DOWNLOAD PDF FUNDAMENTAL ASPECTS OF NORMAL AND MALIGNANT GROWTH.

Chapter 1 : Fundamental aspects of normal and malignant growth.

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An uncontrolled prolifferation of mutated cells Tumour: A new and abnormal growth of tissue, not always a mass. Can be used interchangably with tumour Benign: Non-cancerous tissue which is usually encapulated meanng it isnot capable of spreading Malignant: Rapid growing cells which are not encapsulated meaning that mutated cells can spread to vessels and nearby structures Carcinoma: A cancer that develops in epithelial cells, of the skin and linings of body tissues. This affects squamus and basal cells. Cancer in lympatic tissues. Lymphoma originates in developing B-lymphocytes and T-lymphocytes, which have undergone a malignant cancerous change. These tumours cause swelling in the lymph nodes and other parts of the body. Over time, malignant lymphocytes called lymphoma cells crowd out normal lymphocytes and eventually the immune system becomes weakened and can no longer function properly. Sarcomas grow in connective tissue, cells that connect or support other kinds of tissue in your body. These tumors are most common in the bones, muscles, tendons, cartilage, nerves, fat, and blood vessels of your arms and legs, but they can happen anywhere. These suppress the production of normal blood cells, leading to anaemia and other symptoms. The spread of cancer cells from the place where they first formed to another part of the body. In metastasis, cancer cells break away from the original primary tumor, travel through the blood or lymph system, and form a new tumor in other organs or tissues of the body. Common sites for metastasis are bones, liver, lungs and the brain. Tumor angiogenesis is the growth of new blood vessels that tumors need to grow. This process is caused by the release of chemicals by the tumor and by host cells near the tumor. Tumor suppressor genes are normal genes that slow down cell division, repair DNA mistakes, or tell cells when to die a process known as apoptosis or programmed cell death. In most cases, the p53 gene is mutated, giving rise to a stable mutant protein whose accumulation is regarded as a hallmark of cancer cells. Mutant p53 proteins not only lose their tumor suppressive activities but often gain additional oncogenic functions that endow cells with growth and survival advantages. This video discusses tumour suppressor genes. These genes code for proteins that help regulate cell growth. These important genes are called proto-oncogenes. A change in the DNA sequence of the proto-oncogene gives rise to an oncogene, which produces a different protein and interferes with normal cell regulation. Check this video out which explains oncogenes. Carcinogenesis or oncogenesis or tumorigenesis is the formation of a cancer, whereby normal cells are transformed into cancer cells. The process is characterized by changes at the cellular, genetic, and epigenetic levels and abnormal cell division, in some cancers forming a malignant mass. Development of cancer The fundamental abnormality resulting in the development of cancer is the continual unregulated proliferation of cancer cells. Rather than responding appropriately to the signals that control normal cell behavior, cancer cells grow and divide in an uncontrolled manner, invading normal tissues and organs and eventually spreading throughout the body. The generalized loss of growth control exhibited by cancer cells is the net result of accumulated abnormalities in multiple cell regulatory systems and is reflected in several aspects of cell behavior that distinguish cancer cells from their normal counterparts. Cell growth cycle There are three phases in the development of cancer: This occurs when there is a mutation the the cells DNA structure from exposure to a carcinogen, radiation, or virus, a genetic defect or error during DNA replication. This is a irreversible process but many cells undergo apoptosis when the mutation is detected. Although most carcinogens are safetly removed from the body, failure in protective mechanisms can alter cellular DNA.

Chapter 2 : Benign and Malignant Tumors: What is the Difference?

Book: Fundamental aspects of normal and malignant growth. www.nxgvision.com + pp. Abstract: This is a monumental treatise in which the problems of growth, normal and abnormal, are discussed in their theoretical and practical aspects.

