CELL CYCLE
&
ITS REGULATION

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CELL CYCLE

Cell cycle was described by Howard and Pele in 1953.

Cell cycle is defined as the stages through which a cell passes from one cell division to the next. During this phase the cell grows and prepares for the division.

Whole of the cell cycle is alternated with –

- **Doubling of genome (DNA) in synthesis phase (S phase)**
- **Halving of that genome during mitosis (M phase)**

CELL CYCLE

Cell cycle – Completes in 2 phases

(I) Interphase – Preparatory phase, divided into 3 sub phases

- **(i) G1 (GAP 1) phase**
- **(ii) S (Synthesis) phase**
- **(iii) G2 (GAP 2) phase**

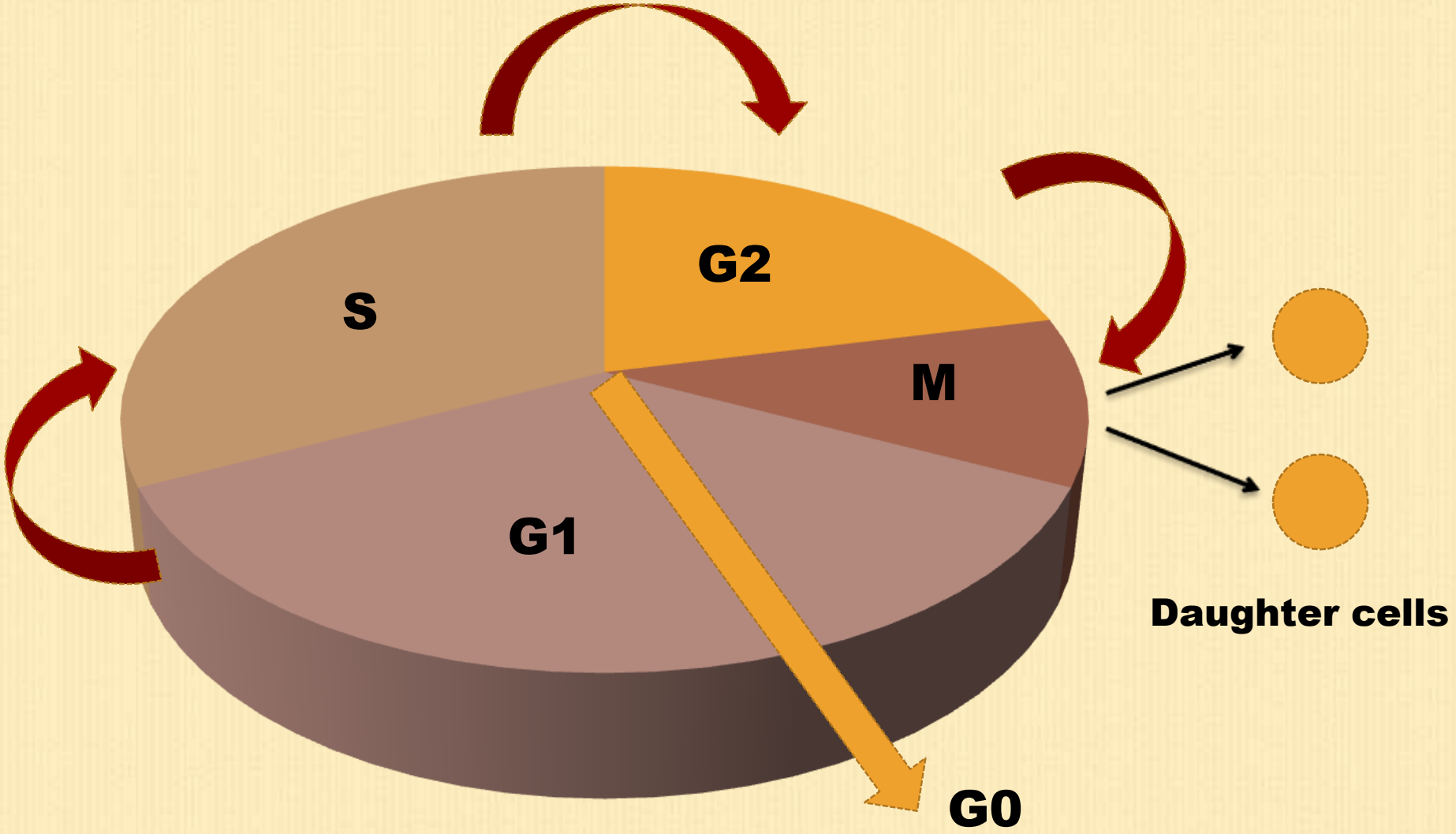
Leading to Doubling of genome (DNA)

