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The cell division cycle protein 20 homolog is an essential regulator of cell division that is encoded by the CDC20 gene in humans. To the best of current knowledge its most important function is to activate the anaphase promoting complex (APC/C), a large 11-13 subunit complex that initiates chromatid separation and entrance into anaphase. The APC/CCdc20 protein complex has two main downstream targets. Firstly, it targets securin for destruction, enabling the eventual destruction of cohesin and thus sister chromatid separation. It also targets S and M-phase (S/M) cyclins for destruction, which inactivates S/M cyclin-dependent kinases (Cdks) and allows the cell to exit from mitosis. A closely related protein, Cdc20homologue-1 (Cdh1) plays a complementary role in the cell cycle.

Using single-cell RNA sequencing, Wang et al. revealed a subcluster of GABAergic neurons characterized by cell division cycle 20 (Cdc20) mRNA expression in the NAc of adult rats. We studied the coexpression of Cdc20 and Gad1 mRNA in the NAc neurons of adult rats and assessed Cdc20 protein expression in the NAc during rat development. Moreover, we microinjected AAV2/9-hSyn-Cdc20 with or without the dual-AAV system into the bilateral NAc for sparse labelling to observe changes in the synaptic morphology of mature neurons and assessed rat behaviours in open field and elevated plus maze tests. Furthermore, we performed the experiments with a Cdc20 inhibitor, Cdc20 overexpression AAV vector, and Cdc20 conditional knockout primary striatal neurons to understand the ubiquitination-dependent degradation of fragile X mental retardation protein (FMRP) in vitro and in vivo. We confirmed the mRNA expression of Cdc20 in the NAc GABAergic neurons of adult rats, and its protein level was decreased significantly 3 weeks post-birth. Upregulated Cdc20 expression in the bilateral NAc decreased the dendritic spine density in mature neurons and induced anxiety-like behaviour in rats. Cdc20-APC triggered FMRP degradation through K48-linked polyubiquitination in Neuro-2a cells and primary striatal neurons and downregulated FMRP expression in the NAc of adult rats. These data revealed that upregulation of Cdc20 in the bilateral NAc reduced dendritic spine density and led to anxiety-like behaviours, possibly by enhancing FMRP degradation via K48-linked polyubiquitination 1).

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