Search term Section In this way we can see the gross properties of the disease â€" the properties that ultimately must be explained by analysis of genes and cells. Metastatic Tumor Cells Are Invasive and Can Spread Tumors arise with great frequency, especially in older animals and humans, but most pose little risk to their host because they are localized and of small size. We call such tumors benign ; an example is warts. It is usually apparent when a tumor is benign because it contains cells that closely resemble, and may function like, normal cells. The surface interaction molecules that hold tissues together keep benign tumor cells, like normal cells, localized to appropriate tissues. Benign liver tumors stay in the liver, and benign intestinal tumors stay in the intestine. A fibrous capsule usually delineates the extent of a benign tumor and makes it an easy target for a surgeon Figure Benign tumors become serious medical problems only if their sheer bulk interferes with normal functions or if they secrete excess amounts of biologically active substances like hormones. Figure Sections of two types of benign tumors. It is organized like a little gland in the midst of normal tissue. In contrast, the cells composing a malignant tumor , or cancer, express some proteins characteristic of the cell type from which it arose, and a high fraction of the cells grow and divide more rapidly than normal. Some malignant tumors remain localized and encapsulated, at least for a time; an example is carcinoma in situ in the ovary or breast. The spread of tumor cells and establishment of secondary areas of growth is called metastasis ; most malignant cells eventually acquire the ability to metastasize. Thus the major characteristics that differentiate metastatic or malignant tumors from benign ones are their invasiveness and spread. Cancer cells can be distinguished from normal cells by microscopic examination. They are usually less well differentiated than normal cells or benign tumor cells. Liver cancers, for instance, express some of but not all the proteins characteristic of normal liver cells and may ultimately evolve to a state in which they lack most liver-specific functions. In a specific tissue, malignant cells usually exhibit the characteristics of rapidly growing cells, that is, a high nucleus -to- cytoplasm ratio, prominent nucleoli, many mitoses, and relatively little specialized structure. The presence of invading cells in an otherwise normal tissue section is the most diagnostic indication of a malignancy Figure Figure Gross and microscopic views of a tumor invading normal liver tissue. The white protrusions on the surface of the liver are the tumor masses. Malignant cells usually retain enough resemblance to the normal cell type from which they arose, as judged by morphology and by expression of cell-specific genes, that it is possible to classify them by their relationship to normal tissue. Normal animal cells are often classified according to their embryonic tissue of origin, and the naming of tumors has followed suit. Cancers occur in most types of cells; compared with the or so different types of cells in the human body, we can recognize different types of human cancers. Malignant tumors are classified as carcinomas if they derive from endoderm or ectoderm and sarcomas if they derive from mesoderm. The leukemias , a class of sarcomas, grow as individual cells in the blood, whereas most other tumors are solid masses. Alterations in Cell-to-Cell Interactions Are Associated with Malignancy The restriction of a normal cell type to a given organ or tissue is maintained by cell-to-cell recognition and by physical barriers. Primary among the physical barriers that keep tissues separated is the basal lamina also called the basement membrane , which underlies layers of epithelial cells as well as surrounds the endothelial cells of blood vessels see Figures and Basal laminae define the surfaces of external and internal epithelia and the structure of blood vessels. Metastatic cells break their contacts with other cells in their tissue of origin and overcome the constraints on cell movement provided by basal laminae and other barriers. As a result, metastatic cells can enter the circulation and establish themselves in another site distant from their original location. In the process of metastasizing, they may invade adjoining tissue before spreading to distant sites through the circulation. Both these events require breach of a basal lamina. Tumor cells often produce elevated levels of cell-surface

receptors specific for the proteins and polysaccharides composing basal laminae e. Many tumor cells also secrete a protease called plasminogen activator, which cleaves a peptide bond in the serum protein plasminogen, converting it to the active protease plasmin. Secretion of a small amount of plasminogen activator causes a large increase in protease concentration by catalytically activating the abundant plasminogen in normal serum. This increased protease activity promotes metastasis by helping tumor cells digest and penetrate the basal lamina. The normally invasive extraembryonic cells of the fetus secrete plasminogen activator when they are implanting in the uterine wall, a compelling analogy to invasion by tumor cells. As the basal lamina disintegrates, some tumor cells will enter the blood, but fewer than 1 in 10, cells that escape the primary tumor survive to colonize another tissue and form a secondary, metastatic tumor see Figure Such a cell first must adhere to an endothelial cell lining a capillary and migrate across or through it into the underlying tissue. To set up a metastasis, a tumor cell must be able to multiply without a mass of surrounding identical cells and to adhere to new types of cells. The wide range of altered behaviors that underlie malignancy may have their basis in new or variant surface proteins made by malignant cells. Tumor Growth Requires Formation of New Blood Vessels Tumors, whether primary or secondary, require recruitment of new blood vessels in order to grow to a large mass. In the absence of a blood supply, a tumor can grow into a mass of about cells, roughly a sphere 2 mm in diameter. At this point, division of cells on the outside of the tumor mass is balanced by death of those in the center due to an inadequate supply of nutrients. Such tumors, unless they secrete hormones, cause few problems. However, most tumors induce the formation of new blood vessels that invade the tumor and nourish it, a process called angiogenesis. Although this complex process is not understood in detail, it can be described as several discrete steps: Many tumors produce growth factors that stimulate angiogenesis; other tumors somehow induce surrounding normal cells to synthesize and secrete such factors. New blood vessels nourish the growing tumor , allowing it to increase in size and thus increase the probability that additional harmful mutations will occur. The presence of an adjacent blood vessel also facilitates the process of metastasis. One of the most mysterious aspects of angiogenesis is that a primary tumor will often secrete a substance that inhibits angiogenesis around secondary metastases. In this case, surgical removal of the primary tumor may stimulate growth of its metastatic secondary tumors. Several natural proteins that inhibit angiogenesis e. While new blood vessels are constantly forming during embryonic development , few form normally in adults; thus a specific inhibitor of angiogenesis might have few adverse side effects. That mutations cause these differences was conclusively established by transfection experiments with a line of cultured mouse fibroblasts called 3T3 cells. These cells normally grow only when attached to the plastic surface of a culture dish and are maintained at a low cell density. Because 3T3 cells stop growing when they contact other cells, they eventually form a monolayer of well-ordered cells that have stopped proliferating and are in the G0 phase of the cell cycle Figure a. Although such quiescent cells in a saturated culture have stopped growing, they remain viable for a long time and can resume growth if they are released from contact inhibition and provided with growth factors present in serum. As is true for other cultured fibroblasts, the exact cell type that gives rise to 3T3 cells is uncertain, but they can differentiate into a range of mesodermally derived cell types, especially fat cells and endothelial cells those that line blood vessels. Figure Scanning electron micrographs of normal and transformed 3T3 cells. The cells are more When DNA from a human bladder carcinoma , mouse sarcoma , or other tumor is added to a culture of 3T3 cells, about one cell in a million incorporates a particular segment of bladder carcinoma DNA that causes a distinctive phenotype. The progeny of the affected cell are more rounded and less adherent to one another and to the dish than are the normal surrounding cells, forming a three-dimensional cluster of cells a focus that can be recognized under the microscope Figure b. Such cells, which continue to grow when the normal cells have become quiescent , have undergone transformation and are said to be transformed. Transformed cells have many properties similar to those of the cells composing malignant tumors, including changes in cell morphology, ability to grow unattached to a basal lamina or other extracellular matrix , reduced requirement for growth factors, secretion of plasminogen activator, and loss of actin microfilaments. Figure outlines the

