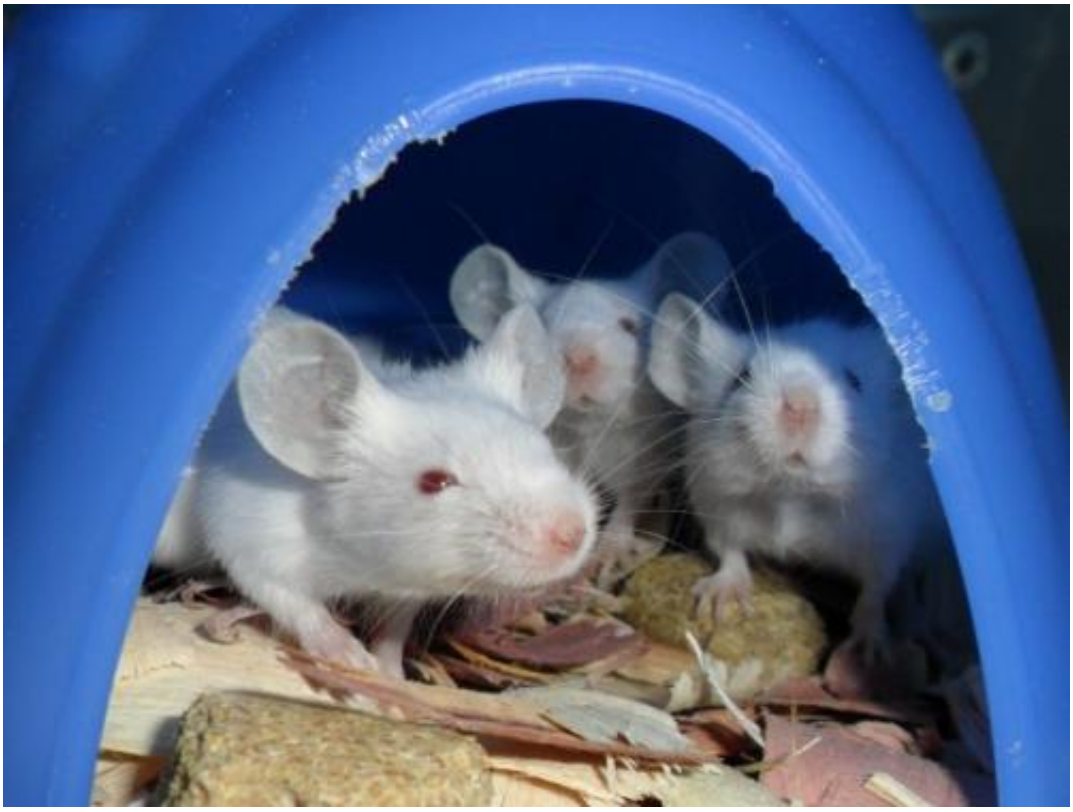
Less effective DNA repair process takes over as mice age

September 9 2014



Credit: Martha Sexton/public domain

As we and other vertebrates age, our DNA accumulates mutations and becomes rearranged, which may result in a variety of age-related illnesses, including cancers. Biologists Vera Gorbunova and Andei Seluanov have now discovered one reason for the increasing DNA damage: the primary repair process begins to fail with increasing age and

is replaced by one that is less accurate.

The findings have been published in the journal *PLOS Genetics*.

"Scientists have had limited tools to accurately study how DNA repair changes with age," said Gorbunova. "We are now able to measure the efficiency with which cells in mice of different ages repair DNA breaks at the same place in the chromosome."

Gorbunova explained that when mice are young, the breaks in DNA strands are repaired through a process called non-homologous end joining (NHEJ), in which the damage is repaired by gluing the DNA together with no or very little overlap. However, Gorbunova and Seluanov found that NHEJ began to fail as the mice got older, allowing a less reliable DNA repair process—microhomology-mediated end joining (MMEJ)—to take over. With MMEJ repairs, broken ends are glued together by overlapping similar sequences that are found within the broken DNA ends. This process leads to loss of DNA segments and the wrong pieces being stitched together.

Gorbunova and her team were able to make their observations by working with genetically-modified mice whose cells produce green fluorescent protein (GFP) that glows each time the breaks are repaired. By tracking how many cells glowed green in different tissues, the researchers determined the efficiency of repair.

"We showed two things with these genetically-modified mice," said Gorbunova. "Not only did the efficiency of DNA repair decline with age, but the mice began using a sloppier repair mechanism, leading to more mutations, particularly in the heart and lungs."

DNA breaks occur frequently because animal cells are under constant assault from routine activities in the environment—whether by a blast of

X-rays from a visit to the doctor or simply breathing in oxygen—and, as a result, the DNA molecules often get damaged.

Using the genetically modified mice, the research team can now look at how diet, medicines, and different genetic factors also affect DNA repair in mice.

"These mice may very well help us devise novel ways to prevent some of the illnesses associated with aging," said Gorbunova.

Provided by University of Rochester