Ubc13 is required for the Chfr-mediated mitotic checkpoint.

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Background. The Chfr checkpoint delays mitotic entry in response to impaired microtubule function - guarding cells against chromosome mis-segregation, genetic instability and cancer. Chfr is a ubiquitin ligase that has been reported to catalyze the formation of Lys-63-linked polyubiquitin chains in vitro in the presence of the Ubc13-Mms2 ubiquitin-conjugation complex. In spite of its significance in cancer, however, the mechanism by which the Chfr checkpoint functions remains obscure. **Methods.** We have used pull-down assays, yeast two-hybrid assays, immunoprecipitations, and RNA interference technology to show that Ubc13 and Chfr physically and functionally interact with each other, and that Ubc13 is required for the Chfr-mediated mitotic checkpoint. **Results.** We have demonstrated the physical interaction between Chfr and Ubc13 in vitro and in vivo and investigated the potential roles of Chfr and ubc13 in cultured human cell lines. Suppression of Ubc13 by interference RNA resulted in a significant increase in mitotic cells when treated with microtubule poisons, reminiscent of the Chfr-deficient cells. Furthermore, suppression of Ubc13 in the Chfr mutant cells did not further increase the microtubule damage-induced increase of the mitotic index, suggesting that Ubc13 and Chfr function in the same signaling pathway. **Conclusions.** Ubc13 is required for the Chfr checkpoint.