

**P053** Cyclin B2 suppresses mitotic failure and DNA re-replication in human somatic cells knocked-down for both cyclins B1 and B2

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CDK1 kinase plays a crucial role in establishing metaphase and has also been shown to prevent DNA re-replication. Inactivation of CDK1 kinase in mammalian cells is sufficient to allow mitosis exit and cytokinesis. Cyclin B1 and cyclin B2 are two known activators of CDK1 operating during mitosis in human cells. Little is known about the specific roles of each of these cyclins in CDK1 activation, but cyclin B2 is thought to play a minor role and to be unable to replace cyclin B1 for mitosis completion. We found that severe reduction by separate RNA interference of either cyclin B1 or cyclin B2 protein levels results in little or no alteration of the cell cycle and, more specifically, of mitosis progression. In contrast, simultaneous depletion of both B-type cyclins leads to massive accumulation of 4N cells, mitotic failure, premature mitosis exit, cytokinesis failure and DNA re-replication. These defects can be corrected by the ectopic expression of a cyclin B2 resistant to the shRNA. Altogether, these data show that, in cycling human cells, cyclin B2 can compensate for the down-regulation of cyclin B1 during mitosis. They also clearly implicate cyclins B1 and B2 as crucial activators of CDK1 in its biological function of DNA re-replication prevention.