Zebrafish shine in medical research

Professor Kathy Crosier and Associate Professor Phil Crosier

Key words:
- leukaemia, cancer, stem cells, zebrafish.

About Zebrafish:
- the first vertebrate found suitable for large scale genetic screens
- their immune system is very similar to the human one
- zebrafish mutants provide models of human disease.

Aims of this research:
- to improve understanding of genetic mechanisms involved in the development of stem cells and the generation of leukaemia
- to identify the key molecules involved, characterise them, and assess their potential as therapeutic targets.

What our research has shown:
- Runx1 controls how blood stem cells develop in zebrafish in the same way it does in humans
- putting the human Runx1 leukaemia variant into a zebrafish embryo leads to it getting an early form of leukaemia
- an accelerated form of leukaemia is induced when the human Runx1 leukaemia variant is introduced into a fish harbouring a mutation that corrupts Runx1 gene expression
- zebrafish provide an important new system for cancer research.

Zebrafish may seem an unusual thing to find in a lab but Professor Kathy Crosier and Associate Professor Phil Crosier from The University of Auckland’s Department of Molecular Medicine & Pathology have been harnessing them for their work on cancer, in particular leukaemia.

Kathy explains, there are now about 350 biomedical research labs around the world using the zebrafish system and there is not really an area of medical research untouched by this.

“Most major biomedical research institutions now have a zebrafish facility. They allow you to do very large-scale screens to look for new genes and gene pathways in a way that’s previously only been possible in yeast and the fruit fly,” she says.

“You can now do these very powerful genetic studies in a vertebrate system which has essentially the same organs and body plan as a human.”

The Crosiers and their team are particularly interested in the Runx family of genes which are critical regulators of stem cell development.

“What we learn about how blood stem cells are regulated by these Runx genes is likely to have a broader application in stem cell research. It is stem cells that hold so much hope for regenerative medicine, and their development is often corrupted in cancer.”

Their lab has been able to show that a mutation in a gene that controls Runx1 can affect how blood stem cells develop and this gene is now a candidate for involvement in leukaemia.

They have also taken the human Runx1 leukaemia variant and shown that when introduced into a zebrafish embryo it causes an early form of leukaemia. When this finding was published in the highly ranked journal Development, it was chosen by the editors of Science as being one of the most important pieces of research published internationally that week.

“It really pushed the zebrafish forward as being a valid system, with exciting potential for cancer research.”

The lab has recently found that if they put the human leukaemia form of Runx1 into a mutant fish that already has corrupted Runx1 gene expression, they can accelerate the leukaemia process.

Professor Crosier says that this means they now appear to have a mutation in a gene that could be pretty important for understanding how cancer develops, and may also represent a new sort of therapeutic target.

While they are some way off commercialising these findings they have been able to commercialise their knowledge of how to successfully grow zebrafish. They have set up a company called “bioFinz” to market a zebrafish nursery and zebrafish adult tank system developed in their lab.

The research is funded by the Health Research Council of New Zealand, The University of Auckland, Marsden Fund, Auckland Medical Research Foundation, the Foundation for Research, Science and Technology.