Using Zebrafish to Shed New Light on Melanoma

"When we look at melanoma from a zebrafish it looks just like melanoma from a person," says researcher Liz Patton, PhD.

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By Cody R. Barnett, MRA Director of Communications

Liz Patton, PhD, an MRA-funded cancer researcher at the Medical Research Council Human Genetics Unit at the University of Edinburgh, is fascinated by learning how things work. Patton has focused her research on better understanding how melanocytes — the cells in our skin that provide us our coloring — develop, divide, migrate, and in some unfortunate circumstances, proliferate uncontrollably turning into melanoma. Her work is providing critical insight into the origin of melanoma and what spurs melanoma to spread throughout the body.

Patton specializes in the use of zebrafish — beautiful, shimmering blue, brown, and black striped fish — to help answer fundamental questions about the function of melanocytes and how these cells give rise to melanoma. She is also pioneering the use of this model to help identify new molecules that could be used to treat and ultimately cure the disease.

In melanoma research, models like zebrafish are used to help scientists explore and test new ideas. Cell lines, computer simulations, mice, and other models are all used to help us better understand melanoma and how potential therapies may work. Each type of model has its own advantages and challenges, but Patton believes that zebrafish are especially suited for melanoma research because of the unique way in which zebrafish can be imaged at the single-cell level, experimented with at a large scale, and the very similar way in which melanoma affects both zebrafish and people.

"The use of zebrafish has opened up an entire new world to follow melanoma from the earliest stages of disease through to metastasis, and how the microenvironment and immune cells interact with melanoma," says Patton. "When we look at melanoma from a zebrafish it looks just like melanoma from a person — something that gives us a great starting point to answer fundamental questions about the disease."

As part of Patton's work, her lab has tested thousands of different drugs in the quest for the next generation melanoma therapy. They are doing this using what she calls a "small-molecule screen;" the scale of which just wouldn't be possible in a vertebrate model without zebrafish. At a very

basic level, the approach can be likened to throwing wet spaghetti against the wall to see what sticks, but it is an effective and efficient way to identify promising drug candidates that may warrant more specialized testing.

“We are able to take 5,000 different drug candidates and from that we may get 10 that seem promising. Then, we’ll take a look at them using more advanced zebrafish or human cell line models to see how and why the drug is working,” says Patton.

Using this technique, her team recently discovered a specific group of melanocytes involved in the start of melanoma that is very sensitive to an experimental drug. Patton’s lab is now following up these observations in other models, with the aim to someday bring this novel molecule into the clinic.

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