is continuous around the cycle and so is the synthesis of most of the cell's proteins.In the absence of Rb, a transcription factor called E2F becomes active and initiates a cascade of gene expression culminating in the resynthesis of cyclins, Cdks and other components needed to initiate S phase.Passage of the G1 checkpoint depends on a similar process operated by a different set of cyclins and Cdks, whose active complexes phosphorylate and activate the enzymes of DNA replication.Asymmetric cell divisions necessarily involve the segregation of different cytoplasmic determi- nants to the two daughter cells, evoking different patterns of gene activity in their nuclei and thus bringing about different pathways of development.Control of the cell cycle depends on a metabolic oscillator comprising a number of proteins called cyclins and a number of cyclin-dependent protein kinases (Cdks).This phosphorylates and thereby activates the various components required for mitosis (nuclear breakdown, spindle formation, chromosome condensation).The asymmetry often arises from auto- segregation of a self-organizing protein complex called the PAR (partitioning defective) complex.In order to pass the M checkpoint and enter mitosis, a complex of cyclin and Cdk (called M-phase promoting factor, MPF) has to be activated.Restitution of growth factors induces the resynthesis of these proteins and the resumption of the cycle starting from the G1 checkpoint.There are various internal controls built into the cycle, for example to ensure that mitosis does not start before DNA replication is completed.The rapid cleavage cycles of early development have short or absent G1 and G2 phases and there is no size check, the cells halving in volume with each division.Stem cells are cells that can both reproduce themselves and generate differentiated progeny for their particular tissue type (Fig.Exit from M phase requires the inactivation of MPF, via the destruction of cyclin.The meiotic cycles require the same active MPF complex to get through the two nuclear divisions, but there is no S phase in between.In the absence of growth factors cells enter a state called G0, in which the Cdks and cyclins are absent.One factor maintaining the G0 state is a protein called Rb (retinoblastoma protein).Although some differentiated cell types can go on dividing, there is a general tendency for differentiation to be accompanied by a slow down or cessation of division.These are early embryo-type cells that can be grown in culture and are capable of repopulating embryos and contributing to all tissue types.These controls operate at checkpoints around the cycle at which the process stops unless the appropriate conditions are fulfilled. 7.5d).

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