Characteristics of cancer cells

Cancer cells

- one of the fundamental features of cancer is tumor clonality (the tumors development from single cell)
- increased ability to survive (they often gain resistance to apoptosis)
- aberrant regulation of cell cycle (mainly is affected transition between G1- and S-phase)
- grow and divide at an abnormally rapid rate
- decreased need of hormones and growth factors coming from outside of the cell
- poorly differentiated
- abnormal membranes, cytoskeletal proteins, and morphology
- a high number of chromosomal breaks and numerous chromosomal aberrations
- presence of so-called tumor neoantigens
- some transformed cells have ability of autocrine stimulation (usually via growth factors)
- intercellular communication and the relationship between tumor cells and neighboring cells is disrupted
- a failure to fix to a solid cell surface

Cancer stem cells (CSC)

- a type of cancer cell with some characteristics of stem cell
- are able to proliferate and change themselves to any type of cancer cell in a given tumor
- it is believed that they occur in all cancer types
- are most often resistant to chemotherapy, therefore subsequent relapse of cancer can appear
- they account for a small percentage of all cells in tumor – they differ from other cancer cells by the presence of special surface markers on their plasma membranes

Cancer Cell Development

- 3 main classes of genes important in controlling cell growth & play a role in cancer cell development

Oncogenes

- cause cells to grow out of control, promote cancer cell growth
- damaged/mutated versions of normal genes called proto-oncogenes
- mutations can be inherited or caused by exposure to a carcinogen in the environment
- mutations are dominant (defect in 1 copy of gene can lead to cancer)

Tumor suppressor genes

- normally protect against cancer (act as brakes and help stop cell growth and control cell death)
- damaged/missing - cell growth, cell division and cell death (apoptosis) may not be controlled
- nearly 50% of all cancers are thought to involve a damaged or missing tumor suppressor gene (e.g. p53, APC, Rb)
- mutations are recessive (both copies of gene need to have a defect to be at risk of developing cancer)

DNA repair genes

- responsible for repairing damaged genes
- fix mistakes (mutations) that commonly occur when DNA is being copied
- damaged genes → mutations may not be repaired and will build up
- mutations are recessive

Forms of cancer

- Sarcoma affecting mesenchymal tissue (muscle, connective tissue, bone).
- Carcinoma affect epithelial tissue.
- Hematopoietic and lymphoid malignant neoplasms (Leukaemia and Lymphoma).

Steps of cancer development

- cells gradually become malignant through a progressive series of alterations (several steps and several genetic mutations are usually required)
- development of cancer is a multistep and multifactorial process and can take a long time (several years) for cancer to develop
- indication of the multistep development of cancer is that most cancers develop in a late life-period

(The incidence of colon cancer increases more than tenfold between the ages of 30 and 50 and another tenfold between 50 and 70. Dramatic increase of cancer incidence with age suggests that most cancers develop as a consequence of multiple abnormalities, which accumulate over periods of many years).

Initiation

- genetic alteration leading to abnormal proliferation of a single cell
- cell proliferation then leads to the outgrowth of a population of clonally derived tumor cells
- ability to spot mutations and either destroy itself (by apoptosis) or fix the mutations → if the repair fails and more mutations occur, the damaged cell is more likely to become cancerous
- initial change may be caused by carcinogens (chemicals, smoking, exposure to radiation) but often the cause is unknown and may be a random

Promotion

- further and repeated damage needs to occur before cancer develops

Progression

- additional mutations occur within cells of the tumor population
- mutations confer a selective advantage to the cell (rapid growth, descendants become dominant within the tumor population)
- clonal selection - new clone of tumor cells has evolved on the basis of its increased growth rate or other properties (such as survival, invasion, or metastasis) that confer a selective advantage
- transformation – different cell behavior, grow and function → turn into a cancer cell
- fast-growing cancer cell may double over 1–4 weeks, a slower growing one over 2–6 months
- as cancer cells grow, they can group together to form a lump (tumor)

Metastasis

- as cancer cells divide, they can invade surrounding tissue
- can also break away from the original (primary) tumor and enter the bloodstream or lymphatic system
- cancer cells escaping detection by the immune system → can be carried by the blood and lymph to distant parts of the body → metastasize

Hallmarks of cancer

- uncontrolled growth of cancer cells results from accumulated abnormalities affecting many of the cell regulatory mechanisms
- cancer cells typically display abnormalities in the mechanisms that regulate normal cell proliferation, differentiation, and survival
- cancer cells never differentiate - continue to divide, cause more damage, and invade new tissue

Uncontrolled proliferation

- normal cells display density-dependent inhibition of cell proliferation = proliferate until they reach a finite cell density → become quiescent (arrested in the G0 stage of the cell cycle)
- cancer cells proliferation is not sensitive to density-dependent inhibition → uncontrolled proliferation (ability to grow on top of other cells in layers resulting in a tumor)
- insensitivity to growth-inhibitory (antigrowth) signals → cancer cells inactivate tumor suppressor genes that normally inhibit growth

Reduced requirements for extracellular growth factors

- self-sufficiency in growth signals = cancer cells can produce growth factors
- abnormal production of growth factors leads to continuous auto-stimulation of cell division
- cancer cells are less dependent on growth factors from other physiologically normal sources
- contributing to the unregulated proliferation of tumor cells

Evasion of programmed cell death (apoptosis)

- normal cells - ability to recognize unrepairable damage and perform a controlled self-destruction for the good of the whole
- cancer cells - allowing their damaged and abnormal features to continue infecting the body
- cancer cells suppress and inactivate genes and pathways that normally enable cells to die

Limitless replication potential

- normal cells - go through senescence through e.g. shortening of telomeres with every cell division
- cancer cells - have telomerase that will sustain the telomere length of the chromosomes rendering the cell virtually immortal even after generations of growth

Sustained angiogenesis

- cancer cells acquire the capacity to draw out their own supply of blood and blood vessels
- ability to form new blood vessels - cancer cells send out chemical signals that promote angiogenesis
- new blood vessels provide the blood supply needed for growth by acting as a type of feeding tube for the delivery of oxygen and nutrients to the cancer cell
- angiogenesis is critical for allowing cancer cells to metastasise or invade neighbouring tissue and distant regions of the body

Tissue invasion and metastasis

- cancer cells acquire the capacity to migrate to other organs, invade other tissues, and colonize these organs, resulting in their spread throughout the body