procedure for transforming 3T3 cells with DNA from a human bladder carcinoma and cloning the specific DNA segment that causes transformation. Subsequent studies showed that the cloned segment included a mutant version of the cellular ras gene , designated rasD. Because the mutated RasD protein hydrolyzes bound GTP very slowly, it accumulates in the active state, sending a growth-promoting signal to the nucleus even in the absence of the hormones normally required to activate the Ras â€" MAP kinase pathway see Figure Figure The identification and molecular cloning of the rasD oncogene. Addition of DNA from a human bladder carcinoma to a culture of mouse 3T3 cells causes about one cell in a million to divide abnormally and form a focus, or clone of transformed cells. Expression of the RasD protein , however, is not sufficient to cause transformation of normal cells in a primary culture of human, rat, or mouse fibroblasts. Unlike cells in a primary culture, however, cultured 3T3 cells have undergone a loss-of-function mutation in the p16 gene ; as discussed later, the p16 gene encodes a cyclin - kinase inhibitor that restricts progression through the cell cycle. Such cells can grow indefinitely if periodically diluted and supplied with nutrients. Transformation of these cells requires both loss of p16 and expression of a constitutively active Ras protein ; for this reason, transfection with the rasD gene can transform 3T3 cells but not normal cultured primary fibroblast cells. A mutant ras gene is found in most human colon, bladder, and other cancers, but not in normal human DNA ; thus it must arise as the result of a somatic mutation in one of the tumor progenitor cells. Any gene, such as rasD or v-src, that encodes a protein capable of transforming cells in culture or inducing cancer in animals is referred to as an oncogene. The normal cellular gene from which it arises is called a proto-oncogene. Development of a Cancer Requires Several Mutations Conversion of a normal body cell into a malignant one is now known to require multiple mutations. Three different types of experimental approaches all converged on this important conclusion: Epidemiology Each individual cancer is a clone that arises from a single cell. Assuming that the rate of mutation is roughly constant during a lifetime, then the incidence of most types of cancer would be independent of age if only one mutation were required to convert a normal cell into a malignant one. In fact, however, the incidence of most types of human cancers increases markedly and exponentially with age Figure Although many explanations of this phenomenon have been considered, the incidence data are most consistent with the notion that multiple mutations are required for a cancer to form. Figure The incidence of several human cancers increases markedly with age. Note that the logarithm of annual incidence is plotted versus the logarithm of age. Kinzler, , Trends Genet. A mutation in one cell would give it a slight growth advantage. One of the progeny cells would then undergo a second mutation that would allow its descendants to grow more uncontrollably and form a small benign tumor ; a third mutation in a cell within this tumor would allow it to outgrow the others, and its progeny would form a mass of cells, each of which would have these three mutations. An additional mutation in one of these cells would allow its progeny to escape into the blood and establish daughter colonies at other sites, the hallmark of metastatic cancer. Since decades are required for these multiple mutations to occur, the exponential increase in cancer incidence with age is predicted by the multi-hit model of cancer induction. Somatic Mutations in Human Tumors Surgeons can produce fairly pure samples of many human cancers, but generally the cells that give rise to these tumors cannot be identified and analyzed. An exception is colon cancer, which evolves through distinct, well-characterized morphological stages Figure Because these intermediate stages â€" polyps, benign adenomas, and carcinomas â€" can be isolated by a surgeon, mutations that occur in each of the morphological stages can be identified. These studies have identified a series of mutations that commonly arise in a welldefined order, providing strong support for the multi-hit model. Invariably the first step in colon carcinogenesis involves loss of a functional APC gene ; however, not every colon cancer acquires all the later mutations or acquires them in the same order. Figure The development and metastasis of human colorectal cancer and its genetic basis. A mutation in the APC tumor-suppressor gene in a single epithelial cell causes the cell to divide, although surrounding cells do not, forming a mass of localized benign tumor more