(II) M phase – Phase of division, divided into 2 sub phases

- **(i) Karyokinesis (Nuclear division) – divided into 4 sub phases**
  - **(a) Prophase**
  - **(b) Metaphase**
  - **(c) Anaphase**
  - **(d) Telophase**
- **(ii) Cytokinesis (Division of cytoplasm)**

Leading to Halving of that genome, passing into daughter cells

CELL CYCLE



Different phases of cell cycle (cell growth & cell division)

CELL CYCLE

EVENTS OCCURRING IN G1 PHASE:

1. SYNTHESIS OF ENZYMES REQUIRED FOR DNA REPLICATION
2. SYNTHESIS OF RNA NEEDED FOR TRANSCRIPTION AND TRANSLATION
3. SYNTHESIS OF ATP
4. SYNTHESIS OF RAW MATERIALS (PENTOSE SUGAR, PHOSPHORIC ACID AND NITROGENASES) FOR DNA DUPLICATION IN S PHASE
5. SO MANY THINGS ARE SYNTHESIZED IN THIS PHASE, THEREFORE, THE SIZE OF THE CELL INCREASES

NOW THE CELL IS READY TO ENTER THE NEXT S PHASE.

CELL CYCLE

EVENTS OCCURRING IN S PHASE:

1. DNA REPLICATION
2. CENTRIOLE DIVIDES (ONLY IN ANIMALS)
3. SYNTHESIS OF HISTOINE PROTEINS

NOW THE CELL IS READY TO ENTER THE NEXT G2 PHASE.

CELL CYCLE

EVENTS OCCURRING IN G2 PHASE:

1. SYNTHESIS OF TUBULIN PROTEIN REQUIRED FOR SPINDLE FORMATION
2. SYNTHESIS OF PROTEIN REQUIRED FOR PLASME MEMBRANE FORMATION
3. CELL ORGANELLES ARE DOUBLED
4. LOTS OF ATP MOLECULES REQUIRED FOR MOVEMENT OF CHROMOSOMES FROM EQUATOR TO POLE (30 ATP/ CHROMOSOME). SO ATP SYNTHESIS INCREASES.
5. RNA SYNTHESIS TAKES PLACE

NOW THE CELL IS READY TO ENTER THE NEXT M PHASE.

CELL CYCLE

EVENTS OCCURRING IN M PHASE:

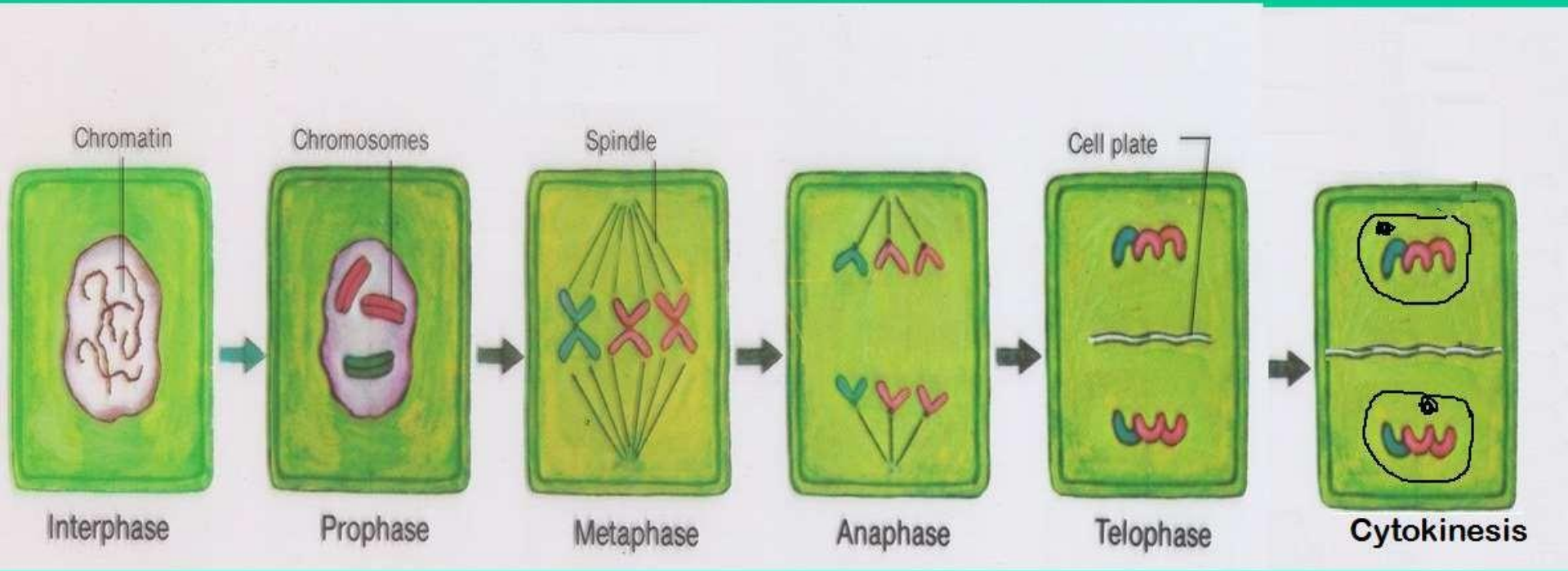
KARYOKINESIS INCLUDES

1. **PROPHASE: CHROMATID COILING, DISINTEGRATION OF NUCLEAR MEMBRANE AND NUCLEOLUS, SPINDLE FORMATION**
2. **METAPHASE: CHROMOSOMAL ORIENTATION AT THE EQUATORIAL PLANE**
3. **ANAPHASE: MOVEMENTS OF CHROMATIDS TOWARDS THE OPPOSITE POLES**
4. **TELOPHASE: RECONSTRUCTION OF DAUGHTER NUCLEI**

CYTOKINESIS INCLUDES

FORMATION OF CELL PLATE LEADING TO EQUAL DIVISION OF CYTOPLASM, NUCLEI, CELL ORGANELLES AND CELL MEMBRANE INTO TWO DAUGHTER CELLS

CELL CYCLE



Stages of cell cycle

CELL CYCLE

AFTER CELL DIVISION, EACH OF THE DAUGHTER CELL BEGINS THE INTERPHASE OF A NEW CYCLE.

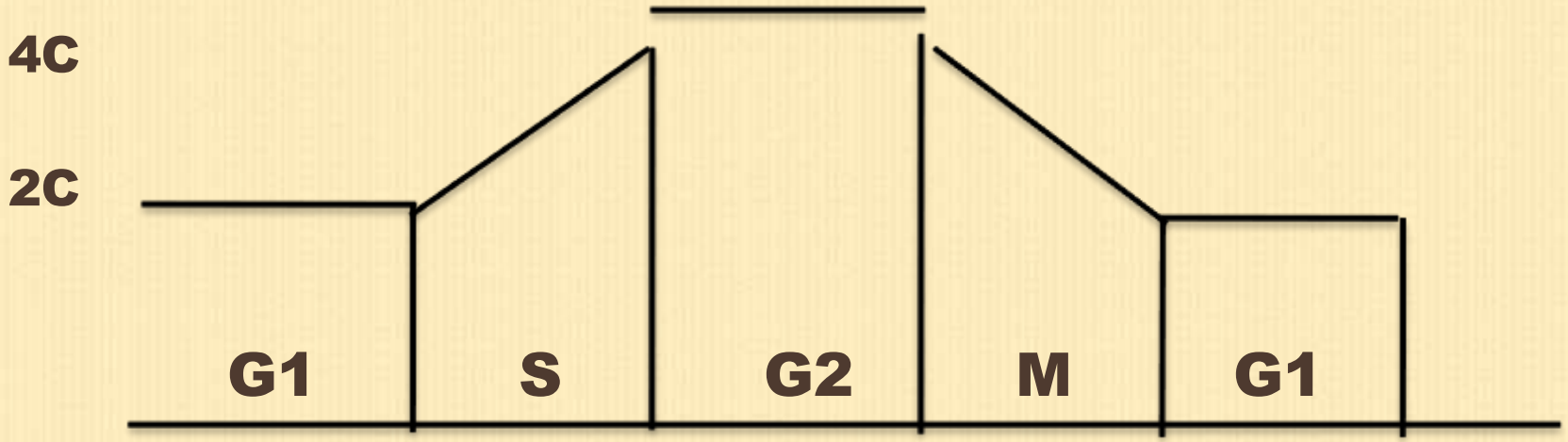
SOME CELLS (eg. CELLS OF HEART, KIDNEY, LIVER, NEURONS etc.) AFTER REMAINING IN G1 PHASE FOR SOMETIME COME OUT OF THE CELL CYCLE AND ENTER Go PHASE KNOWN AS QUIESCENT PHASE.

IN QUIESCENT PHASE THE CELL DIVISION STOPS BUT OTHER ACTIVITIES OF THE CELL CONTINUE.

SOMETIMES THE CELL REENTERS THE CELL CYCLE FROM QUIESCENT PHASE WHEN REQUIRED.

Eg. DURING FORMATION OF PERIDERM

CELL CYCLE



Cell cycle of a cell showing the changes in DNA content during various phases

REGULATION OF CELL CYCLE

Cell cycle does not occur in unchecked manner. The preparations of the cell are checked by regulatory molecules. It includes the detection and repair of genetic damage as well as prevention of uncontrolled cell division.

