

Using Zebrafish to Understand and Design New Approaches to Treat Melanoma

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- Melanoma is a cancer of the melanocytes, the skin cells that provide pigment to the skin, hair and eyes.
- Melanoma accounts for greater than 80% of the deaths from skin cancer, and incidence continues to rise rapidly.
- Metastatic melanoma is aggressive and resistant to all chemotherapy; afflicted individuals have a median life expectancy of less than one year.
- People who live in Scotland have among the highest incidence of melanoma in the UK.
- Increase in sun bed use and holiday sun tanning has promoted melanoma to one of the most common cancers in young adults.

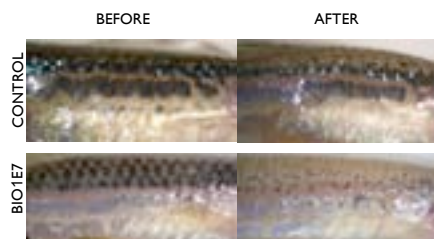
• Melanoma in zebrafish



Zebrafish models of melanoma allow us to study the genetic and environmental factors that lead to the development of moles and melanoma. Here, we have expressed melanoma cancer genes in the fish, and the fish develops a mole and then melanoma.



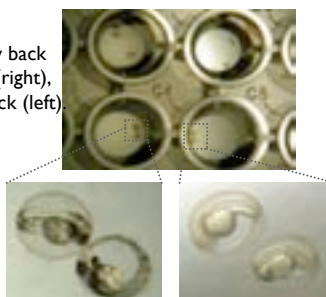
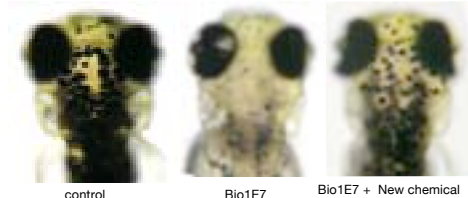
• Testing new chemical compound on our melanoma models



Zebrafish models of melanoma allow us to study the effects of new chemical compounds on the developing cancers. Here, the fish melanocytes all express a mutant gene, called BRAF^{V600E}. This is the most common mutation in human moles and melanoma. We find the melanocytes on these fish highly sensitive to our new compound, BIO1E7.

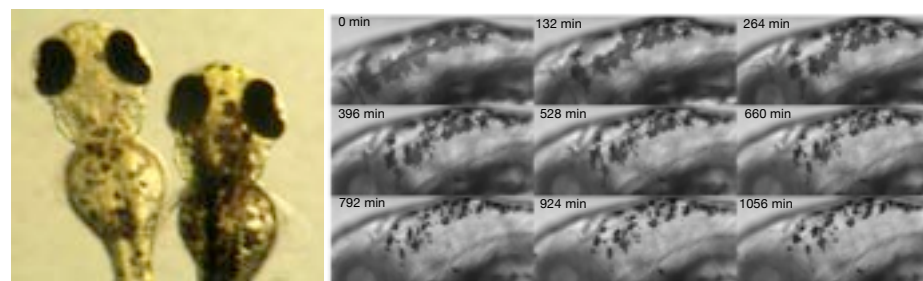
• New insight into melanocyte stem cells

Fish treated with BIO1E7 lose their melanocytes and they do not grow back properly. By testing large numbers of chemicals on zebrafish embryos (right), we have identified a new pathway that allows melanocytes to grow back (left).



• A new chemical compound that kills melanocytes in zebrafish

Zebrafish melanocytes – the dark brown cells – can be viewed easily under a light microscope. We have tested thousands of chemicals and clinical drugs for a specific effect on melanocyte biology and have found that one set of chemicals can specifically kill zebrafish melanocytes.



Zebrafish embryos treated with a new chemical have fewer melanocytes (left) compared with untreated fish (right)

Time-lapse images of a zebrafish embryo treated with a new chemical that causes the melanocytes to lose their normal shape and die.

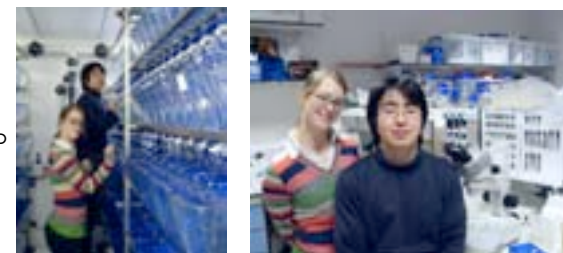
• Who we are!

Our laboratory uses zebrafish as a model organism to answer fundamental questions about melanoma, melanocyte development and the MAPK-signalling pathway in development and disease.

• Dr Hironori Ishizaki, BSc, MD, PhD: Dr Ishizaki trained as a clinical doctor and scientist in Japan, before moving to Edinburgh

• Ms Kerrie Taylor, BSc: Ms Taylor studied biochemistry at the University of Leeds and is a PhD student at the MRC Human Genetics Unit

• Dr Elizabeth Patton, BSc, PhD: Dr Patton trained as a scientist in Canada and the United States, before moving to the UK to set up a laboratory



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