

New mouse model may lead to new therapies for degenerative diseases

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Most degenerative diseases begin with a gradual loss of specific cell types that progresses, eventually leading to symptoms. For example, in type I diabetes, hyperglycemia commonly develops when approximately 80 percent of the beta cells in the pancreas are lost; in Parkinson's disease, motor dysfunction typically begins when neurons in a certain portion of the brain are decreased by 70 to 80 percent. Finding ways to stop early cell destruction is vital, but methods to do so have proven challenging because of limitations of models for early stages of cell loss.

A research team led by Albert Edge, Ph.D., principal investigator at the Massachusetts Eye and Ear Infirmary's Eaton-Peabody Laboratory and associate professor at Harvard Medical School, have engineered a new mouse that that can be used for research on degenerative disease. Their paper describing the findings, "Cre/lox mediated in vivo mosaic cell ablation to generate novel mouse models of degenerative disease," was published on May 16 in the [Journal of Clinical Investigation](#).

The "Mos-iCsp3" mouse (for "mosaic inducible caspase 3 mouse") is engineered so that administration of a drug initiates destruction of cells in specifically designated tissues, explains Dr. Edge. Selection of the cell type to be killed is achieved by mating the Mos-iCsp3 mouse with a "Cre" mouse in which an enzyme called Cre recombinase is contained in selected tissues. Any cell that contains the enzyme begins to produce caspase 3. This protein, a so-called "cell death" protein, is subsequently kept in an inactive form until the mouse is treated with a drug that activates caspase 3. Upon treatment with the drug the selected cells die.

Several hundred Cre mice exist and cover a broad array of cell types.

"The mouse provides a way to study [degenerative diseases](#) and a [model organism](#) in which to develop therapies for those diseases," Dr. Edge said. "We targeted inner ear [hair cells](#), beta cells in the pancreas, and epidermal cells. We found that whereas the [beta cells](#) and skin cells showed some regeneration in response to cellular loss, inner ear hair cells were not capable of regeneration and thus hair cell death caused partial deafness. The mouse will expedite our efforts to replace inner ear cells lost in deafness."

Provided by Massachusetts Eye and Ear Infirmary

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