Chapter 3 : Fundamental aspects of normal and malignant growth. - Biodiversity Heritage Library

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Angiogenesis inhibitor can be endogenous or come from outside as drug or a dietary component. Application in medicine[edit] Angiogenesis as a therapeutic target[edit] Angiogenesis may be a target for combating diseases characterized by either poor vascularisation or abnormal vasculature E. The presence of blood vessels where there should be none may affect the mechanical properties of a tissue, increasing the likelihood of failure. The absence of blood vessels in a repairing or otherwise metabolically active tissue may inhibit repair or other essential functions. Several diseases, such as ischemic chronic wounds , are the result of failure or insufficient blood vessel formation and may be treated by a local expansion of blood vessels, thus bringing new nutrients to the site, facilitating repair. Other diseases, such as age-related macular degeneration , may be created by a local expansion of blood vessels, interfering with normal physiological processes. The modern clinical application of the principle of angiogenesis can be divided into two main areas: Whereas anti-angiogenic therapies are being employed to fight cancer and malignancies, [27] [28] which require an abundance of oxygen and nutrients to proliferate, pro-angiogenic therapies are being explored as options to treat cardiovascular diseases , the number one cause of death in the Western world. One of the first applications of pro-angiogenic methods in humans was a German trial using fibroblast growth factor 1 FGF-1 for the treatment of coronary artery disease. There are still serious, unsolved problems related to gene therapy. Difficulties include effective integration of the therapeutic genes into the genome of target cells, reducing the risk of an undesired immune response, potential toxicity, immunogenicity , inflammatory responses, and oncogenesis related to the viral vectors used in implanting genes and the sheer complexity of the genetic basis of angiogenesis. Oral, intravenous, intra-arterial, or intramuscular routes of protein administration are not always as effective, as the therapeutic protein may be metabolized or cleared before it can enter the target tissue. Cell-based pro-angiogenic therapies are still early stages of research, with many open questions regarding best cell types and dosages to use. Tumor angiogenesis[edit] Without angiogenesis a tumor cannot grow beyond a limited size Cancer cells are cells that have lost their ability to divide in a controlled fashion. A malignant tumor consists of a population of rapidly dividing and growing cancer cells that progressively accrues mutations. Growth factors such as bFGF and VEGF can induce capillary growth into the tumor, which some researchers suspect supply required nutrients, allowing for tumor expansion. Unlike normal blood vessels, tumor blood vessels are dilated with an irregular shape. In normal cells but not in cancerous ones , PKG apparently limits beta-catenin , which solicits angiogenesis. In either case, angiogenesis is a necessary and required step for transition from a small harmless cluster of cells, often said to be about the size of the metal ball at the end of a ball-point pen, to a large tumor. Angiogenesis is also required for the spread of a tumor, or metastasis. Single cancer cells can break away from an established solid tumor, enter the blood vessel, and be carried to a distant site, where they can implant and begin the growth of a secondary tumor. Evidence now suggests the blood vessel in a given solid tumor may, in fact, be mosaic vessels, composed of endothelial cells and tumor cells. This mosaicity allows for substantial shedding of tumor cells into the vasculature, possibly contributing to the appearance of circulating tumor cells in the peripheral blood of patients with malignancies. Endothelial cells have long been considered genetically more stable than cancer cells. For this reason, endothelial cells are thought to be an ideal target for therapies directed against them. Angiogenic stimulators are then released by the tumor cells. These then travel to already established, nearby blood vessels and activates their endothelial cell receptors. This induces a release of proteolytic enzymes from the vasculature. These enzymes target a particular point on the blood vessel and cause a pore to form. This is the point where the new blood vessel will grow from. The reason tumour cells need a blood supply is because

