Age-related methylation changes in the human sperm epigenome

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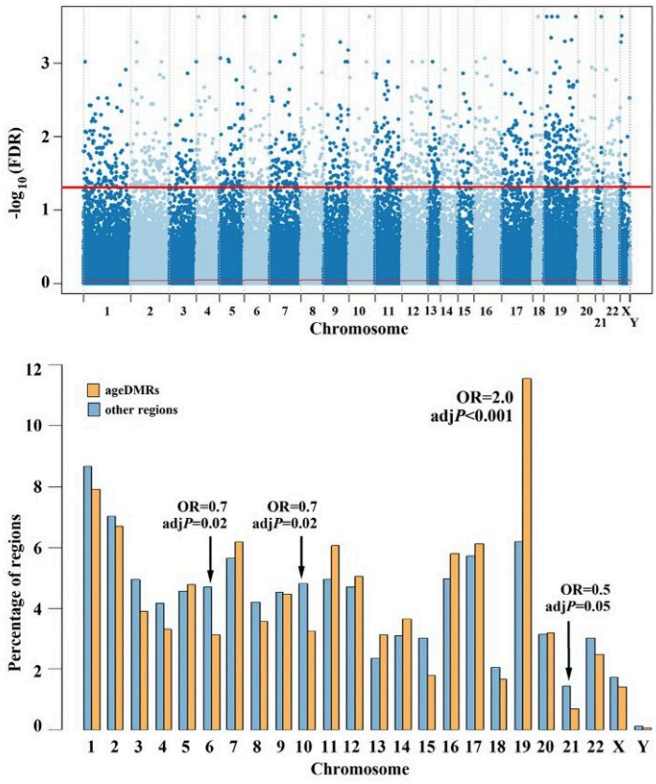

Chromosomal distribution of human sperm ageDMRs. Credit: *Aging* (2023). DOI: 10.18632/aging.204546

A new research paper titled "Age-related methylation changes in the human sperm epigenome" has been published in *Aging*.

Advanced paternal age is associated with increased risks for reproductive and offspring medical problems. Accumulating evidence suggests age-related changes in the sperm epigenome as one underlying mechanism. In a recent study, researchers from Julius Maximilians University, Partner Site Göttingen and Fertility Center Wiesbaden performed reduced representation bisulfite sequencing (RRBS) on 73 sperm samples of males attending a fertility center in Germany.

The researchers write, "[...] we identified 1,162 (74%) regions which were significantly (FDR-adjusted) hypomethylated and 403 regions (26%) being hypermethylated with age."

There were no significant correlations with paternal BMI, semen quality, or ART outcome. The majority (1,152 of 1,565; 74%) of age-related differentially methylated regions (ageDMRs) were located within genic regions, including 1,002 genes with symbols. Hypomethylated ageDMRs were closer to transcription start sites than hypermethylated DMRs, half of which reside in gene-distal regions.

In this and conceptually related genome-wide studies, so far 2,355 genes have been reported with significant sperm ageDMRs, however most (90%) of them in only one study. The 241 genes that have been replicated at least once showed significant functional enrichments in 41 biological processes associated with development and the nervous system and in 10 cellular components associated with synapses and neurons.

This supports the hypothesis that paternal age effects on the sperm methylome affect offspring behavior and neurodevelopment. The researchers found it interesting to note that sperm ageDMRs were not randomly distributed throughout the human genome; chromosome 19 showed a highly significant twofold enrichment with sperm ageDMRs. Although the high gene density and CpG content have been conserved, the orthologous marmoset chromosome 22 did not appear to exhibit an

increased regulatory potential by age-related DNA methylation changes.

"Collectively, our data support the conclusion that age-induced methylation changes in the sperm epigenome contribute to the increased offspring disease susceptibility for neurodevelopmental disorders," the researchers conclude.

More information: Laura Bernhardt et al, Age-related methylation changes in the human sperm epigenome, *Aging* (2023). DOI: 10.18632/aging.204546

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