AIP regulates stability of Aurora-A at early mitotic phase coordinately with GSK-3β

Abstract

Glycogen synthase kinase-3 (GSK-3β) regulates microtubule dynamics and cellular polarity through phosphorylating various microtubule associating proteins and plus-end tracking proteins. Although it was also reported that GSK-3β is inactivated by protein kinase B at the spindle poles, functions and targets of GSK-3β in the mitotic phase are unknown. Here, we identified Aurora-A-interacting protein (AIP), a negative regulator of Aurora-A, as a binding partner of GSK-3β. AIP was colocalized with Aurora-A and GSK-3β to the spindle poles in metaphase, and its depletion in cells stabilized and activated Aurora-A in early mitotic phase and caused mitotic cell arrest. Treatment of the cells with a GSK-3β inhibitor reduced the protein level of Aurora-A and this reduction was suppressed by AIP knockdown. AIP was phosphorylated by GSK-3β, and an AIP mutant in which the GSK-3β phosphorylation site was mutated could bind and downregulate Aurora-A more efficiently. These results suggest that GSK-3β modulates the early mitotic Aurora-A level through binding and phosphorylating AIP.