they cannot grow any more than millimeters in diameter without an established blood supply which is equivalent to about cells. It is a potent, physiological process that underlies the natural manner in which our bodies respond to a diminution of blood supply to vital organs, namely the production of new collateral vessels to overcome the ischemic insult. Reproducible and credible successes in these early animal studies led to high enthusiasm that this new therapeutic approach could be rapidly translated to a clinical benefit for millions of patients in the Western world suffering from these disorders. A decade of clinical testing both gene- and protein-based therapies designed to stimulate angiogenesis in underperfused tissues and organs, however, has led from one disappointment to another. Although all of these preclinical readouts, which offered great promise for the transition of angiogenesis therapy from animals to humans, were in one fashion or another, incorporated into early stage clinical trials, the FDA has, to date , insisted that the primary endpoint for approval of an angiogenic agent must be an improvement in exercise performance of treated patients. It may be necessary to present these proteins in a way that mimics natural signaling events, including the concentration , spatial and temporal profiles, and their simultaneous or sequential presentation with other appropriate factors. While arteriogenesis produces network changes that allow for a large increase in the amount of total flow in a network, angiogenesis causes changes that allow for greater nutrient delivery over a long period of time. Capillaries are designed to provide maximum nutrient delivery efficiency, so an increase in the number of capillaries allows the network to deliver more nutrients in the same amount of time. A greater number of capillaries also allows for greater oxygen exchange in the network. This is vitally important to endurance training, because it allows a person to continue training for an extended period of time. However, no experimental evidence suggests that increased capillarity is required in endurance exercise to increase the maximum oxygen delivery. In wet macular degeneration , VEGF causes proliferation of capillaries into the retina. Since the increase in angiogenesis also causes edema , blood and other retinal fluids leak into the retina , causing loss of vision. Anti-angiogenic drugs targeting the VEGF pathways are now used successfully to treat this type of macular degeneration Quantification[edit] Quantifying vasculature parameters such as microvascular density has various complications due to preferential staining or limited representation of tissues by histological sections. Recent research has shown complete 3D reconstruction of tumor vascular structure and quantification of vessel structures in whole tumors in animal models.

Chapter 4 : At Brain Tumor Diagnosis: Glossary

Comment: A readable copy. All pages are intact, and the cover is intact. Pages can include considerable notes-in pen or highlighter-but the notes cannot obscure the text.

A type of radiosurgery that uses a focused beam of gamma raysto destroy tumor cells. Glioblastoma There are more than types of brain and central nervous system CNS tumors. A detailed list of tumor types, their characteristics, symptoms and potential treatments can be found here link to the Tumor Type page. In other words, the process by which the information from a specific gene is manifested into a biological structure or activity in the cell. Gene Regulation The control of gene expression. Genomic changes may include the entire set of small DNA mutations, the deletion of genes, extra copies of genes gene amplification or gene rearrangements relative to each other within, for example, a tumor. Genomic changes provide evidence as to which DNA alterations drive the growth of a tumor. Genomic Sequencing A laboratory method that is used to determine the entire genetic makeup of a specific organism or cell type. This method can be used to find changes in areas of the genome that may be important in the development of specific diseases, such as cancer. Genomic Characterization A laboratory method that is used to learn about all the genes in a person or in a specific cell type, and the way those genes interact with each other and with the environment. Genomic characterization may be used to find out why some people get certain diseases while others do not, or why people react in different ways to the same drug. It may also be used to help develop new ways to diagnose, treat, and prevent diseases, such as cancer. Also called genomic profiling. Glioma There are more than types of brain and central nervous system CNS tumors. A detailed list of tumor types, their characteristics, symptoms and potential treatments can be found here. Different approaches can include stimulating the immune system to enhance immune response, modifying immune cells, suppressing cells that dampen the immune response, viruses and vaccines. Back to Top Malignant brain tumors Contain cancer cells and often do not have clear borders. They are considered to be life-threatening because they grow rapidly and invade surrounding brain tissue. Although malignant brain tumors very rarely spread to other areas of the body, they can spread throughout the brain or to the spine. These tumors can be treated with surgery, chemotherapy and radiation, but they may recur after treatment. Meduloblastoma There are more than types of brain and central nervous system CNS tumors. Meningioma There are more than types of brain and central nervous system CNS tumors. Metastatic or secondary brain tumors Begin in another part of the body and then spread to the brain. These tumors are more common than primary brain tumors and are named by the location in which they begin. They are treated based on where they originate, such as the lung, breast, colon or skin. Model Systems Model Systems: They are created to better understand the tumor and test therapies outside of actual humans. Molecular analysis In medicine, a laboratory test that checks for certain genes, proteins, or other molecules in a sample of tissue, blood, or other body fluid. Molecular tests also check for certain changes in a gene or chromosome that may cause or affect the chance of developing a specific disease or disorder, such as cancer. A molecular test may be done with other procedures, such as biopsies, to help diagnose some types of cancer. It may also be used to help plan treatment, find out how well treatment is working, or make a prognosis. Some molecular analyses use microscopes but others use liquid-based specimens. A molecular marker may be used to see how well the body responds to a treatment for a disease or condition. Also called biomarker and signature molecule. Molecular Profiling Comprehensive molecular profiling of specific tumors identifies biological targets such as genes that allow for interventions, including targeted drug therapies that will be effective for those specific tumor types. We also believe that comprehensive molecular profiling is transforming the research landscape for some tumor types. Mouse-model Mice are the species of choice for modeling the complex interactions between tumor cells, a host environment, and drugs, as mouse genetics are easily manipulated. Mouse models allow investigators to better study and understand relationships between specific genetic alterations and tumors, utilize new imaging techniques, and test novel therapies. MRI

