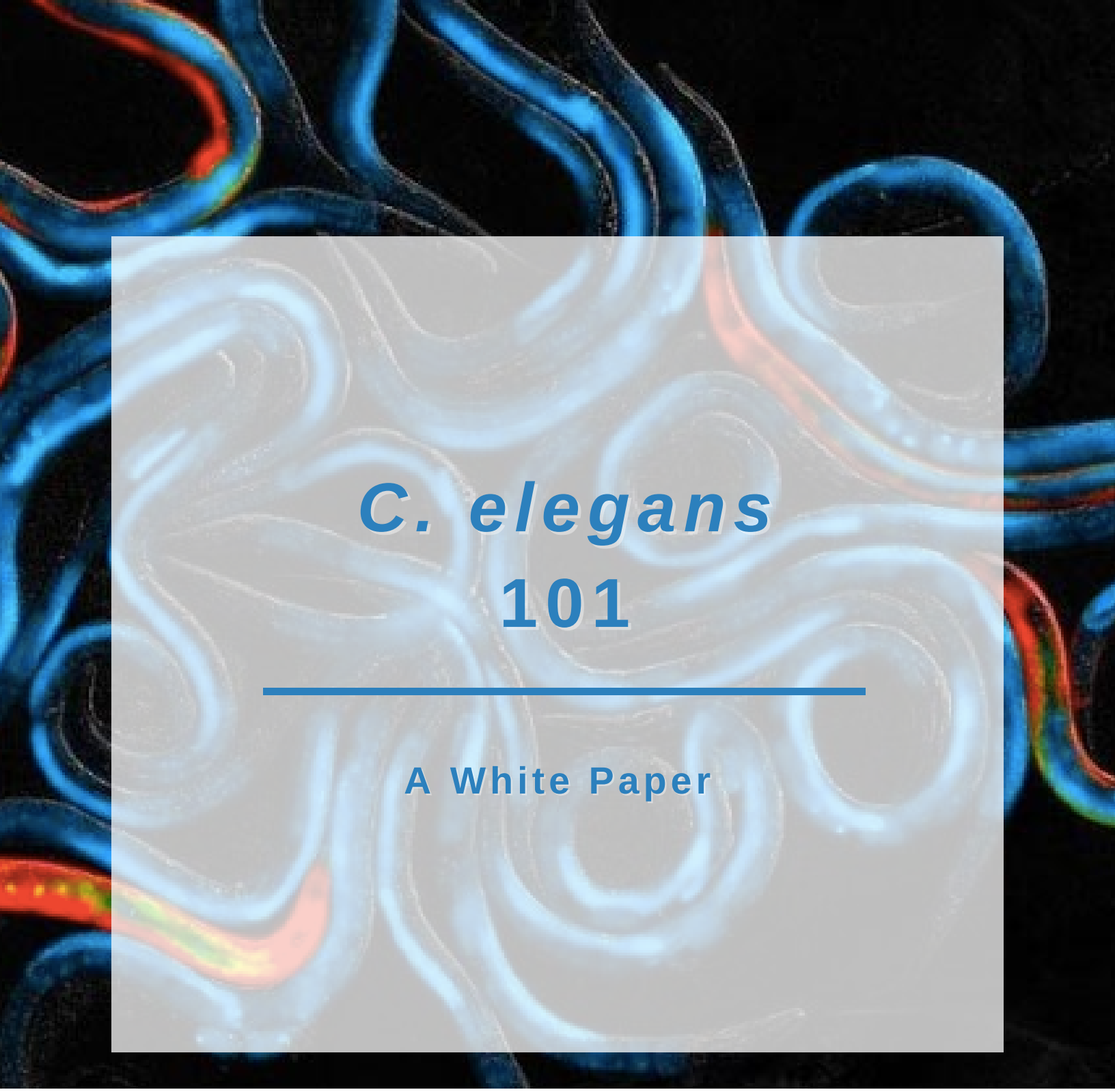

# *C. elegans* 101

A White Paper

InVivo Biosystems

## Summary

The nematode *C. elegans* has been used as a model organism for nearly sixty years and has made significant contributions to science in that time. In this white paper we will discuss the attributes of *C. elegans*, their advantages and limitations, and how they are currently being used in research to answer the question: is a *C. elegans* model right for my research?


