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Study unmasks regulator of healthy life span

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A new series of studies in mouse models by Mayo Clinic researchers uncovered that the aging process is characterized by high rates of whole-chromosome losses and gains in various organs, including heart, muscle, kidney and eye, and demonstrate that reducing these rates slows age-related tissue deterioration and promotes a healthier life span. The findings appear in today's online issue of *Nature Cell Biology*.

"We've known for some time that reduced levels of BubR1 are a hallmark of aging and correspond to age-related conditions, including muscle weakness, cataract formation and tumor growth," says co-author Jan van Deursen, Ph.D., of Mayo Clinic. "Here we've shown that a high abundance of BubR1, a regulator of chromosome segregation during mitosis, preserves genomic integrity and reduces tumors, even in the face of some genetic alterations that promote inaccurate cell division. Our findings suggest that controlling levels of this regulator provides a unique opportunity to extend healthy life span."

Researchers studied two lines of transgenic mice, one with moderate expression of BubR1 and the other with high expression. Outcomes of a series of experiments showed that mice with high expression of the gene were dramatically effective in preventing or limiting age-related disease compared to those with moderate expression and especially to wild type mice.

The findings were significant. Only 33 percent of these high expressing mice developed lung and skin tumors compared to 100 percent of the control group. BubR1 overexpression markedly reduced aneuploidy (a

state of having an abnormal number of chromosomes), which causes birth defects. Other results showed these mice were protected from muscle fiber deterioration, that they were better performers in treadmill tests, that they had much reduced levels of renal sclerosis, intestinal fibrosis and tubular atrophy—all signs of aging. They also showed higher cardiac-stress tolerance and resistance to age-related retinal atrophy.

Co-author Darren Baker, Ph.D., of Mayo Clinic, says the findings show BubR1 and its associated regulators are "promising targets for a broad spectrum of aneuploid human cancers and key age-related disorders that dictate human health."

Provided by Mayo Clinic