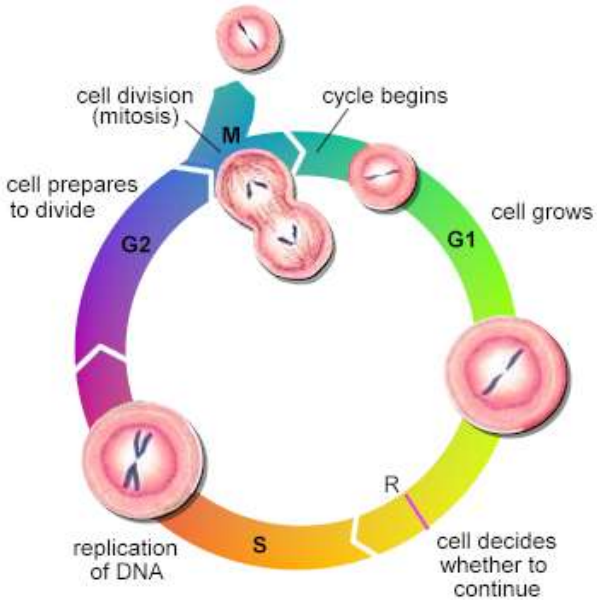
Proliferation & Cell Turnover

Judith Barbaro-Brown



The Cell Cycle.

In order for growth to occur, and maintenance, it is essential that cells have the ability to replicate.

The cell cycle, or cell-division cycle, is the series of events that take place in a eukaryotic cell leading to its replication.

These events can be divided in two brief periods:

1. interphase, during which the cell grows, accumulating nutrients needed for mitosis and duplicating its DNA

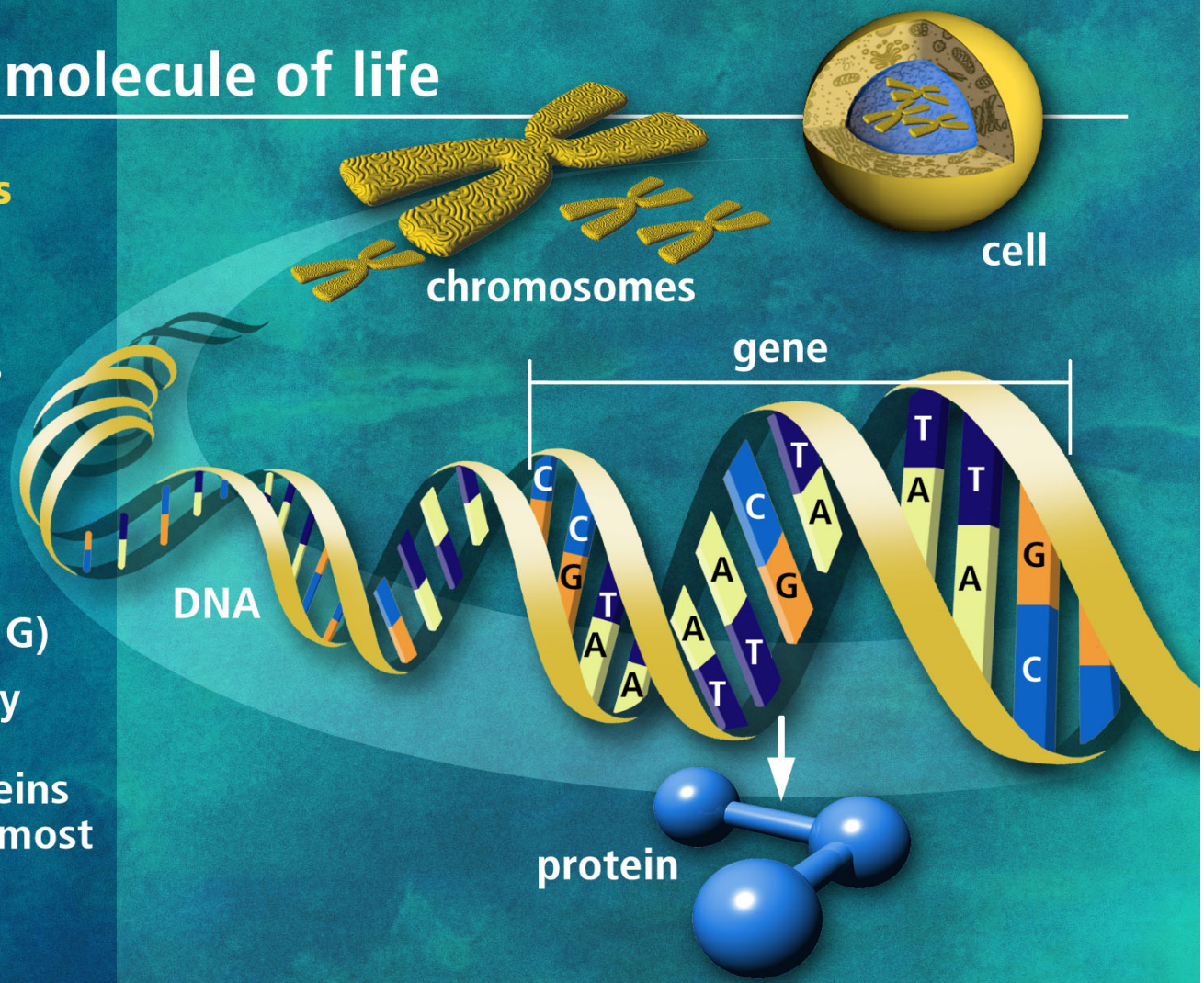
2. mitotic (M) phase, during which the cell splits itself into two distinct cells, often called "daughter cells“, both containing an exact replica of the original cell DNA.