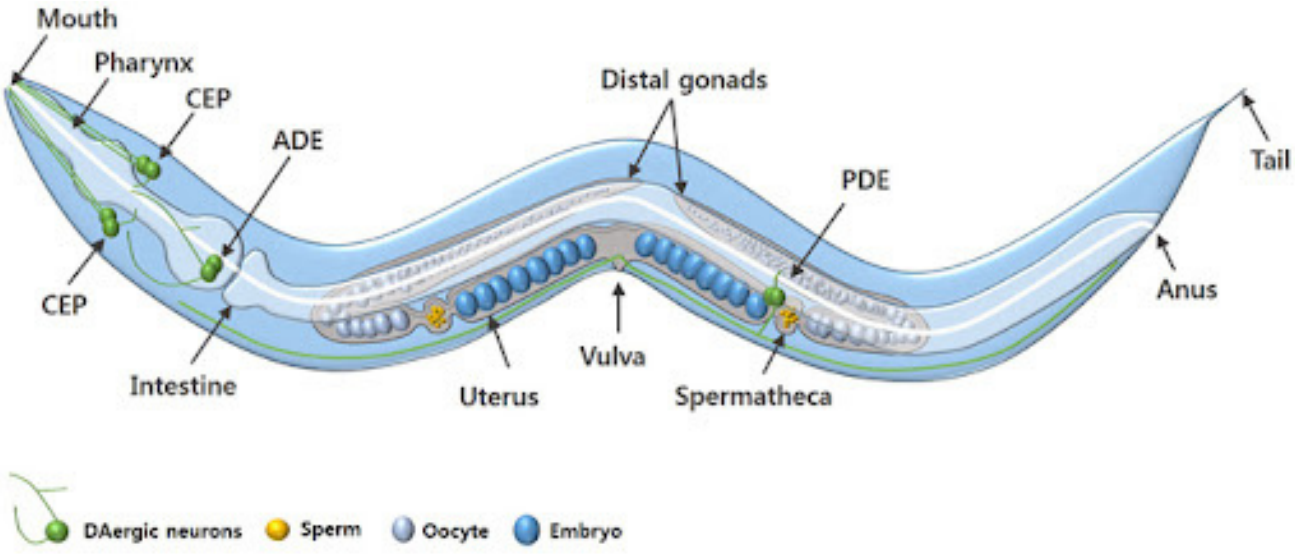


**Figure 1. An adult C. elegans hermaphrodite.** The DAergic neurons include 4 cephalic (CEP) neurons, 2 anterior deirid (ADE) neurons, and 2 posterior deirid (PDE) neurons. Males have 6 additional DAergic neurons located in the tail (Chege & McColl, 2014)

## What is a *C. elegans*?: Biological Sketch

*C. elegans* is a free-living nematode, a member of the phylum Nematoda [See Figure 1]. A roundworm, *C.elegans* is a relatively small organism, growing to 1mm, which mainly consists of their reproductive system (Edgley & the Riddle Lab, 2015). There are two sexes: male or hermaphrodite, but they are easily differentiated by the shape of their tails [Figure 2] (Yokoyama, 2020; Meneely, Dahlberg & Rose, 2019). Its body has three layers: an epidermal, a muscular, and an intestinal layer.

