Fbx7 functions in the SCF complex regulating Cdk1-Cyclin B-phosphorylated HURP proteolysis by protein-rich region

李元綺
Hsu JM;Lee YCG;Yu CTR;Huang CYF

Abstract

F-box proteins, components of SCF ubiquitin-ligase complexes, are believed to be responsible for substrate recognition and recruitment in SCF-mediated proteolysis. F-box proteins that have been identified to function in the SCF complexes to date mostly have substrate-binding motifs, such as WD repeats or leucine-rich repeats in their C termini. However, many F-box proteins lack recognizable substrate-binding modules; whether they can function in the SCF complexes remains unclear. We show here that Fbx7, an F-box protein without WD repeats and leucine-rich repeats, is required for the proteasome-mediated proteolysis of the hepatoma up-regulated protein (HURP). Depletion of Fbx7 by small interfering RNA leads to depression of HURP ubiquitination and accumulation of HURP abundance. In the SCFFbx7 complex, Fbx7 recruits HURP through its C-terminal proline-rich region in a Cdk1-cyclin B-phosphorylation dependent manner. Mutation of the multiple Cdk1-cyclin B phosphorylation sites on HURP or the proline-rich region of Fbx7 abolishes the association between Fbx7 and HURP. Thus, Fbx7 is a functional adaptor of the SCF complex with a proline-rich region as the substrate-binding module. In addition to Fbx7, data base analyses reveal two putative mammalian proline-rich region-containing F-box proteins, KIAA1783 and RIKEN cDNA 2410015K21. Taken together, these findings further expound the diverse substrate-recognition abilities of the SCF complexes.