DNA the molecule of life

Trillions of cells

Each cell:

- 46 human chromosomes
- 2 meters of DNA
- 3 billion DNA subunits (the bases: A, T, C, G)
- Approximately 30,000 genes code for proteins that perform most life functions

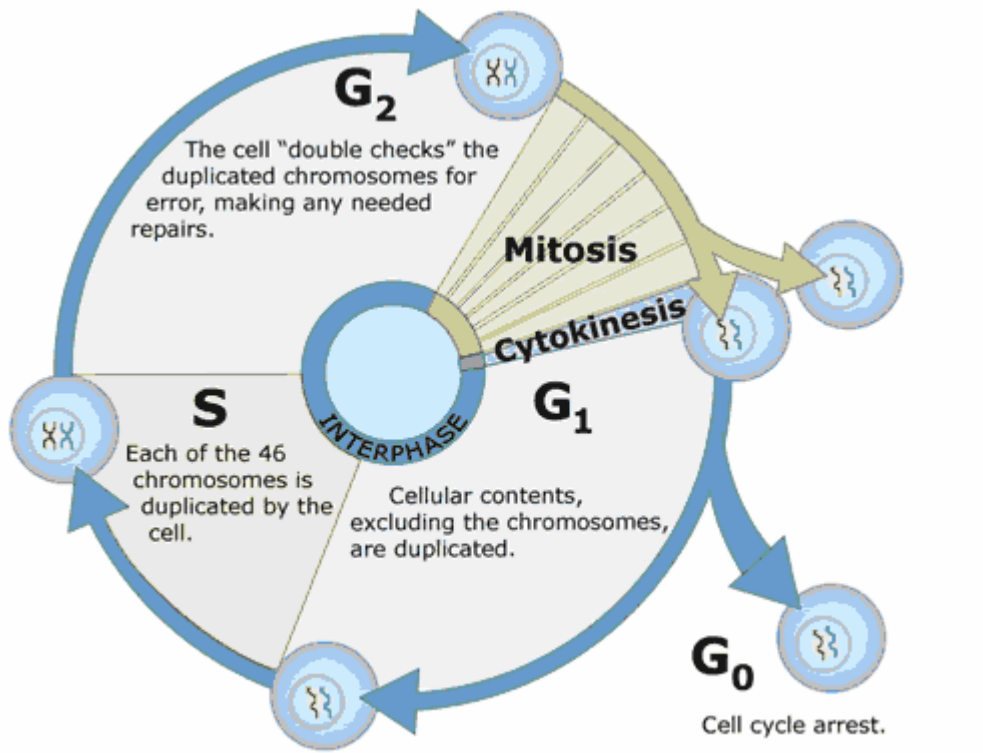


Y-GG 01-0085

The cell cycle consists of four distinct phases :