Magnetic resonance imaging â€" A medical imaging technique that uses powerful magnetic fields to make detailed pictures of the inside of the body. Back to Top Nanotechnology The field of research that deals with the engineering and creation of things from materials that are less than nanometers one-billionth of a meter in size, especially single atoms or molecules. Nanotechnology is being studied in the detection, diagnosis, and treatment of cancer. For example, they are being engineered to deliver therapeutic agents to brain tumor cells. The NCI coordinates the U. Neuroblastoma There are more than types of brain and central nervous system CNS tumors. NF2 Neurofibromatosis type 2 â€" a hereditary condition characterized by the growth of noncancerous tumors of the central nervous system. Neurology The branch of medicine dealing with the diagnosis and treatment of diseases of the nervous system. Neuro-Oncology The branch of medicine dealing with the diagnosis and treatment of brain tumors. Neuropsychology The study of how the structure and function of the brain relate to behavior and other psychology processes. Oligodendroglioma oligo There are more than types of brain and central nervous system CNS tumors. Oncogene A gene that is a mutated changed form of a gene involved in normal cell growth. Oncogenes may cause the growth of cancer cells. Mutations in genes that become oncogenes can be inherited or caused by being exposed to substances in the environment that cause cancer. Back to Top Palliative Care Palliative care will address the symptoms of a serious illness as well as the side effects of medical therapies used to treat the illness, such as nausea, pain, anxiety, insomnia, lack of appetite and fatigue. Pathology A branch of medical science and clinical care primarily concerning the examination of tissues and bodily fluids in order to understand diseases, make medical diagnoses and guide clinical care. Pathologist A doctor who identifies diseases by studying cells and tissues under a microscope and through analysis of liquid-based specimens e. Pathology Report The description of cells and tissues made by a pathologist based on microscopic evidence, and sometimes used to make a diagnosis of a disease. PET Positron emission tomography â€" A type of nuclear medicine imaging which is used to show how tissues are working. PI Principal Investigator â€" The lead researcher for a study or trial. PIP Pediatric Investigational Plan â€" A plan that pharmaceutical companies must submit in Europe that outlines their intention to develop a pediatric equivalent of an adult therapy. Primary Whether cancerous or benign, tumors that start in cells of the brain are called primary brain tumors. Primary brain tumors may spread to other parts of the brain or to the spine, but rarely to other organs.

