Researchers identify mechanism involved in causing cataracts in mice

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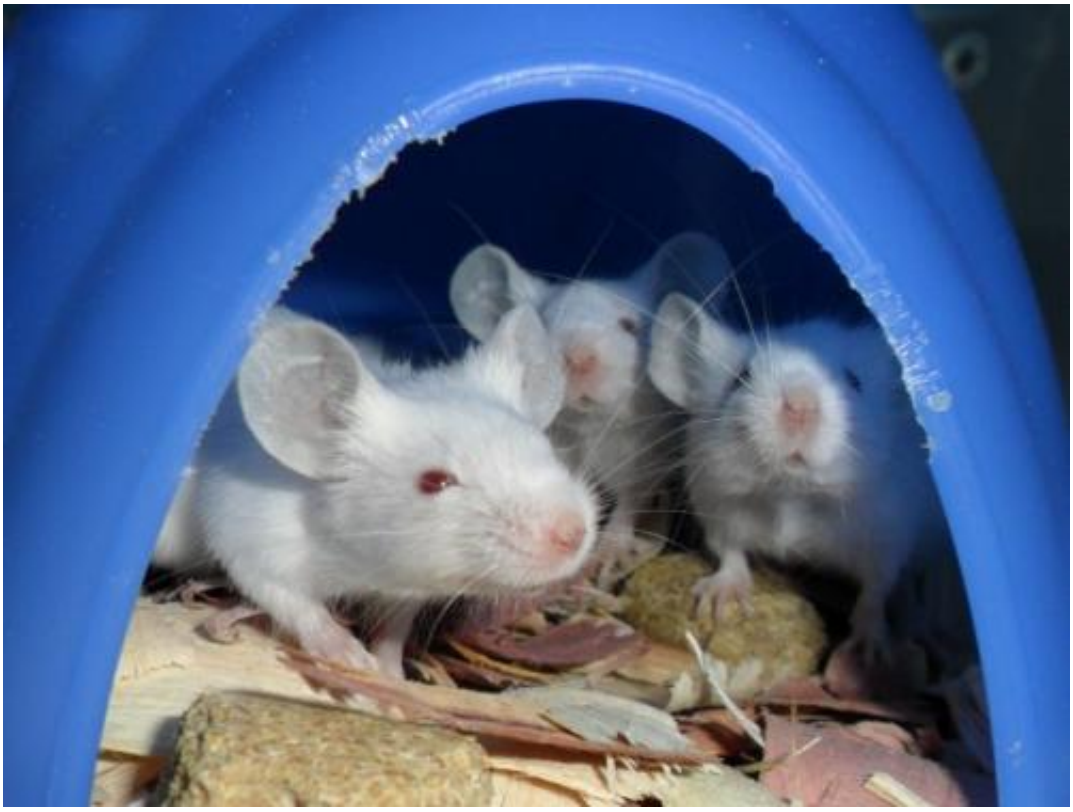

Credit: Martha Sexton/public domain

Cataract is one of the most common eye diseases, becoming more prevalent as people age. Over half of adults in the United States develop cataracts before age 80 and more than six million have undergone surgery to prevent vision loss caused by the clouding of the eye lens.

Now, a team of scientists have established that a breakdown in communication between two biochemical pathways in the eye is involved in causing cataracts. The new information could help researchers develop pharmaceutical and dietary approaches to delaying the onset of cataracts. Scientists from the Jean Mayer USDA Human Nutrition Research Center on Aging (USDA HNRCA) at Tufts University led the study in mice and their results are published in the January 12-16 Online Early Edition of the *Proceedings of the National Academy of Sciences*.

Cataracts are caused in part by the accumulation of abnormal proteins. Normally, obsolete or damaged proteins are removed by the ubiquitin and lysosomal pathways. The authors noticed when the ubiquitin pathway falters calcium flows into the cells of the lens, causing a third pathway to activate. It is this third pathway that causes cataract-related damage in the eye.

"We discovered that the ubiquitin pathway and the calpain pathway communicate with one another. When their conversation goes awry, cells start a vicious cycle in which proteins are improperly degraded," said senior and corresponding author Allen Taylor, Ph.D., the director of Laboratory for Nutrition and Vision at the USDA HNRCA and a professor at the Friedman School of Nutrition Science and Policy at Tufts University. "This leads to alterations in proteins and the beginning of the clouding of the lens that signals the onset of cataract."

The Laboratory for Nutrition and Vision Research at the USDA HNRCA seeks to define and understand how aging and poor diet quality contributes to the abnormal accumulation of proteins that cause eye diseases. The newfound relationship between the ubiquitin and calpain pathways provides a new avenue for researching drugs and dietary approaches that could prolong the function of these pathways and delay the onset of cataract.

The findings may carry implications for other diseases. "Ubiquitin is found in every cell in plants, animals and people; therefore it's possible this interaction with calpain is occurring elsewhere in the body," said Taylor who is also a member of the Cell Molecular & Developmental Biology program faculty at the Sackler School of Graduate Biomedical Sciences and a professor of ophthalmology at Tufts University School of Medicine. "If it is, that would provide the opportunity to learn more about how abnormal proteins may accumulate in other disease states that are similar to cataract, including neurodegenerative diseases such as Alzheimer's and Parkinson's."

Additional authors of this study from the USDA HNRCA are Ke Liu, a former visiting professor from Sichuan University; Lei Lyu, a former visiting graduate student from Sichuan University; Fu Shang, Andrea Caceres, Min-Lee Chang and Sheldon Rowan. Other authors include David Chin and Junmin Pang of St. Jude Children's Research Hospital; Hideko Kasahara of the University of Florida, College of Medicine; and Richard Mathias, Junyuan Gao and Xiurong Sun of Stony Brook University.

More information: Liu K; Lyu L; Chin D; Gao J; Sun X; Shang F; Caceres A; Chang M; Rowan S; Peng J; Mathias R; Kasahara H; Jian S; and Taylor A. "Altered ubiquitin causes perturbed calcium homeostasis, hyperactivation of calpain, dysregulated differentiation and cataract." *Proceedings of the National Academy of Science* Online Early Edition, Jan. 12-16, 2015. DOI: 10.1073.pnas.1404059112

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