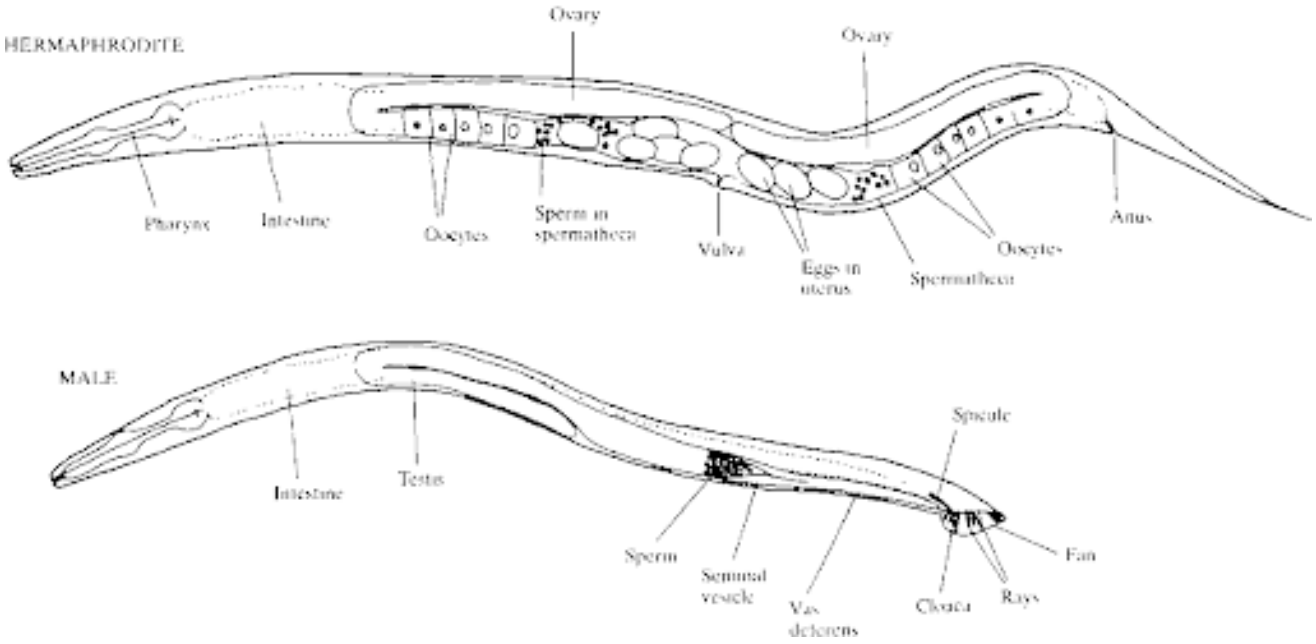


**Figure 2. Primary sex determination in the nematode *C. elegans* (Hodgkin, 1987).**

## Origins of the Model: Out of all the Worms - Why *C. elegans?*

When asking 'why are *C. elegans* widely used as a model organism instead of another type of nematode (worm)', the credit belongs to Sydney Brenner. Sydney Brenner was a genetic biologist who had the foresight to specifically choose *C. elegans* because it was well-suited to genetic analysis — his work on this model would lead him to receive a Nobel Prize in Physiology or Medicine in 2002 (Brenner, 2002).

Brenner first started thinking about the model in 1963 when he wrote to the chairman of the Medical Research Council's Laboratory of Molecular Biology (MRC-LMB) outlining the future of molecular biology research. In this letter Brenner actually suggested the nematode *Caenorhabditis briggsae* as the model organism to shepard in the next decade of discoveries, however, Brenner later changed his mind, settling on the *Caenorhabditis elegans* in 1965 because it grew better in the lab (Corsi, Wightman & Chalfie, 2015; Riddle, Blumenthal, Meyer & Priess, 1997).

## Advantages to using the C. elegans Model

*C. elegans* is an ideal laboratory organism because it is inexpensive, requiring low maintenance, and little space. Only growing to ~1mm, *C. elegans* can be grown in petri dishes, stored in large numbers in the lab, and don't require many other resources commonly needed for other organisms, such as special diets or environmental enrichment that is needed for mammals.(Corsi., Wightman & Chalfie, 2015). Their short life cycle (2-3 weeks) also enables lifespan studies to be conducted much faster than traditional mammalian models [Figure 3]. Furthermore, because of their hermaphroditic nature, *C. elegans* can self-fertilize, enabling them to reproduce quickly in high numbers ( ~300 offspring, with a reproductive cycle of 3.5 days) (Meneely, Dahlberg & Rose, 2019). *C. elegans* have the added advantage of withstanding a ‘’starved’ state for months or, for longer storage periods, they can be frozen at -80C and later revived. Their ability for cryopreservation is especially beneficial for genetic research, as mutant strains can be preserved without the concern that background mutations, suppressors, or other modifiers will occur (Corsi., Wightman & Chalfie, 2015).

