

Gene expressions related to DNA changes due to aging found to be related to CpG islands

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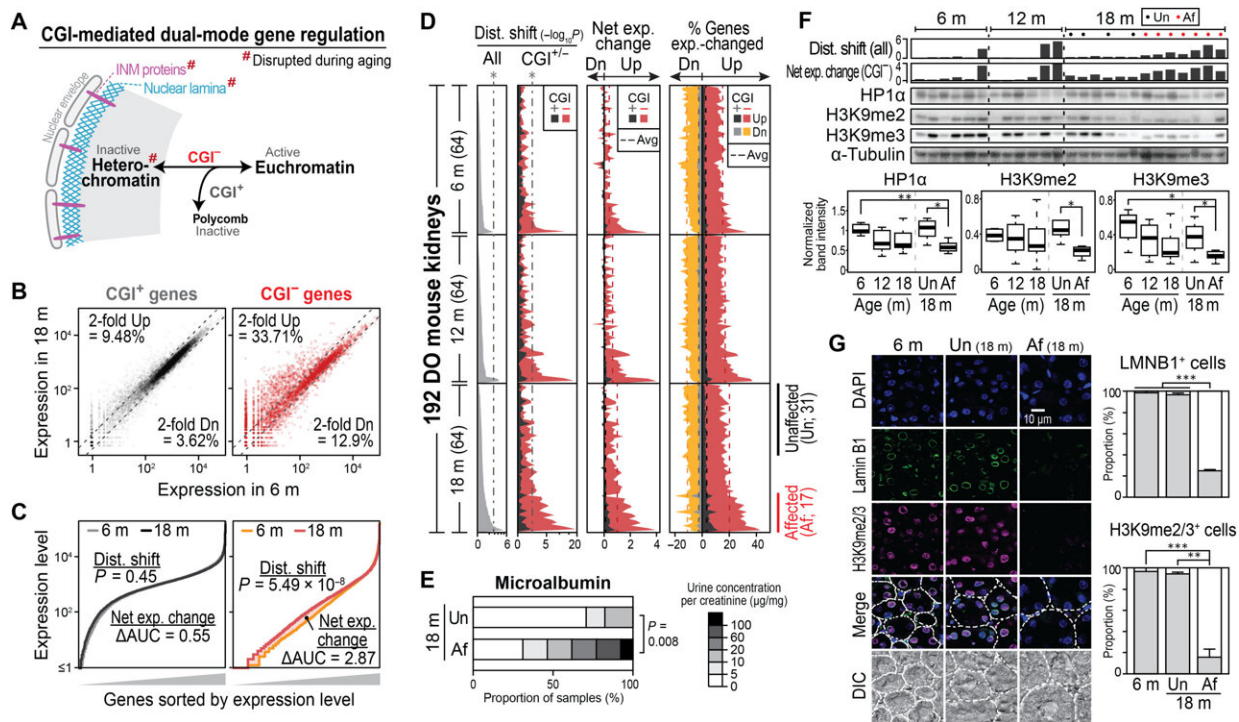


FIG. 1. CGI⁻ gene misexpression and nuclear architecture disruption in aged kidneys. (A) Schematic showing dual mode gene regulation mediated by CGI. Only CGI⁻ genes form lamina-associated heterochromatin, which is disrupted during aging (see also fig. S1A). (B) Example comparison of CGI⁺ and CGI⁻ gene expression in kidney from a young (6 months) and an old (18 months) diversity outbred (DO) mouse showing genes that are ≥2-fold up/down-regulated. Dotted lines indicate twofold difference in expression. (C) Analysis of distribution shift and net expression change for the example shown in (B). Genes

were sorted by expression level. AUC, area under curve. (D) Global gene expression changes in 192 DO mouse kidneys. Each row indicates each kidney; therefore, values (distribution shift, net expression change, and percent genes expression-changed) on the same horizontal line are from the same tissue. Kidneys were sorted by distribution shift of all genes within each age group. Affected (Af) and unaffected (Un) kidneys reflecting distinct physiological ages were determined with distribution shift of all genes as shown in the right bottom. (E) Microalbumin concentration in urine from DO mice with affected and unaffected kidneys. (F) Western blotting of heterochromatin marks and proteins in DO mouse kidneys. (G) Immunofluorescence staining of DO mouse kidneys for lamin B1 and heterochromatin mark (H3K9me_{2/3}). White dotted lines indicate the boundaries of renal tubules. Error bars indicate SD of three replicates. *P

A team of researchers from the Davis Center for Regenerative Biology and Medicine, MDI Biological Laboratory, the University of Texas at Austin and the Jackson Laboratory has found evidence that gene expressions related to DNA changes during aging are related to a lack of CpG islands (long stretches of cytosine-guanine repeats). Their paper is published in *Science Advances*.

One of the great mysteries of science is biological aging. No one really knows why organisms age or the drivers that are behind it, and scientists have been trying to solve the mystery for centuries. Doing so, it is assumed, could someday prevent the process from starting or stopping it at a given point in time. In this new effort, the researchers have found what they believe could be a clue—a possible explanation for why [genes](#) that lack CpG islands begin behaving in destructive ways.

Prior research has shown that as cells grow older, problems begin to arise with chromatin—the material cells are composed of: DNA, RNA and proteins. Researchers have wondered if such changes were contributors to the aging process in general, or just a result of it. To find out, they focused their efforts on CpG islands, which are present in approximately 60 percent of promoters in [human genes](#); they are known as CGI⁺ genes—those without them, quite naturally, are called CGI⁻ genes. Prior research has shown that CGI⁻ genes remain dormant early in life. As people grow older, however, the lamina holding

them in place weakens, allowing them to begin expressing things such as cytokines.

In studying the CGI⁻ genes in mice, the researchers found it tended to be upregulated more (more [gene expression](#) occurred) as tissues aged. And they also found that mice with such upregulation had higher rates of renal dysfunction. They suggest this is evidence of an association between the misexpression of CGI⁻ genes and aging. They also found that when a receptor known as Lamin B, which binds heterochromatin to the [nuclear envelope](#), does not function as it should, the result is looser heterochromatin, allowing CGI⁻ genes to become more active.

More information: Jun-Yeong Lee et al, Misexpression of genes lacking CpG islands drives degenerative changes during aging, *Science Advances* (2021). [DOI: 10.1126/sciadv.abj9111](https://doi.org/10.1126/sciadv.abj9111)

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