

## Evidence for forward and reverse aging via epigenetic manipulation

Jae-Hyun Yang, Ph.D.

Paul F. Glenn Center for Biology of Aging Research, Department of Genetics, Blavatnik Institute, Harvard Medical School, Boston, MA, USA

All living things experience entropy, manifested as a loss of inherited genetic and epigenetic information. In mammals, epigenetic information is also lost over time, but what causes it to be lost and whether it is a cause or a consequence of aging is not known. Using a system called "ICE" (Inducible Changes to the Epigenome), we find the act of faithful DNA repair advances aging at physiological, cognitive, and molecular levels, including erosion of the epigenetic landscape, cellular exdifferentiation, senescence, and advancement of the DNA methylation clock, which can be reversed by OSK-mediated epigenetic reprogramming. These data support a model in which a loss of epigenetic information is a cause of aging in mammals.