

PARP1 regulates 3D structure and function of super-enhancers and hormone-control regions

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Poly (ADP-ribose) polymerase 1 (PARP1) has been linked to various genomic pathways and in the maintenance of genomic stability. PARP1 also regulates enhancers activity, but its role at super-enhancers (SE) remains unknown. Here, we employed genomic approaches to show how PARP1 occupies SE of T47D breast cancer cells and how PARP1 is also dynamically sequestered from SE by progesterone treatment to lodge into control regions regulated by the hormone. Disruption of PARP1 or inhibition of its PAR-ylation activity cause transcriptome reprogramming altering the expression of both SE-associated and hormone-regulated genes. This is achieved through a coordinated action in the establishment of long-range chromatin loops by PARP1 which are lost upon PARP1 ablation and/or catalytic inhibition. Our results reveal PARP1 as a chromatin looper and SE-associated protein, gatekeeping genes linked to cell identity and hormonal response via 3D genome looping in breast cancer cells.

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