Identification of AIP as a GSK-3 binding protein

Abstract

GSK-3, a well-known serine/threonine kinase is one of the key players controlling numerous cellular and physiological processes such as protein synthesis, cell poliferation, cellular differentiation, apoptosis and microtubule dynamics. Therefore, GSK-3 phosphorylates and regulates the functions of a diverse group of substrates including many transcription factors, components regulating the cell cycles and signaling proteins. However, the mechanisms by which GSK-3 regulates the functions of many substrates specifically and selectively are not known. In order to understand the molecular basis of GSK-3 regulation and specificity, we attempt to search for novel GSK-3 binding proteins using yeast two-hybrid screening. We have identified AIP (Aurora-A Kinase Interacting Protein) as a protein that interacts with GSK-3. AIP has been reported to be a novel negative regulator of Aurora-A kinase where it might down-regulates Aurora-A kinase through proteasome dependent degradation. Our study showed that AIP is able to bind both the homologous forms of GSK-3, GSK-3a and GSK-3b in intact cells. This binding is not affected by SB216763, a specific GSK-3 inhibitor, indicating that the kinase activity of GSK-3 is not required for the interaction. AIP has the consensus motif –S-X-X-X-S- for substrate phosphorylation by GSK-3b and i sphosphorylated by GSK-3b in vitro. Our results suggest that AIPis a novel binding partner of GSK-3.