Control of the Cell Cycle

- The timing and rates of cell division in different parts of an animal or plant are crucial for normal growth, development, and maintenance.
- The frequency of cell division varies with cell type.
    - Some human cells divide frequently throughout life (skin cells), others have the ability to divide, but keep it in reserve (liver cells), and mature nerve and muscle cells do not appear to divide at all after maturity.
- Investigation of the molecular mechanisms regulating these differences provide important insights into how normal cells operate, but also how cancer cells escape controls.
- Molecular control systems drive the cell cycle
- The cell cycle appears to be driven by ***specific chemical signals in the cytoplasm.***
    - Fusion of an S phase and a G_1 phase cell, induces the G_1 nucleus to start S phase.
    - Fusion of a cell in mitosis with one in interphase induces the second cell to enter mitosis.
- The distinct events of the cell cycle are directed by a distinct **cell cycle control system**.
    - These molecules, many of which are enzymes, trigger and coordinate key events in the cell cycle.
    - The control cycle has a built-in clock, but it is also regulated by external adjustments and internal controls.
- A **checkpoint** in the cell cycle is a critical control point where stop and go signals regulate the cycle.
    - Many signals registered at checkpoints come from cellular surveillance mechanisms .
    - These indicate whether key cellular processes have been completed correctly.
    - Checkpoint also register signals from outside the cell.
- Three major checkpoints are found in the G_1, G_2, and M phases.
- For many cells, the G_1 checkpoint, the restriction point in mammalian cells, is the most important.
    - If the cells receives a go-ahead signal, it usually completes the cell cycle and divides.
    - If it does not receive a go-ahead signal, the cell exits the cycle and switches to a nondividing state, the **G_0 phase**.
        - Most human cells are in this phase.
        - Liver cells can be “called back” to the cell cycle by external cues (growth factors), but highly specialized nerve and muscle cells never divide.

Cancer cells have escaped from cell cycle controls

- Cancer cells divide excessively and invade other tissues because they are free of the body’s control mechanisms.
- If and when cancer cells stop dividing, they do so at random points, not at the normal checkpoints in the cell cycle.
- Cancer cell may divide indefinitely if they have a continual supply of nutrients.
    - In contrast, nearly all mammalian cells divide 20 to 50 times under culture conditions before they stop, age, and die.
    - Cancer cells may be “immortal”.
        - Cells (HeLa) from a tumor removed from a woman (Henrietta Lacks) in 1951 are still reproducing in culture
- The abnormal behavior of cancer cells begins when a single cell in a tissue undergoes a **transformation** that converts it from a normal cell to a cancer cell.
    - Normally, the immune system recognizes and destroys transformed cells.
    - However, cells that evade destruction proliferate to form a **tumor**, a mass of abnormal cells.
- If the abnormal cells remain at the originating site, the lump is called a **benign tumor**.
    - Most do not cause serious problems and can be removed by surgery.
- In a **malignant tumor**, the cells leave the original site to impair the functions of one or more organs.
    - This typically fits the colloquial definition of cancer.
    - In addition to chromosomal and metabolic abnormalities, cancer cells often lose attachment to nearby cells, are carried by the blood and lymph system to other tissues, and start more tumors in a event called **metastasis**.
- Treatments for metastasizing cancers include high-energy radiation and chemotherapy with toxic drugs.
    - These treatments target actively dividing cells.
- Researchers are beginning to understand how a normal cell is transformed into a cancer cell.
    - The causes are diverse.
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