DOWNLOAD PDF THE LIFE HISTORY OF 21 BREAST CANCERS

Chapter 1 : Early History of Cancer | American Cancer Society

Newly developed algorithms allow the reconstruction of the genomic history of different breast cancers, tracing the temporal evolution of each tumor and the emergence of the dominant subclones that will eventually trigger diagnosis.

Risk factors can be divided into two categories: One study indicates that exposure to light pollution is a risk factor for the development of breast cancer. List of breast carcinogenic substances Obesity and drinking alcoholic beverages are among the most common modifiable risk factors. Smoking tobacco appears to increase the risk of breast cancer, with the greater the amount smoked and the earlier in life that smoking began, the higher the risk. The risk is not negated by regular exercise, though it is lowered. Drinking alcoholic beverages increases the risk of breast cancer , even at relatively low one to three drinks per week and moderate levels. A review found that studies trying to link fiber intake with breast cancer produced mixed results. Diabetes mellitus might also increase the risk of breast cancer. Carcinogenesis Overview of signal transduction pathways involved in programmed cell death. Mutations leading to loss of this ability can lead to cancer formation. Breast cancer, like other cancers , occurs because of an interaction between an environmental external factor and a genetically susceptible host. Normal cells divide as many times as needed and stop. They attach to other cells and stay in place in tissues. Cells become cancerous when they lose their ability to stop dividing, to attach to other cells, to stay where they belong, and to die at the proper time. Normal cells will commit cell suicide programmed cell death when they are no longer needed. Until then, they are protected from cell suicide by several protein clusters and pathways. Sometimes the genes along these protective pathways are mutated in a way that turns them permanently "on", rendering the cell incapable of committing suicide when it is no longer needed. This is one of the steps that causes cancer in combination with other mutations. The familial tendency to develop these cancers is called hereditary breastâ€”ovarian cancer syndrome. The best known of these, the BRCA mutations , confer a lifetime risk of breast cancer of between 60 and 85 percent and a lifetime risk of ovarian cancer of between 15 and 40 percent. These mutations are either inherited or acquired after birth. Presumably, they allow further mutations, which allow uncontrolled division, lack of attachment, and metastasis to distant organs. This is caused by unobserved risk factors. GATA-3 directly controls the expression of estrogen receptor ER and other genes associated with epithelial differentiation, and the loss of GATA-3 leads to loss of differentiation and poor prognosis due to cancer cell invasion and metastasis. Also, there are types of breast cancer that require specialized lab exams. The two most commonly used screening methods, physical examination of the breasts by a healthcare provider and mammography, can offer an approximate likelihood that a lump is cancer, and may also detect some other lesions, such as a simple cyst. Together, physical examination of the breasts, mammography, and FNAC can be used to diagnose breast cancer with a good degree of accuracy. Other options for biopsy include a core biopsy or vacuum-assisted breast biopsy , [82] which are procedures in which a section of the breast lump is removed; or an excisional biopsy , in which the entire lump is removed. Very often the results of physical examination by a healthcare provider, mammography, and additional tests that may be performed in special circumstances such as imaging by ultrasound or MRI are sufficient to warrant excisional biopsy as the definitive diagnostic and primary treatment method. High-grade invasive ductal carcinoma, with minimal tubule formation, marked pleomorphism , and prominent mitoses , 40x field. Micrograph showing a lymph node invaded by ductal breast carcinoma, with an extension of the tumor beyond the lymph node. Neuropilin-2 expression in normal breast and breast carcinoma tissue. A breast cancer metastasis to the right scapula Needle breast biopsy. Elastography shows stiff cancer tissue on ultrasound imaging. Ultrasound image shows irregularly shaped mass of breast cancer. Infiltrating Invasive breast carcinoma. Breast cancer classification Breast cancers are classified by several grading systems. Each of these influences the prognosis and can affect treatment response. Description of a breast cancer optimally includes all of these factors. Breast cancer is usually classified primarily by its histological appearance. Most breast cancers are derived from the epithelium lining the ducts or lobules, and these cancers are classified as ductal or lobular carcinoma. Carcinoma in situ is growth of low-grade cancerous or precancerous cells within a particular tissue

