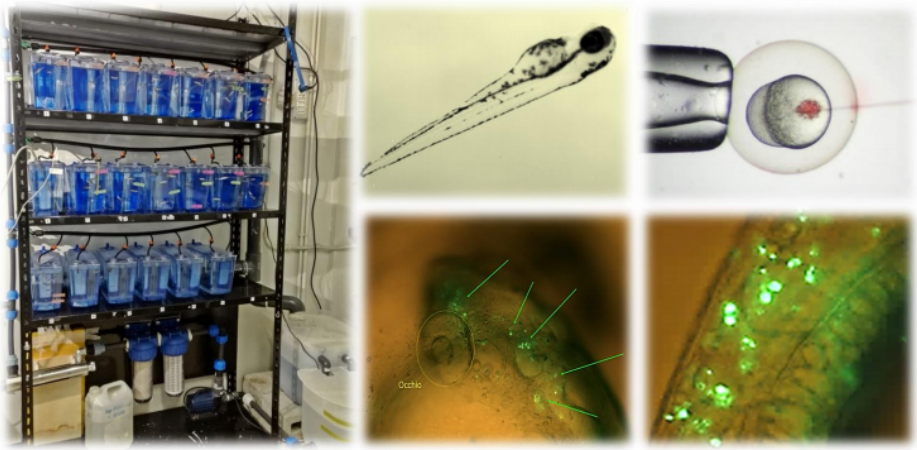
ZEBRAFISH MODEL FOR HUMAN DISEASE



CREATION OF A ZEBRAFISH MODEL FOR ALEXANDER DISEASE

The zebrafish (Danio rerio) is a small tropical teleost fish model often used to study vertebrate biology due to its features including external development, rapid sexual maturity, and embryo transparency. By means of fluorescence microscopy, this last property allows to observe fusion proteins whose expression can be driven in embryos, thus making it an useful model for the study of genetic diseases. In the Laboratory of Developmental Neurobiology we are developing a zebrafish model for Alexander disease, an autosomal dominant and orphan of care neurodegenerative disease caused by heterozygous mutations in the gene encoding GFAP, the intermediate filament of astrocytes. *In vitro* models represented by cell cultures that express the mutated GFAP protein show that the mutations prevent the formation of a correct filamentous structure of the protein and induce its aggregation in the form of numerous cytoplasmic inclusions. However, these models suffer from limitations because, especially for the study of proteins involved in the nervous system, they are unable to recapitulate the numerous interactions between the different cell types.
The aim of this project is therefore to produce a model of Alexander disease more complex than those represented by cell cultures, that could allow both cell biology studies and screenings of compounds to identify molecules effective in counteracting the formation of aggregates.

Keywords: zebrafish, GFAP, microinjection, transgenesis, fluorescence microscopy, molecular biology. Dedicated equipment: DISTAV zebrafish housing and husbandry room

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