## FISH- FORGOTTEN VICTIMS OF RESEARCH

When it comes to animal experiments, most people think of mice, rats or even primates, but few consider the vast number of fish that are used every year.

## Overview

Since the early 1990s, fish have been increasingly used in research:

- as models of human development and disease
- in toxicity testing as subjects for measuring harmful effects of chemicals
- in aquaculture research to expand the farming of fish for food

From a researcher's perspective, fish provide simpler systems for the study of complex processes. Stem cells live throughout their bodies, allowing them to regenerate, providing many avenues for exploratory biomedical research. Moreover, because fish are small, inexpensive, easy to breed and relatively easy to house, they have become a "convenient" test subject for many scientists.<sup>1</sup>

The zebrafish (*Danio rerio*), in particular, is used in research. Since zebrafish embryos are transparent, develop outside of the mother, and grow rapidly (hatching in just three days), they are frequently used to study vertebrate development and physiology. Scientists are increasingly creating mutant zebrafish to identify genes that are essential for normal development.

Aside from zebrafish; platyfish and sword-tails, another kind of small fish, have been used as cancer models for more than 70 years. The Japanese medaka is one of the most commonly used fish models for carcinogenicity testing.<sup>1</sup>



Zebrafish embryo

There is a long tradition of using cephalopods as experimental animals, particularly squid and octopus, in the field of neurophysiology.<sup>2</sup> However, ethical guidelines for the use and handling of animals in science do not typically include cephalopods. The **Australian Code for the Care and Use of Animals for Scientific Purposes** applies to the care and use of all live non-human vertebrates and cephalopods but reporting on the use of fish and cephalopods is not mandatory in all Australian States and Territories.

Globally, it remains unclear just how many fish are used annually, with estimates of over 5 million of zebrafish alone.<sup>3</sup> In Australia, 2,700,640 fish were as used in research in 2017, which is almost double the number of mice.

Lister et al (2017) International survey on the use and welfare of zebrafish Danio rerio in research. Journal of Fish Biology. 90, 1891–1905



American Anti-Vivisection Society (2020) Animals in Science: Fish. Available at: https://aavs.org/animals-science/animals-used/fish/

Moltschaniwskyj, N, et al (2007) Ethical and welfare considerations when using cephalopods as experimental animals. Rev Fish Biol Fisheries 17:455–476

Seahorses are the only fish that swim upright. Most
fish have
taste buds all
over their
body.

of low-pitched sounds to convey messages to each other. They moan, grunt, croak, boom, hiss, whistle, creak, shriek, and wail. They rattle their bones and gnash their teeth. However, fish do not have vocal cords. They use other parts of their bodies to make noises, such as vibrating muscles against their swim bladder.

Fun Facts sourced from Lehnardt, K (2016) 63 Fun Fish Facts. Available at: https://www.factretriever.com/fun-fish-facts

# WHAT YOU CAN DO

We need your help. Fill in the form below today and donate or become a member. Help us to continue the fight to end cruel and ineffective animal experiments and promote more human-relevant research.

Visit our website www.humaneresearch.org.au to read about other ways in which you can help our work to end animal experiments.



Name:	
Address:	
Postcode: Email:	
Phone: Mobile:	Date of Birth:
2 Payment details	3 I would like to make a regular monthly donation of:
l am paying by: Cheque/Money Order Mastercard Visa	\$100 \$50 \$30 Other per month until further notice \$
Number:	I understand that this payment can be stopped by me at any time.
	4 I would like to make a once off donation of:
Expiry Date: CCV No.	\$100 \$50 \$25 Other: \$
Name on Card:	5 I would like to become a member: \$30
Signature:	6 Have you considered leaving a bequest to Humane Research Australia in your Will? Yes No
	7 Would you like us to send you information about bequests to HRA? Yes No





# hra

## Sentience

Scientists often view fish as an alternative to studies that more traditionally use mice and rats, thus, in theory, reducing animal costs by using a phylogenetically lower species and meeting refinement objectives.

Indeed, it has been shown that animals that are closer relatives of humans tend to evoke more-positive feelings and those animals perceived as "cute" tend to be preferred.<sup>4</sup>

Species such as fish and invertebrates are typically rated below mammals, which may in part explain why there is not huge public opposition to the use of fish in research. Yet, whilst the welfare of laboratory fish has received little academic interest and there is lack of certainty on a range of issues, such as anaesthesia or euthanasia methods or enrichment, the mounting evidence that fish are sentient and have the capacity to feel pain is clear.



