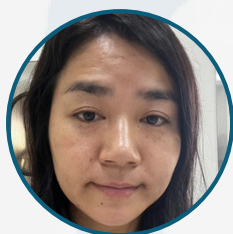


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FBXO47 Is Key Component of The Centromeric SCF E3 Ligase Complex That Regulates Centromere Pairing for Pachynema Progression in Mouse Spermatocytes

Abstract:

Centromere pairing is crucial for synapsis in meiosis. This study delves into the Skp1-Cullin1-F-box protein (SCF) E3 ubiquitin ligase complex, specifically focusing on F-box protein 47 (FBXO47), in mouse meiosis. Here, we discovered that spermatocytes deficient in centromere-expressed FBXO47 encounter difficulties with double-strand break (DSB) repair and arrest at a stage resembling pachytene, displaying unstable centromere pairing. Defective centromere pairing leads to the disintegration of the synaptonemal complex (SC) in chromosomes and disrupts the telomere-nuclear envelope (NE) attachment system during the pachytene stage. Immunoblotting analysis revealed that the deletion of FBXO47 impairs the expression of centromere protein C (CENP-C) and SC components beginning at this pachytene-like stage. This coincides with the depletion of its partner SKP1 at centromeres and chromosomes in *Fbxo47*^{-/-} spermatocytes. Notably, the patterns observed in FBXO47-deficient mice—specifically, the return recruitment of HORMAD1 on chromosomes and the reduction of CENP-C are similar to those in SKP1-deficient mice. Furthermore, co-immunoprecipitation (Co-IP) analysis indicates that FBXO47 interacts with SKP1, playing a crucial role in stabilizing it by reducing its ubiquitination in the HEK293 cell line. Our findings suggest that the SCF complex formed at centromeres is essential for stabilizing centromere pairing, likely through the regulation of HORMAD1 during meiosis.

Keywords: FBXO47, meiosis, DSB, synapsis, centromere pairing

Biography :

- 1) meiosis focusing on FBXO47
- 2) endocrinology focusing on Spexin