- The core of this system is an ordered series of biochemical switches that control the main events of cycle, including DNA replication and the segregation of the replicated chromosomes

- Intracellular and extracellular signals act on the control system to regulate cell division in a multicellular organism
- In most cells, additional layers of regulation enhance the fidelity of cell division and allow the control system to respond to various signals from both inside and outside the cell
  - Inside the cell, the control system monitors progression through the cell cycle and delays later events until earlier events have been completed
  - The control systems also monitors the conditions outside the cell
    - In the multicellular animal, the system is highly responsive to signals from other cells, stimulating cell division when more cells are needed and blocking it when they are not

- When the cell malfunctions, excessive cell divisions can result in cancer

Key components of the central cell-cycle control system

- It is a **protein-kinase-based machine**
- The proteins of this control system are well conserved in evolution

- The cell-cycle control system is based on two key families of proteins
  - Cyclin-dependent protein kinases (Cdk)
  - Cyclins (CdK activating proteins)

- These protein complexes exert control through their **kinase activities**, which are abruptly **switched on or off** at particular points in the cycle
- The cyclic assembly, activation and disassembly of cyclin-Cdk complexes are the pivotal events driving the cell cycle

- The details of cell cycle regulation, such as the number of different cyclins and kinases and the combinations in which they act, differ from species to species, but the basic mechanism has been conserved in the evolution of all eukaryotic cells

- A typical cyclin is present at low levels for most of the cycle, but increases strongly at the stage where it is needed
- e.g.,
  - G1 cyclins are needed for much of the cycle
  - M cyclin peaks dramatically at the transition from G2 to M phase

- Decrease in cyclin is due to
  - Decreased expression of cyclin gene and decreased synthesis
  - Proteolysis of existing cyclins
- Increase in cyclin is due to
  - Increased expression of cyclin gene

Cell Cycle Control System – Role of cyclin dependent kinase (CdKs)

Activation of CdK

Cyclin-CdK complex

CdK activation is timed - Cyclin expression cycle in mammals

Regulation of CdK – written under separate heading

Proteins phosphorylated by CdK or Substrates of CdK – written under separate heading

Regulation of DNA replication