Confined Migration Induces Heterochromatin Formation and Alters Chromatin Accessibility

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Cell migration is required for many physiological and pathological functions. *In vivo*, cells frequently migrate through tight spaces, requiring extensive deformation of the cell body and nucleus. We hypothesized that nuclear deformation associated with such confined migration could alter chromatin organization and function. Studying cells migrating through collagen matrices and microfluidic devices that mimic interstitial spaces in vivo, we found that confined migration results in increased H3K9me3 and H3K27me3 heterochromatin marks that persist for several days. This confined migration-induced heterochromatin ("CMiH") was distinct from heterochromatin formation during migration initiation. CMiH predominantly decreased chromatin accessibility at intergenic regions near centromeres or telomeres, suggesting heterochromatin spreading from existing heterochromatin sites. Consistent with the overall decrease in chromatin accessibility, global transcription was decreased during confined migration. Inhibiting CMiH reduced migration speed, suggesting that it promotes confined migration. Intriguingly, we also identified increased accessibility at promoter regions of gene linked to chromatin silencing, tumor invasion, and DNA damage response. Together, our study indicates that confined migration can induce chromatin changes that regulate confined migration and other cellular functions.