Zebrafish

Fish are sentient animals who form friendships, experience "positive emotions" and have individual personalities<sup>5</sup>. In the European Union, a scientific panel commissioned by the EU commission recently adopted its general approach to fish welfare and to the concept of sentience in fish. Having examined the research that has been done for some species of fish, it concluded fish feel fear and pain.<sup>6</sup> Similarly, a University of Liverpool study has concluded that the anglers myth that "fish don't feel pain" can be dispelled. Fish do indeed feel pain, with a similarity to that experienced by mammals, including humans.<sup>7</sup>

## Fish Research Cases

As outlined previously, zebrafish are used as an alternative vertebrate model to bridge the gap between simple in vitro cellular studies and complex in vivo models. Two Australian cases are:

- The Australian Institute of Regenerative Medicine at Monash university use zebrafish to research brain and spinal cord injuries and how stem cells work in repair.8
- The Leukaemia Foundation's Research Unit at the Queensland Institute of Medical Research use zebrafish to research gene functions associated with leukaemia.<sup>9</sup>

Fish may also be used in behavioural studies. Such studies often "discover" previously known or trivial conclusions which can easily be concluded by interviewing or observing human subjects. For instance, research into the effects of alcohol by the New York University Polytechnic Institute showed that alcohol-exposed fish swam faster in a group than they did alone, and that drunk zebrafish don't fear robotic predators. <sup>10</sup>

<sup>10</sup> Preston, E (2019). Drunk Fish Convince Sober Ones to Follow Them Around. Available at: <a href="https://www.discovermagazine.com/mind/drunk-fish-convince-sober-ones-to-follow-them-around#.VSyNNPnF-Ck">https://www.discovermagazine.com/mind/drunk-fish-convince-sober-ones-to-follow-them-around#.VSyNNPnF-Ck</a>



<sup>4</sup> Ormandy, E et al (2012) Factors Affecting People's Acceptance of the Use of Zebrafish and Mice in Research. ATLA 40, 321–333

<sup>5</sup> Johnson, I (2017) Fish are sentient animals who form friendships and experience "positive emotions", landmark study suggests. Available at: <a href="https://www.independent.co.uk/news/science/fish-sentient-animals-friends-positive-emotions-study-study-source-ethics-eating-pescaterians-vegans-a7660756.">https://www.independent.co.uk/news/science/fish-sentient-animals-friends-positive-emotions-study-study-source-ethics-eating-pescaterians-vegans-a7660756.</a>

<sup>6</sup> European Food Safety Authority (2020) Fish Welfare. Available at: https://www.efsa.europa.eu/en/topics/topic/fish-welfare

<sup>7</sup> University of Liverpool (2019) September 25, 2019. Fish experience pain with "striking similarity" to mammals. Available at: <a href="https://news.liverpool.ac.uk/2019/09/25/fish-experience-pain-with-striking-similarity-to-mammals/">https://news.liverpool.ac.uk/2019/09/25/fish-experience-pain-with-striking-similarity-to-mammals/</a>

<sup>8</sup> Monash University (2018). Zebrafish and their leading role in regeneration research. Available at: <a href="https://lens.monash.edu/2018/12/04/1358462/zebrafish-and-their-leading-role-in-regeneration">https://lens.monash.edu/2018/12/04/1358462/zebrafish-and-their-leading-role-in-regeneration</a>

<sup>9</sup> Leukaemia Foundation of Queensland (2007) The Carer. Available at: <a href="https://www.leukaemia.org.au/wp-content/uploads/2014/04/LOWTheCarer2\_2007.pdf">https://www.leukaemia.org.au/wp-content/uploads/2014/04/LOWTheCarer2\_2007.pdf</a>

### Concerns

HRA challenges the use of ALL animal experiments, regardless of how "cute" the animal is. Zebrafish have a similar genetic structure to humans. They share approximately 70 per cent of genes with us. However, the dissimilarities and differences in genetic expression mean that research outcomes cannot be translated to humans. Therefore, we propose that human-relevant alternatives are used as a superior method of research.

Furthermore, due to the lower perceived value of fish and lack of understanding of fish welfare, there is a risk that protocols may be approved that would not be permitted for other species afforded a higher value.

These concerns have been substantiated in academic studies. An international survey was conducted regarding zebrafish use for scientific research<sup>11</sup>. This survey highlighted animal welfare issues associated with anaesthesia, lighting, and euthanasia methods, as well as highlighting resistance and confusion over enrichment.

Besides resistance on cost and practicalities, it has also been found that there is lack of consensus about the need for enrichment and how it can be met in fish. Stakeholder interviews in the UK with animal technicians, aquarium managers, scientists, veterinarians and regulators found that there is limited knowledge of what constitutes appropriate environmental enrichment for zebrafish and disagreements over the ability of fish to feel pain and suffer, can hamper the implementation of refinements, despite regulatory encouragement.12

The interviews highlighted that even within laboratory settings technologists, researchers and vets can struggle to relate to fish in contrast with mammals.

It is disappointing that despite their increasing use in research, fish welfare has usually been less of a focus of public interest or regulatory attention than the welfare of more familiar terrestrial and mammalian laboratory animals. It's time to address this and challenge the notion that a "fish is just a fish".



Metriaclima Estharae



Seahorse



Goldfish

<sup>12</sup> Message, R and Greenhough, (2019) "But It's Just a Fish": Understanding the Challenges of Applying the 3Rs in Laboratory Aquariums in the UK. Animals. Available at: https://animalresearchnexus.org/sites/default/files/publications/other-files/animals-09-01075.pdf





<sup>11</sup> Lister et al (2017) International survey on the use and welfare of zebrafish Danio rerio in research. Journal of Fish Biology. 90, 1891–1905