typical of Alzheimer's disease).

Killifish, an alternative to laboratory mice

The efficacy of a drug is usually tested in animals before it can be clinically tested in patients. This is the case, for example, of the anti-aging treatments that Alejandro Ocampo's team hopes to find. These treatments will aim at increasing the period of good health of the elderly by delaying the onset of diseases as much as possible.

The increasing restrictions on animal experimentation in Switzerland provide a secure framework and ensure the ethical treatment of animals used in research. “In aging studies, switching to killifish might help to reduce the number of experiments with mice and in our case, even stop the use of genetically modified mouse models of premature aging,” adds Professor Ocampo. “The killifish make it now possible to investigate the mechanisms of natural aging.” Everything is under control in the animal house: lighting, temperature, acidity, conductivity; development, and reproduction are monitored regularly, lastly, killifish are fed twice per day, seven days a week. At present, the new small fish available at UNIL could be of interest to other teams in the scientific community of the FBM, or even throughout Switzerland, working in the field of biomedical research.