There are two key classes of regulatory molecules that determine a cell's proper progress through the cell cycle. These are -

- Cyclins
- Cyclin dependent kinases (Cdk)

The Nobel Prize in Physiology or Medicine 2001 was awarded jointly to Leland H. Hartwell, Tim Hunt and Sir Paul M. Nurse for their discoveries of key regulators of the cell cycle.

REGULATORY MOLECULES

Cyclins-

G1 Cyclins (D cyclins)

S-phase cyclins (cyclins E and A)

M-phase cyclins (B cyclins)

- **Their levels in the cell rise and fall with the stages of the cycle.**

Cyclin dependent kinases

G1 Cdk (Cdk 4)

S-phase Cdk (Cdk 2)

M-phase Cdk (Cdk 1)

- **Their levels in the cell remain stable.**
- **Remain inactive.**
- **Bind to the appropriate cyclin in order to be activated.**
- **Their function is to provide phosphate group to a number of proteins that control processes in the cell cycle.**

REGULATORY MOLECULES

Table 1: Cyclin – Cyclin dependent kinases (Cdk) complexes formed during cell cycle reguation and their functions

Phase of cell cycle	Cyclin	Cdk	Cyclin-Cdk complx	Function
G1	Cyclin D	Cdk 4	G1 Cyclin-G1 Cdk	Inhibits Rb (Retinoblastoma) protein and signals the cell to prepare the chromosome for replication
S	Cyclin E and Cyclin A	Cdk 2	S phase cyclin – S phase Cdk	Activates DNA replication
G2	Cyclin B	Cdk 1	Mitotic cyclins – M phase Cdk	Activates mitosis

CELL CYCLE CHECKPOINTS

CELL CYCLE CHECKPOINTS ARE USED BY THE CELL TO MONITOR AND REGULATE THE PROGRESS OF THE CELL CYCLE. THE CELL CANNOT PROCEED TO THE NEXT PHASE UNTIL CHECKPOINT REQUIREMENTS HAVE BEEN MET.

THREE MAIN CHECKPOINTS ARE:

(I) G1/S CHECKPOINT (before cell enters S phase)

(II) G2/M CHECKPOINT (after S phase)

(III) APC/C CHECKPOINT (during mitosis)
(Anaphase Promoting Complex / Cyclosome)

CELL CYCLE CHECKPOINTS

(I) G1/S CHECKPOINT (before cell enters S phase):

- **Checks for cell size**
- **Checks for nutrients**
- **Checks for DNA damage**
- **Checks for all the preparations (all proteins, ATP etc. requires in S phase)**
- **Checks whether S phase Cyclins and Cdk complex is activated to initiate DNA replication**

Then the cell passes to next S phase.

CELL CYCLE CHECKPOINTS

(I) G2/M CHECKPOINT (after S phase):

- **Checks for proper DNA replication**
- **Checks for all the preparations (all proteins, ATP etc. required in M phase)**
- **Checks for Tubulin synthesis**
- **Checks whether M phase Cyclins and Cdk complex is activated to initiate mitosis**

Then the cell passes to next M phase.

APC / C CHECKPOINT

Anaphase Promoting Complex / Cyclosome Checkpoint

- **It refers to a critical control point in the cell cycle that regulates the timing of anaphase**
- **It ensures that all chromosomes are properly aligned and attached to the mitotic spindle before separation occurs.**
- **It is part of the spindle assembly checkpoint (SAC), which prevents premature progression into anaphase and ensures genomic stability.**

CELL CYCLE CHECKPOINTS

ALL THE CHECKPOINTS REQUIRE THE SERVICES OF A COMPLEX OF PROTEINS. THE LEVELS OF THESE PROTEINS ARE INCREASED IN DAMAGED CELLS. THEY ALLOW TIME TO REPAIR DNA BY BLOCKING THE CELL CYCLE.

P53 IS ONE SUCH PROTEIN WHICH SENSES DNA DAMAGE AND CAN HALT PROGRESSION OF THE CELL CYCLE IN G1 PHASE BY BLOCKING THE ACTIVITY OF Cdk 2 UNTIL DAMAGE CAN BE REPAIRED. IF THE DAMAGE IS SO SEVERE THAT IT CAN NOT BE REPAIRED, THEN THE CELL DESTRUCTS ITSELF BY APOPTOSIS.

IN CASE OF DAMAGE TO DNA AFTER S PHASE, THE ACTION OF CDK 1 IS INHIBITED, THUS STOPPING PROGRESSION OF THE CELL FROM G2 TO MITOSIS.

THANK YOU