Stem cell breakthrough: Monitoring the on switch that turns stem cells into muscle

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In a genetic engineering breakthrough that could help everyone from bed-ridden patients to elite athletes, a team of American researchers—including 2007 Nobel Prize winner Mario R. Capecchi—have created a "switch" that allows mutations or light signals to be turned on in muscle stem cells to monitor muscle regeneration in a living mammal.

For humans, this work could lead to a genetic switch, or drug, that allows people to grow new muscle cells to replace those that are damaged, worn out, or not working for other reasons (e.g., muscular dystrophy). In addition, this same discovery also gives researchers a new tool for the study of difficult-to-treat muscle cancers. The full report containing details of this advance is available online in The FASEB Journal (http://www.fasebj.org).

"We hope that the genetically-engineered mouse models we developed will help scientists and clinicians better understand how to make muscle stem cells regenerate muscle tissue," said Charles Keller, M.D., assistant professor at the University of Texas Health Science Center and a senior researcher involved in the work. "For our own work on childhood muscle cancers, we also hope to understand how tumors start and progress, and to develop therapies that are less toxic than chemotherapy."

The scientists made their discovery by breeding special mice with a specific gene, called "Cre," which, when activated, can trigger mutations

in muscle stem cells. This Cre trigger is restricted to muscle stem cells and requires a special drug for it to be activated. In one part of the study, using fluorescent techniques, the researchers were able to visualize stem cells and their derivatives in order to pinpoint exactly where muscle tissue was being made. In another part of the study, the scientists were able to activate tumor-causing mutations in muscle stem cells, providing valuable insights into the origins of muscle tumors, which have been previously elusive.

"This is basic science at its best," said Gerald Weissmann, M.D, Editor-in-Chief of The *FASEB Journal*. "This study in mice has not only shown us how stem cells turn into muscle in the living body, but brought us closer to the day when we can use stem cells to repair wounded flesh or a maimed physique."

More information: Biomarker system for studying muscle, stem cells, and cancer in vivo FASEB J. doi:10.1096/fj.08-128116. www.fasebj.org/cgi/content/abstract/fj.08-128116v1

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