Rules of *C. elegans* model organism in science.

Sciandrone B.[1], Pensotti R.[1], Regonesi M.E[1].
E-mail: Barbara.sciandrone@unimib.it
[1] Biotechnology and Bioscience Dept., Università Milano-Bicocca.

Keywords: *C. elegans*, 3R, neurodegeneration, aging, toxicology, natural extracts.

Abstract:

The *"classical problems of molecular biology have either been solved or will be solved"*. With these words, Sydney Brenner in 1963 proposed the roundworm *C. elegans* as a new model organism, in particular for development and nervous system studies. From the identification of mutations that affect animal behaviour in 1974, to the first pluricellular genome sequenced in 1997-2003, *C. elegans* helps researchers in different scientific areas, asserting itself as a valid model organism also in molecular biology, aging and neurodegeneration.

In our laboratory *C. elegans* has been employed in different topics: neurodegeneration, aging, toxicity assessment and supplement foods development.
Neurodegeneration: we have developed a platform that combines *in vitro*, *in situ* and *in vivo* methods to identify lead compound(s) able to counteract the Spinocerebellar Ataxia type 3 (SCA3), an inherited neurodegenerative disease caused by the aggregation of an expanded variant of the ataxin 3 protein, leading to the formation of amyloid fibrils. In particular, our lab focuses on the discovering of natural compounds from plant matrix able to prevent and contrast SCA3 onset. We demonstrated that epigallocatechin-3-gallate, polyphenols from cocoa *Lavado* beans and canella buds are able to prevent ATX3 fibrillation and ameliorates SCA3 phenotypes in a SCA3 *C. elegans* model.
Aging: we characterized the aging process from a phenotypic and molecular point of view in order to correlate the main physiological parameters of lifespan/healthspan to the major aging pathways. Moreover, we analyze the impact of natural extracts, e.g. *Cinnamomum cassia* buds, on *C. elegans* aging.
Toxicity assessment: we employ *C. elegans* to test the effects of natural extracts in aging and malnutrition, and to test the potential toxicity of the promising anticancer Justicidin B lignan, contributing to the reduction of the use of superior model organisms, according with the 3R principles (reduction, refinement and replacement).

In the next future, we are interested in the employment of our *C. elegans* models to study the effects of probiotics both in aging and malnutrition, and in our *C. elegans* SCA3 model to explore the potential gut-brain axis role in this neurodegenerative disease.