

Epigenomic regulation of prefrontal microglia induced by social defeat stress

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Stress is caused by various adverse environments, and often causes emotional changes. Using social defeat stress (SDS) in mice, we previously reported that repeated SDS activates microglia in the medial prefrontal cortex (mPFC), and then leads to social avoidance. Recently, we found that microglial activation in the mPFC occurs more rapidly and strongly with repetition of SDS. This finding led us to speculate that repetition of SDS induced persistent epigenomic changes of microglia in the mPFC. However, due to the limited sensitivity of chromatin immune precipitation sequencing (ChIP-seq), a brain region- and cell type-specific epigenomic analysis has been challenging. Here we optimized the protocol of ChIP-seq for epigenomic analyses of mPFC microglia. This protocol allows us to detect enrichment of active histone marks near microglia-specific genes in mPFC microglia. Our preliminary findings reveal that whole-genome epigenomic profiles of microglia reflected the experience of single SDS or repeated SDS. Interestingly, these epigenomic profiles in mPFC microglia were different from the profiles in the nucleus accumbens, indicating brain-region-specific epigenomic changes. We are currently investigating transcription factors related to regulation of mPFC microglial epigenomic changes associated with emotional changes.