Another advantage of *C. elegans* is that, unlike mammalian models which have to adhere to numerous animal testing regulations, *C. elegans* have few ethical concerns (Zhang, et al., 2020). An early criticism of *C. elegans* was that they were too simplistic to be used as an alternative model to these mammalian models, however, in 1974 Brenner published the first genetic map of the organism, revealing that the *C. elegans* has over 100 genetic loci dispersed over 6 chromosomes, all of which are behavioural or morphological markers (Corsi., Wightman & Chalfie, 2015). This publication made it apparent that *C. elegans* were particularly powerful for genetic research, as their simplistic qualities lend themselves to research on complex genetics: their transparent body enables observation at the single-cell level. Additionally, in 1998 they became the first organism to have their genome fully sequenced (*C. elegans* Sequencing Consortium, 1998). Thus, *C. elegans* are extremely advantageous for developmental studies (Corsi., Wightman & Chalfie, 2015). *C. elegans*’ transparent body also enables the use of fluorescent protein reporters, such as Cameleon and gCaMP3 that allow researchers to measure electrophysiology in vivo (Corsi., Wightman & Chalfie, 2015).

Despite *C. elegans* being a simplistic model there are many structural overlaps between humans and *C. elegans* such as the: digestive system, nervous system, and reproductive system. *C. elegans* also display complex behaviour and have ~65% of

disease genes in common with humans (Baumeister & Ge, 2002). Taken together, these characteristics make *C.elegans* capable of a wide range of studies, and able to produce robust and translatable data.

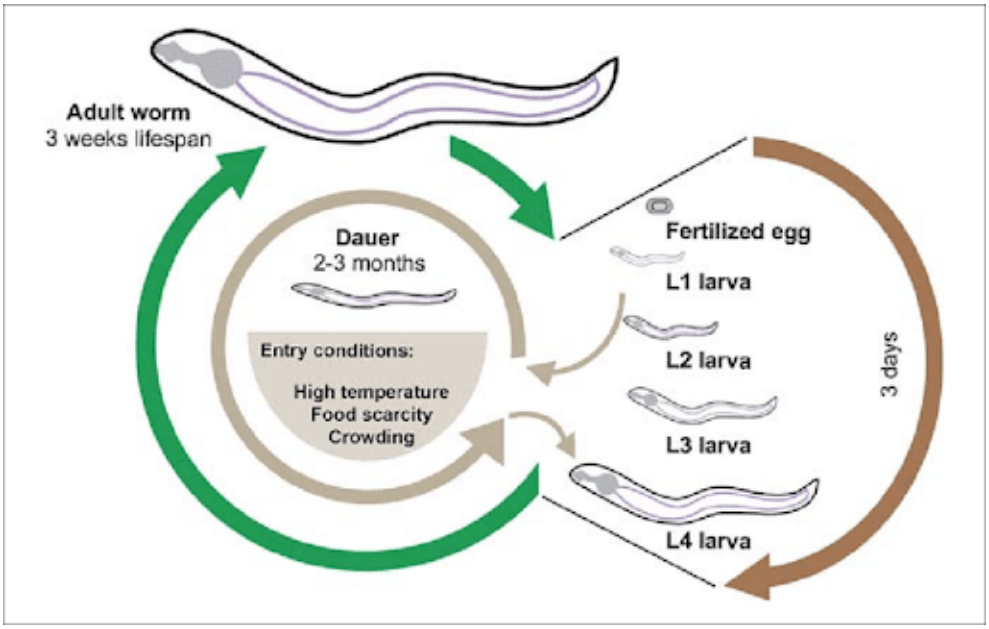


**Figure 3. The lifecycle of the *C. elegans* (Ewald, Castillo-Quan & Blackwell, 2017).**

From a practical standpoint, *C. elegans* are also an advantageous model because they are easy to work with without the hindrances to researchers that other models can pose: there is little health risk as the worm cannot bite, scratch, or grow at body temperature (cannot grow in humans), and there are no recorded allergic reactions (Corsi., Wightman & Chalfie, 2015). Moreover, the active, and collaborative, *C. elegans* community means there are vast resources available for *C. elegans* researchers. These include databases such as: WormBase (https://wormbase.org), which houses nearly all of the known genetic and genomic information of *C. elegans*, the Caenorhabditis Genetics Center (http://cgc.umn.edu), which distributes strains and has information on gene names and laboratory contacts, and WormBook (https://wormbook.org), which collects up-to-date articles on *C. elegans* discoveries and laboratory practices. The access to a complete cell lineage map, these knockout (KO) mutant libraries, and established genetic methodologies including mutagenesis, transgenesis, and RNA interference (RNAi) provide a variety of options to manipulate and study *C. elegans* at the molecular level (Leung et al., 2008).

