NC State develops more precise genetic 'off switches'

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Researchers at North Carolina State University have found a way to "cage" genetic off switches in such a way that they can be activated when exposed to UV light. Their technology gives scientists a more precise way to control and study gene function in localized areas of developing organisms.

The off switches, called morpholino oligonucleotides, are like short snippets of DNA that, when introduced into cells, bind to target RNA molecules, effectively turning off specific genes. Morpholinos have been used as genetic switches in many animal models, including the zebrafish embryo. However, morpholinos are distributed throughout dividing cells in a developing embryo, thereby turning off the specific gene everywhere. Moreover, they are active right after injection, silencing the targeted gene throughout development of the organism. Such uncontrolled genetic disruption makes studying tissue-specific and time-specific gene function difficult.

Dr. Alex Deiters, associate professor of chemistry, Dr. Jeffrey Yoder, associate professor of molecular biomedical sciences, and a team of NC State researchers developed a new methodology to turn off genes at a specific time and in a specific region of an organism. Deiters' team devised a way to synthesize morpholinos that would only bind with RNA molecules after a brief exposure to UV light, effectively "caging" the morpholino and providing a method for precisely controlling the genetic off switch. Yoder's team then tested the new photo-caged morpholinos in a zebrafish model and confirmed that they performed as expected: the

caged morpholinos did not disrupt gene function unless the embryos were briefly exposed to UV light.

The researchers' results appear online in the Journal of the American Chemical Society.

More information: "Photocaged Morpholino Oligomers for the Light-Regulation of Gene Function in Zebrafish and Xenopus Embryos" Authors: Alexander Deiters, R. Aaron Garner, Hrvoje Lusic, Jeane M. Govan, Mike Dush, Nanette M. Nascone-Yoder, and Jeffrey A. Yoder, NC State University Published: online in the *Journal of the American Chemical Society*.

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