

Microglial methylation "landscape" in human brain

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In the central nervous system, microglial cells play critical roles in development, aging, brain homeostasis, and pathology. Recent studies have shown variation in the gene-expression profile and phenotype of microglia across brain regions and between different age and disease states. But the molecular mechanisms that contribute to these transcriptomic changes in the human brain are not well understood.

Now, a new study targets the methylation profile of microglia from human brain.

The study appears in *Biological Psychiatry*.

Microglia, the brain's own immune cells, were once thought of as a homogenous population that was either "activated" or "inactivated," with either pro-inflammatory or neuroprotective effects. But the cells are now recognized to have a vast array of phenotypes depending on environmental conditions with myriad functional consequences. Microglia are increasingly appreciated as critical players in neurologic and psychiatric disorders.

Fatemeh Haghghi, Ph.D., senior author of the new work, said that "to address this gap in knowledge, we set out to characterize the DNA methylation landscape of human primary microglia cells and factors that contribute to variations in the microglia methylome."

DNA methylation is the main form of epigenetic regulation, which determines the pattern of which genes are being turned "on" or "off" in various circumstances over time.

The researchers studied isolated microglia cells from post-mortem [human brain](#) tissue from 22 donors of various age, including 1 patient with schizophrenia, 13 with mood disorder, and 8 controls with no psychiatric disorder, taken from 4 [brain regions](#). They analyzed the microglia using genome-scale methylation microarrays.

Unsurprisingly, microglia showed DNA methylation profiles that were distinct from other cells in the central nervous system. But less expected, said Haghghi, "we found that interindividual differences rather than brain region differences had a much larger effect on the DNA methylation variability." In addition, an exploratory analysis showed

differences in the methylation profile of microglia from brains of subjects with psychiatric disorders compared to controls.

John Krystal, MD, Editor of *Biological Psychiatry*, said of the work, "These promising data point to pathology of the microglia, key immune cells of the brain, in the biology of depression."

More information: Lot D. de Witte et al, Contribution of age, brain region, mood disorder pathology, and interindividual factors on the methylome of human microglia., *Biological Psychiatry* (2021). [DOI: 10.1016/j.biopsych.2021.10.020](https://doi.org/10.1016/j.biopsych.2021.10.020)

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