> **C. elegans *has always been collaborative, so I do love that part of the worm community.”***
>
> ***- Dr Anne Hart, 17 Minutes of Science***

## Limitations to the *C. elegans* Model

Like any model, *C. elegans* has its limitations. Mainly, their simple body plan, and lack of certain human anatomical features such as bones, blood, a defined fat cell, and internal organs (heart or circulatory system) make them unable to model certain conditions. Similarly, for certain research, *C. elegans'* small size may also prove challenging (Tissenbaum, 2015).

## Awards *C. elegans* Have Contributed to: Six Nobel Prizes

As previously mentioned, *C. elegans* was used in Sydney Brenner's work on organ development and programmed cell death, for which he, John E. Sulston, and H. Robert Horvitz shared the 2002 Nobel prize. *C. elegans* also enabled the Nobel-winning work of three other researchers: Andrew Z. Fire and Craig C. Mello's discovery of the phenomenon “RNA interference” (2006), and Martin Chalfie's discovery and development of the Green Fluorescent Protein (GFP) (2008) (Nobel Prize Outreach, 2021; Chalfie, 2008). Thus, despite only gaining prominence as a model organism a few decades ago, Brenner rightly foresaw *C. elegans'* power as a model.

## Research Areas *C. elegans* are widely/regularly used in

### *C. elegans* & the Nervous System: Recent & Notable Publications

1. *C. elegans* as a model to study glial development
2. The Use and Predictability of C. elegans as an Alternative and Complementary Model in Neurotoxicological Studies: Focus on the Dopaminergic System
3. What about the males? the C. elegans sexually dimorphic nervous system and a CRISPR-based tool to study males in a hermaphroditic species

### *C. elegans* & the Immune System : Recent & Notable Publications

1. Neuronal GPCR NMUR-1 regulates distinct immune responses to different pathogens
2. Interspecies bacterial competition regulates community assembly in the C. elegans intestine
3. The Microbial Zoo in the C. elegans Intestine: Bacteria, Fungi and Viruses

### *C. elegans* & Rare Disease Research : Recent & Notable Publications

1. *Caenorhabditis elegans* for rare disease modeling and drug discovery: strategies and strengths
2. NGLY1: insights from *Caenorhabditis elegans*
3. Modeling brain dopamine-serotonin vesicular transport disease in *Caenorhabditis elegans*

### *C. elegans* & Aging / Longevity

1. *Caenorhabditis elegans* as a model system for studying aging-associated neurodegenerative diseases
2. Age-dependent changes and biomarkers of aging in *Caenorhabditis elegans*
3. Lifespan Extension of *Caenorhabditis elegans* by Butyricicoccus pullicaecorum and Megasphaera elsdenii with Probiotic Potential

### *C. elegans* & Toxicology Research

1. *Caenorhabditis elegans*: An Emerging Model in Biomedical and Environmental Toxicology
2. *Caenorhabditis elegans* As a Promising Alternative Model for Environmental Chemical Mixture Effect Assessment—A Comparative Study
3. The *C. elegans* model in toxicity testing
4. *Caenorhabditis elegans* for predictive toxicology

## About InVivo Biosystems

Founded in Eugene, Oregon in 2011, InVivo Biosystems is working to accelerate deep in-vivo insights into human biology and enable researchers to develop and deliver solutions that improve human health. An expert in CRISPR genome editing, InVivo Biosystems provides a unique capability for creating custom genome edited zebrafish and *C. elegans* that enable therapeutic research on genetic models of aging, developmental, and neurodegenerative disease, uncovering potential cures. The company's *in vivo* analytical testing platforms and technologies provide faster, cost-effective investigations that focus on proof-of-principle experiments for rapid go/no go decision making so that biopharma and nutraceutical companies around the world can better understand aging and aging related diseases and explore potential treatments.

All our projects include on-call project status updates, as well as regularly scheduled communication. We also provide on-call consulting and interpretation with our Ph.D. level, subject-matter experts.

## What we do:

- Deliver scientific data on test results in less than 5 months.
- Produce the best outcome measures for anti-aging products.
- Provide information about mechanisms of action (MoA).
- Support your Marketing and IP claims with real science.

Contact us to start a conversation about how our services can support your innovation.


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