Light switch added to gene tool opens new view of cell development

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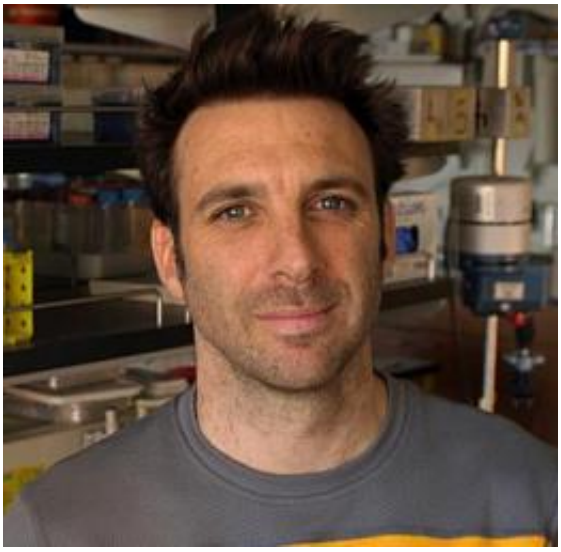

University of Oregon biologist Phil Washbourne collaborated with an Oregon company to develop a UV light-activated on-off switch for the vital gene-blocking molecule, an accomplishment that may help researchers around the world who are studying early developmental processes. Credit: University of Oregon

University of Oregon scientists collaborating with an Oregon company that synthesizes antisense Morpholinos for genetic research have developed a UV light-activated on-off switch for the vital gene-blocking molecule. Based on initial testing in zebra-fish embryos, the enhanced molecule promises to deliver new insights for developmental biologists and brain researchers.

The seven-member team describes the advancement in an open-access paper published in the May issue of the journal *Development*. UO neuroscientist Philip Washbourne, a professor of biology, says the paper is a "proof-of-concept" on an idea he began discussing with scientists at Gene Tools LLC in Philomath, Ore., about four years ago. Gene Tools was founded in the 1980s by James Summerton, who first invented Morpholino oligos. The company holds the exclusive license to distribute these molecules to researchers around the world.

Morpholinos are short-chain, artificially produced oligomers that bind to RNA in cells and block protein synthesis. For a decade, biologists have used them in zebra fish, mice and African clawed toads to study development, but they remained in the active, or on, position. Gene Tools created and introduced a light-sensitive linker, allowing researchers to control the molecule -- even leaving one on in one cell and off in an adjacent cell -- with a pinpoint UV laser beam.

Researchers in Washbourne's lab -- led by neuroscience research associate Alexandra Tallafuss -- were challenged to give the new molecules a test run. They applied them to their work in zebra fish. "Now we can turn them on and off," Washbourne said. "You can insert them and then manipulate them to learn just when a gene is important, and we learned two things right away."

Researchers have known that if a gene known as "no tail" is blocked in development, zebra fish fail to grow tails. They now know that the no-tail gene does not need to produce protein for tail formation until about 10 hours, or very late, into an embryo's development.

Secondly, the researchers looked at the gene sox10, which is vital in the formation of neural crest cells, which give rise to dorsal root ganglion cells -- neurons that migrate out of the spinal cord -- and pigment cells. "Again, we found that sox10 is not needed as early in development as

theorized," Washbourne said.

"These light-sensitive molecules significantly expand the power and precision of molecular genetic studies in zebrafish," said Robert Riddle, a program director at the National Institute of Neurological Disorders and Stroke (NINDS). "Researchers from many fields will be able to use these tools to explore the function of different genes in embryonic regions, specific cell types and at precise times in an animal's lifespan."

The NINDS and National Institute of Child Health and Human Development, both at the National Institutes of Health, supported the research through grants to Washbourne and Eisen.

"This successful collaboration between our scientists and this Oregon-based company shows that commercial innovation can come quickly by jointly addressing common needs," said Kimberly Andrews Espy, vice president for research and innovation at the UO. "This is a remarkable example of turning a concept into a working tool that likely will benefit many researchers around the world."

Provided by University of Oregon