Chapter 5 : " Growth in tissue culture." by C Waymouth

Sinauer Associates ; Search term The Development and Causes of Cancer The fundamental abnormality resulting in the development of cancer is the continual unregulated proliferation of cancer cells. Rather than responding appropriately to the signals that control normal cell behavior, cancer cells grow and divide in an uncontrolled manner, invading normal tissues and organs and eventually spreading throughout the body. The generalized loss of growth control exhibited by cancer cells is the net result of accumulated abnormalities in multiple cell regulatory systems and is reflected in several aspects of cell behavior that distinguish cancer cells from their normal counterparts. Types of Cancer Cancer can result from abnormal proliferation of any of the different kinds of cells in the body, so there are more than a hundred distinct types of cancer , which can vary substantially in their behavior and response to treatment. The most important issue in cancer pathology is the distinction between benign and malignant tumors Figure A tumor is any abnormal proliferation of cells, which may be either benign or malignant. A benign tumor , such as a common skin wart, remains confined to its original location, neither invading surrounding normal tissue nor spreading to distant body sites. A malignant tumor , however, is capable of both invading surrounding normal tissue and spreading throughout the body via the circulatory or lymphatic systems metastasis. Only malignant tumors are properly referred to as cancers, and it is their ability to invade and metastasize that makes cancer so dangerous. Whereas benign tumors can usually be removed surgically, the spread of malignant tumors to distant body sites frequently makes them resistant to such localized treatment. Micrographs of normal uterus A and a section of a uterine sarcoma B. Note that the cancer cells darkly stained have invaded the surrounding normal tissue. Both benign and malignant tumors are classified according to the type of cell from which they arise. Most cancers fall into one of three main groups: Sarcomas , which are rare in humans, are solid tumors of connective tissues, such as muscle, bone, cartilage, and fibrous tissue. Tumors are further classified according to tissue of origin e. For example, fibrosarcomas arise from fibroblasts, and erythroid leukemias from precursors of erythrocytes red blood cells. Although there are many kinds of cancer , only a few occur frequently Table More than a million cases of cancer are diagnosed annually in the United States, and more than , Americans die of cancer each year. The Development of Cancer One of the fundamental features of cancer is tumor clonality, the development of tumors from single cells that begin to proliferate abnormally. The single-cell origin of many tumors has been demonstrated by analysis of X chromosome inactivation Figure As discussed in Chapter 8, one member of the X chromosome pair is inactivated by being converted to heterochromatin in female cells. X inactivation occurs randomly during embryonic development, so one X chromosome is inactivated in some cells, while the other X chromosome is inactivated in other cells. Thus, if a female is heterozygous for an X chromosome gene , different alleles will be expressed in different cells. Normal tissues are composed of mixtures of cells with different inactive X chromosomes , so expression of both alleles is detected in normal tissues of heterozygous females. In contrast, tumor tissues generally express only one allele of a heterozygous X chromosome gene. The implication is that all of the cells constituting such a tumor were derived from a single cell of origin, in which the pattern of X inactivation was fixed before the tumor began to develop. Normal tissue is a mosaic of cells in which different X chromosomes X1 and X2 have been inactivated. Tumors develop from a single initially altered cell, so each tumor cell displays the same pattern of X inactivation X1 inactive, X more The clonal origin of tumors does not, however, imply that the original progenitor cell that gives rise to a tumor has initially acquired all of the characteristics of a cancer cell. On the contrary, the development of cancer is a multistep process in which cells gradually become malignant through a progressive series of alterations. One indication of the multistep development of cancer is that most cancers develop late in life. The incidence of colon cancer, for example, increases more than tenfold between the ages

of 30 and 50, and another tenfold between 50 and 70 Figure Such a 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. Annual death rates from colon cancer in the United States. Science and Society, New York: At the cellular level, the development of cancer is viewed as a multistep process involving mutation and selection for cells with progressively increasing capacity for proliferation, survival, invasion, and metastasis Figure The first step in the process, tumor initiation, is thought to be the result of a 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. Tumor progression continues as additional mutations occur within cells of the tumor population. Some of these mutations confer a selective advantage to the cell, such as more rapid growth, and the descendants of a cell bearing such a mutation will consequently become dominant within the tumor population. The process is called clonal selection, since a 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. Clonal selection continues throughout tumor development, so tumors continuously become more rapid-growing and increasingly malignant. The development of cancer initiates when a single mutated cell begins to proliferate abnormally. Additional mutations followed by selection for more rapidly growing cells within the population then result in progression of more Studies of colon carcinomas have provided a clear example of tumor progression during the development of a common human malignancy Figure The earliest stage in tumor development is increased proliferation of colon epithelial cells. One of the cells within this proliferative cell population is then thought to give rise to a small benign neoplasm an adenoma or polyp. Further rounds of clonal selection lead to the growth of adenomas of increasing size and proliferative potential. Malignant carcinomas then arise from the benign adenomas, indicated by invasion of the tumor cells through the basal lamina into underlying connective tissue. The cancer cells then continue to proliferate and spread through the connective tissues of the colon wall. Eventually the cancer cells penetrate the wall of the colon and invade other abdominal organs, such as the bladder or small intestine. In addition, the cancer cells invade blood and lymphatic vessels, allowing them to metastasize throughout the body. Development of colon carcinomas. A single initially altered cell gives rise to a proliferative cell population, which progresses first to benign adenomas of increasing size and then to malignant carcinoma. The cancer cells invade the underlying connective more Causes of Cancer Substances that cause cancer , called carcinogens , have been identified both by studies in experimental animals and by epidemiological analysis of cancer frequencies in human populations e. Since the development of malignancy is a complex multistep process, many factors may affect the likelihood that cancer will develop, and it is overly simplistic to speak of single causes of most cancers. Nonetheless, many agents, including radiation, chemicals, and viruses, have been found to induce cancer in both experimental animals and humans. Radiation and many chemical carcinogens Figure These carcinogens are generally referred to as initiating agents, since the induction of mutations in key target genes is thought to be the initial event leading to cancer development. Some of the initiating agents that contribute to human cancers include solar ultraviolet radiation the major cause of skin cancer , carcinogenic chemicals in tobacco smoke, and aflatoxin a potent liver carcinogen produced by some molds that contaminate improperly stored supplies of peanuts and other grains. The carcinogens in tobacco smoke including benzo a pyrene, dimethylnitrosamine, and nickel compounds are the major identified causes of human cancer. In total, it is estimated that smoking is responsible for nearly one-third of all cancer deathsâ€”an impressive toll for a single carcinogenic agent. Other carcinogens contribute to cancer development by stimulating cell proliferation, rather than by inducing mutations. Such compounds are referred to as tumor promoters , since the increased cell division they induce is required for the outgrowth of a proliferative cell population during early stages of tumor development. The phorbol esters that stimulate cell proliferation by activating protein kinase C see Figure Their activity was defined by studies of chemical induction of skin tumors in mice Figure Tumorigenesis in this system can be initiated by a single treatment with a mutagenic carcinogen. Tumors do not develop, however, unless the mice are subsequently treated with