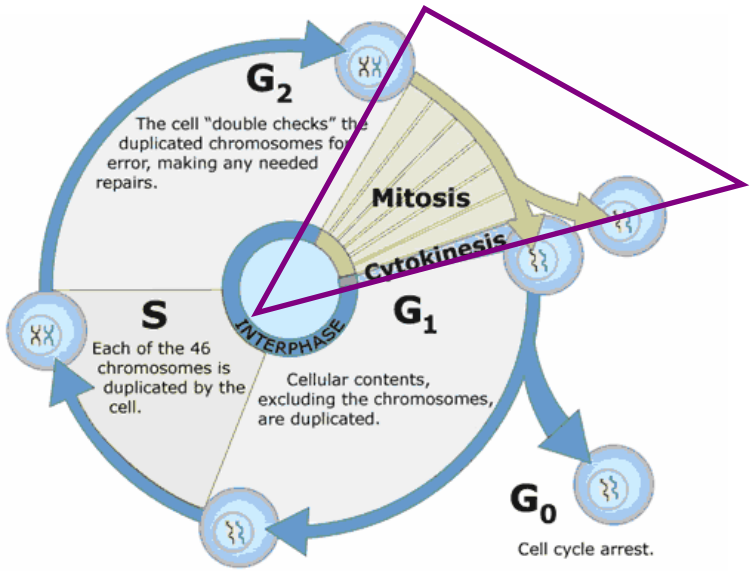
G1 phase
S phase
G2 phase
} INTERPHASE

M phase – mitosis
cytokinesis



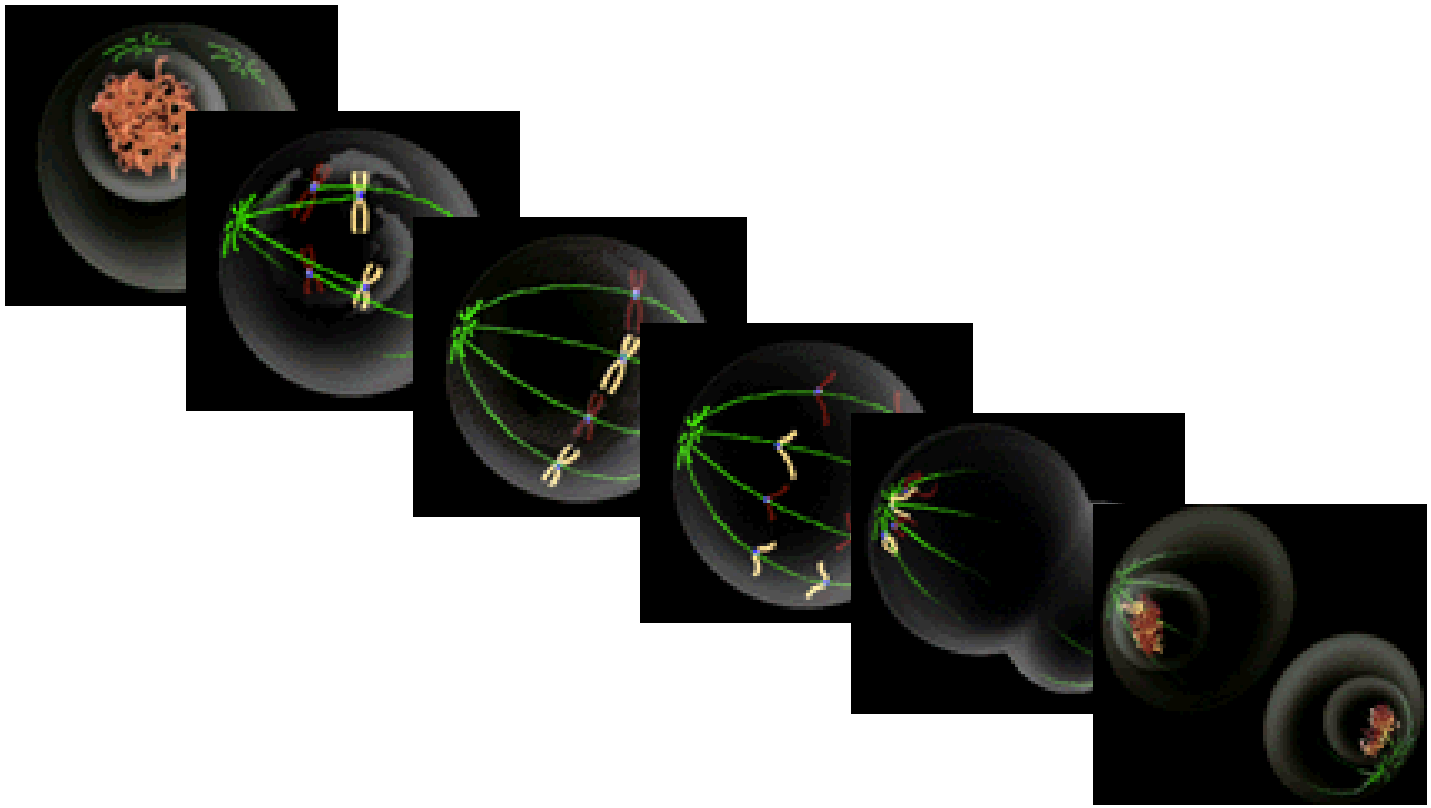
M Phase

Relatively brief phase consisting of nuclear division (karyokinesis) and cytoplasmic division (cytokinesis).



- Mitosis is the division of nuclear material, and itself is divided into prophase, prometaphase, metaphase, anaphase, and telophase.
- Cytokinesis is the actual splitting of the cell into two new cells.

