1. Record Nr. TD16001646

Titolo	THE INTERPLAY BETWEEN CDK1/CLBS AND PP2A/CDC55 IN ADAPTATION TO THE SPINDLE ASSEMBLY CHECKPOINT (SAC) [Tesi di dottorato]
Editore	UniversitÃ degli Studi di Milano, 2014-03-25
Lingua di pubblicazione	Inglese
Formato	Tesi di dottorato
Livello bibliografico	Monografia
Note	diritti: info:eu-repo/semantics/openAccess
Sommario	Abstract The spindle assembly checkpoint (SAC) monitors that all sister chromatids are correctly attached to microtubules of the mitotic spindle during prometaphase. The correct attachment is known as biorientation, and it is the prerequisite for proper partitioning of the duplicated DNA from the mother to the two daughter cells. Until the last kinetochores are bioriented, the SAC arrests progression into anaphase by inhibiting the Anaphase Promoting Complex or Cyclosome (APC/C) bound to its coactivator Cdc20, therefore stabilizing the cohesin rings that hold pairs of sister chromatids together. When the SAC is continuously activated, cells remain arrested in prometaphase for some hours, but not indefinitely; even if the checkpoint is not satisfied, eventually cells separate the duplicated DNA material and progress into anaphase. This phenomenon is known as adaptation to the SAC and is poorly understood from the molecular viewpoint. By using budding yeast (S. cerevisiae) as a model organism, in this work I show that adaptation to the SAC requires phosphorylation of the APC/C, which is stimulated by the Cyclin dependent kinase 1 (Cdk1) bound to its mitotic regulatory subunit, Clb2, and is opposed by the phosphatase PP2ACdc55. I propose that PP2ACdc55 and the APC/C are implicated in a double negative feedback loop of reciprocal inhibition, which regulates transition into anaphase in adapting cells: when

	accumulating Clb2 provides sufficient Cdk1:Clb2 activity to allow initial activation of APC/CCdc20, the antagonist of the APC/C, PP2ACdc55, starts to be inhibited. This strongly reinforces APC/CCdc20, and leads to a rapid and irreversible transition into anaphase.
Localizzazioni e accesso	http://memoria.depositolegale.it/*/http://hdl.handle.net/2434/234138