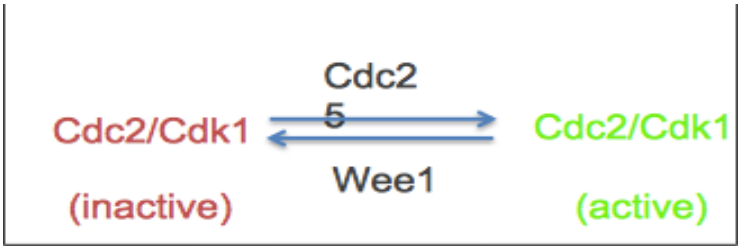
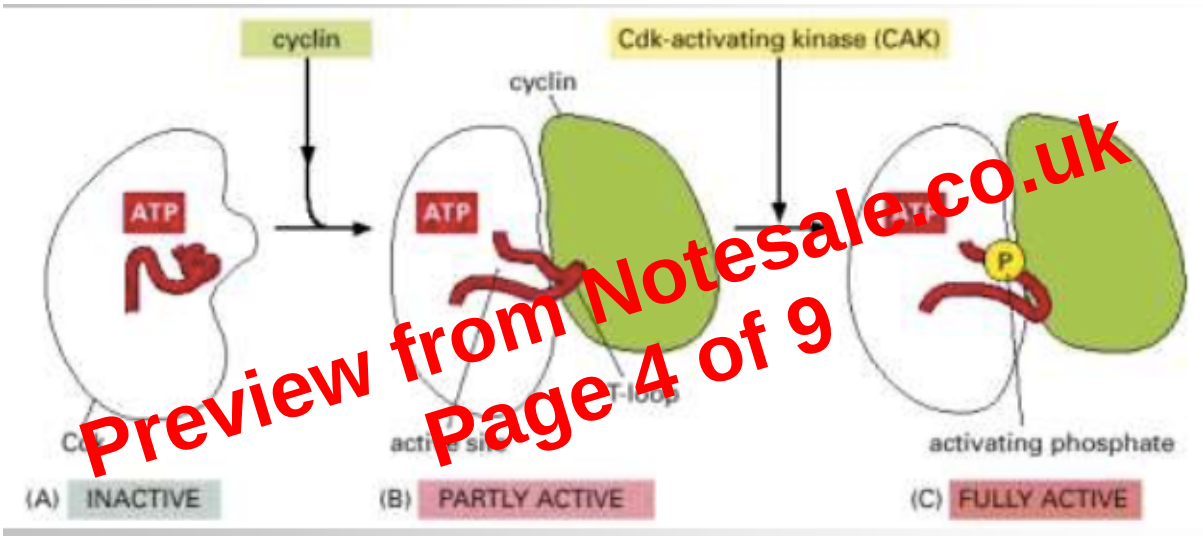


Regulation of Cdk/Cyclin Activity:

1. Cyclin binding to Cdk displaces the T-loop from the Cdk's active site – **partial activation.**
2. Phosphorylation of the T-loop (T161 [threonine at 161] in CDK1) by **cyclin activating kinase (CAK) – full activation.**
3. CAK itself is a cyclin-dependent kinase – a complex of CDK7/cyclin H in mammalian cells.



4. The cell needs a lot of Cdk1/cyclin complexes to drive mitosis, but levels of this complex are built gradually through G2.
5. Therefore, the cell needs to maintain this Cdk1/cyclin complex in an **inactive state,** then *suddenly* activate it upon mitotic entry.
6. As well as activating phosphorylation, i.e. CAK, there are also inhibitory phosphorylations on Cdks, which keep the complex inactive until they are removed.
7. Cyclin binding to Cdk also exposes Tyrosine 15 (**Y15**) and threonine 14 (**T14**) in the active site.
8. Wee1 and **Myt1,** both negative regulators of mitosis**,** can phosphorylate these residues.
9. Phosphorylation of Y15 and T14 prevents **ATP-binding to Cdk's active site**, thus blocking the activity of this complex.
10. The phosphorylation of Cdk1 by the negative regulators allows Cdk1/Cyclin to accumulate to high levels in the *inactive form* and stops cells from entering mitosis.