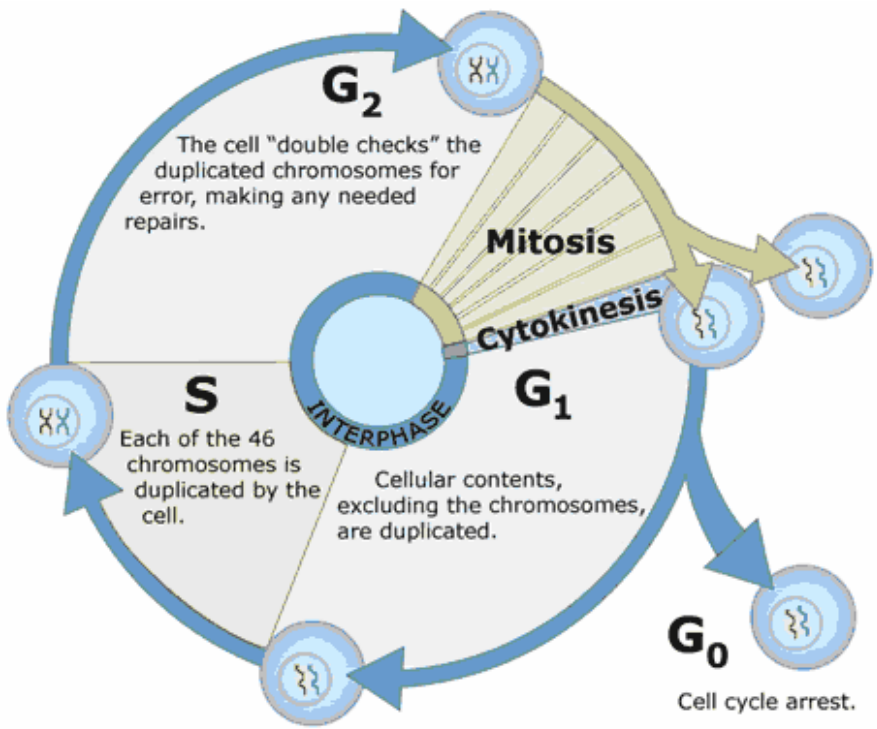
Mitosis and Cytokinesis



http://www.biology.arizona.edu/cell_bio/tutorials/cell_cycle/cells3.html

Interphase

- G_1 phase
- S phase
- G_2 phase
- G_0 phase



Regulation

- Regulation of the cell cycle involves steps crucial to the cell, including detecting and repairing genetic damage, and provision of various checks to prevent uncontrolled cell division.

- The molecular events that control the cell cycle are ordered and directional; that is, each process occurs in a sequential fashion and it is impossible to "reverse" the cycle.

Regulatory molecules

Cyclins

Cyclin-dependent kinases (Cdks)

Control progress through the cell cycle. Usually described with an identifying number, eg, cdc25, where cdc refers to ‘cell division cycle’.

- Cdks and cyclins are major control switches for the cell cycle, causing the cell to move from G1 to S or G2 to M.
- MPF (Maturation Promoting Factor) includes the CdK and cyclins that triggers progression through the cell cycle.

Cell cycle inhibitors

The *cip/kip* family and the INK4a/ARF (*In*hibitor of *K*inase 4/*A*lternative *R*eading *F*rame) group of genes prevent the progression of the cell cycle.

These genes are instrumental in prevention of tumour formation and are known as tumor suppressors.

Cip/kip family – prevent the action of Cdks and cyclins, halting the cell cycle in G_1, eg, p21, p27, p53, p57.

By preventing movement through a phase, the cell cannot move through it's 'checkpoints' and onto the next phase.

Genetic defects in the inhibitor families leads to an increased frequency of tunour development.

Hyaluronic acid

This is a glycosaminoglycan present in all cells. It is essential for cell proliferation, and is found at it's highest concentrations within the skin, bound together with collagen.

It's highly hygroscopic properties increase the water content around the cell, helping the dividing cells separate from each other (mitosis), and encouraging cell motility. It is not directly involved with mitogenic activity itself.

Role of CD44

Clinical applications – MSK

wound healing

ophthalmic

Proliferative problems

- Psoriasis – autoimmune cause
- Atopic dermatitis – external agent
- Callus - mechanical
- Verrucae – viral

Summary

- Normal cell proliferation is needed for the replication of DNA, and the production of identical ‘daughter’ cells.
- Regulation of the cell cycle is essential in managing cell proliferation, thereby maintaining a ‘normal’ population of cells.
- Changes to regulatory mechanisms can occur due to either external or internal forces, and can manifest in a number of ways, both benign and malignant.

That’s all for the moment ……