a tumor promoter usually a phorbol ester to stimulate proliferation of the mutated cells. Tumors are initiated by mutations induced by a carcinogen. Development of a tumor then requires treatment with a tumor promoter to stimulate proliferation of the mutated cells. Hormones, particularly estrogens, are important as tumor promoters in the development of some human cancers. The proliferation of cells of the uterine endometrium, for example, is stimulated by estrogen , and exposure to excess estrogen significantly increases the likelihood that a woman will develop endometrial cancer. The risk of endometrial cancer is therefore substantially increased by long-term postmenopausal estrogen replacement therapy with high doses of estrogen alone. Fortunately, this risk is minimized by administration of progesterone to counteract the stimulatory effect of estrogen on endometrial cell proliferation. However, long-term therapy with combinations of estrogen and progesterone may lead to an increased risk of breast cancer. In addition to chemicals and radiation, some viruses induce cancer both in experimental animals and in humans. These viruses are important not only as causes of human cancer; as discussed later in this chapter, studies of tumor viruses have played a key role in elucidating the molecular events responsible for the development of cancers induced by both viral and nonviral carcinogens. Properties of Cancer Cells The uncontrolled growth of cancer cells results from accumulated abnormalities affecting many of the cell regulatory mechanisms that have been discussed in preceding chapters. This relationship is reflected in several aspects of cell behavior that distinguish cancer cells from their normal counterparts. Cancer cells typically display abnormalities in the mechanisms that regulate normal cell proliferation, differentiation, and survival. Taken together, these characteristic properties of cancer cells provide a description of malignancy at the cellular level. The uncontrolled proliferation of cancer cells in vivo is mimicked by their behavior in cell culture. A primary distinction between cancer cells and normal cells in culture is that normal cells display density-dependent inhibition of cell proliferation Figure Normal cells proliferate until they reach a finite cell density, which is determined in part by the availability of growth factors added to the culture medium usually in the form of serum. They then cease proliferating and become quiescent, arrested in the G0 stage of the cell cycle see Figure The proliferation of most cancer cells, however, is not sensitive to density-dependent inhibition. Rather than responding to the signals that cause normal cells to cease proliferation and enter G0, tumor cells generally continue growing to high cell densities in culture, mimicking their uncontrolled proliferation in vivo. Normal cells proliferate in culture until they reach a finite cell density, at which point they become quiescent. Tumor cells, however, continue to proliferate independent of cell density. A related difference between normal cells and cancer cells is that many cancer cells have reduced requirements for extracellular growth factors. As discussed in Chapter 13, the proliferation of most cells is controlled, at least in part, by polypeptide growth factors. For some cell types, particularly fibroblasts, the availability of serum growth factors is the principal determinant of their proliferative capacity in culture. The growth factor requirements of these cells are closely related to the phenomenon of density-dependent inhibition, since the density at which normal fibroblasts become quiescent is proportional to the concentration of serum growth factors in the culture medium. The growth factor requirements of many tumor cells are reduced compared to their normal counterparts, contributing to the unregulated proliferation of tumor cells both in vitro and in vivo. In some cases, cancer cells produce growth factors that stimulate their own proliferation Figure Such abnormal production of a growth factor by a responsive cell leads to continuous autostimulation of cell division autocrine growth stimulation , and the cancer cells are therefore less dependent on growth factors from other, physiologically normal sources.

Chapter 6 : Angiogenesis - Wikipedia

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