

P025 JunB breakdown in G2 is required for proper mitosis
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The AP-1 transcription complex comprises a collection of homo- and heterodimers of bZip proteins, the best known being the Jun and Fos family proteins. AP-1 regulates proliferation, differentiation, apoptosis and responses to stresses and it is essential for many physiological functions at the whole organism level. JunB, a member of the Jun family, is a negative regulator of cell proliferation that has been demonstrated to have tumour suppressor activity. With respect to cell cycle control, it has been shown to exert a dual function. Thus, sustained JunB accumulation leads to cell cycle arrest in G1 via induction of p16INK4 α and down regulation of the cyclin D1. On the other hand, rapid progression through S phase depends on JunB, whose expression positively regulates transcription of the cyclin A2 gene. Finally, JunB levels are low in mitotic cells. Using cell synchronization experiments we show that phosphorylation-induced accelerated degradation of JunB occurs in mid/late G2 and is dependent on the ubiquitin-proteasome pathway. Inducible expression of ectopic JunB in late G2 indicates that JunB decay is necessary for subsequent reduction of cyclin A2 levels, the latter event being essential for proper mitosis. Consistently, abnormal JunB expression in late G2 entails a variety of mitotic defects. As these aberrations may cause genetic instability, our findings contrast with the acknowledged tumor suppressor activity of JunB and reveal a mechanism by which JunB might contribute to tumorigenesis.