compartment such as the mammary duct without invasion of the surrounding tissue. In contrast, invasive carcinoma does not confine itself to the initial tissue compartment. Grading compares the appearance of the breast cancer cells to the appearance of normal breast tissue. Normal cells in an organ like the breast become differentiated, meaning that they take on specific shapes and forms that reflect their function as part of that organ. Cancerous cells lose that differentiation. In cancer, the cells that would normally line up in an orderly way to make up the milk ducts become disorganized. Cell division becomes uncontrolled. Cell nuclei become less uniform. Pathologists describe cells as well differentiated low grade , moderately differentiated intermediate grade , and poorly differentiated high grade as the cells progressively lose the features seen in normal breast cells. Poorly differentiated cancers the ones whose tissue is least like normal breast tissue have a worse prognosis. Breast cancer staging using the TNM system is based on the size of the tumor T , whether or not the tumor has spread to the lymph nodes N in the armpits, and whether the tumor has metastasized M i. Larger size, nodal spread, and metastasis have a larger stage number and a worse prognosis. The main stages are: Stages 1â€”3 are within the breast or regional lymph nodes. Stage T1 breast cancer Stage T2 breast cancer Stage T3 breast cancer Where available, imaging studies may be employed as part of the staging process in select cases to look for signs of metastatic cancer. However, in cases of breast cancer with low risk for metastasis, the risks associated with PET scans , CT scans , or bone scans outweigh the possible benefits, as these procedures expose the person to a substantial amount of potentially dangerous ionizing radiation. Breast cancer cells have receptors on their surface and in their cytoplasm and nucleus. Chemical messengers such as hormones bind to receptors , and this causes changes in the cell. Breast cancer cells may or may not have three important receptors: DNA testing of various types including DNA microarrays have compared normal cells to breast cancer cells. The specific changes in a particular breast cancer can be used to classify the cancer in several ways, and may assist in choosing the most effective treatment for that DNA type. Stage 1A breast cancer.

Chapter 2 : The life history of 21 breast cancers - CORE

These processes mark the genome, such that a cancer's life history is encrypted in the somatic mutations present. We developed algorithms to decipher this narrative and applied them to 21 breast.

Driver mutations occur in the subset of genes known as cancer genes. We have relatively limited understanding, however, of the DNA damage and repair processes that have been operative during the lifetime of the patient and that are responsible for the somatic mutations that underlie the development of all cancers in the first place. Historically, analysis of mutation patterns to investigate underlying DNA damage and repair processes in human cancers has predominantly been restricted to reporter cancer genes, notably TP These mutations are enriched at CpG dinucleotides and exhibit a transcriptional strand bias reflecting past activity of transcription-coupled nucleotide excision repair TCR on bulky adducts of guanine caused by tobacco carcinogens Hainaut and Pfeifer, Although these studies have been highly informative, they have limitations. Because they depend upon driver mutations, effects of selection have been superimposed upon mutational patterns generated by DNA damage and repair processes. Moreover, only a single mutation from each cancer sample is usually incorporated into each data set. Thus, they have been well placed to report strong exposures and dominant repair processes operative across most cases of a particular tumor type. However, where there is heterogeneity of mutational process in a cancer class, a composite of different processes will be reported. These bystanders bear the imprints of the DNA damage and repair processes operative during the development of the cancer, unmodified by selection. The several hundreds to tens of thousands of somatic mutations in each cancer, therefore, potentially allow much greater resolution of mutational patterns and insights into underlying mutational processes. In both cancers, mutations were more common in poorly expressed than in highly expressed genes, both on the transcribed and untranscribed strands. The mechanisms underlying these expression-related phenomena are unknown. Compared to melanoma and lung cancer, the mutational processes underlying other cancer types are poorly understood. Therefore, in this study, we document essentially the full repertoire of somatic mutations of 21 breast cancers to investigate the mutational mechanisms shaping these cancer genomes. Results Sequencing of Breast Cancers We sequenced the complete genomes of 21 primary breast cancers and matched normal DNAs from the same individuals. All substitutions were therefore included in the analyses. For indels and rearrangements only confirmed variants were included Table S1 B. From 17 of the 21 cases mRNA expression data were also obtained. In protein coding regions, there were 1, missense, nonsense, 2 stop-lost, 37 essential splice-site, and silent mutations. Of the 2, indels identified, 2, were deletions, insertions and 92 complex. There were 21 coding indels, of which 15 were predicted to result in a translational frameshift and six were in-frame. In addition, 1, structural variants rearrangements , 16 homozygous deletions, and 14 regions of increased copy number amplifications were identified Table S1 C. Each process leaves a mutation signature on the cancer genome defined by the mechanisms of DNA damage and repair that constitute it. The final catalog of mutations is determined by the strength and duration of exposure to each mutational process. We set out to extract the mutation signatures characterizing the mutational processes operative in the 21 breast cancers studied. Because there are six classes of base substitution and 16 possible sequence contexts for each mutated base there are 96 possible mutated trinucleotides. We have represented the fraction of mutations at each of the 96 mutated trinucleotides as a heat map for each cancer and normalized it according to the prevalence of each trinucleotide in the genome.

Chapter 3 : The Life History of 21 Breast Cancers | Ludmil B Alexandrov - calendrierdelascience.com

such that a cancer's life history is encrypted in the somatic mutations present. We developed algo-rithms to decipher this narrative and applied them The Life History of 21 Breast Cancers.

ShareCompartir Being a woman and getting older are the main risk factors for breast cancer. Studies have shown that your risk for breast cancer is due to a combination of factors. The main factors that influence your risk include being a woman and getting older. Most breast cancers are found in women who are 50 years old or older. Some women will get breast cancer even without any other risk factors that they know of. Having a risk factor does not mean you will get the disease, and not all risk factors have the same effect. Most women have some risk factors, but most women do not get breast cancer. If you have breast cancer risk factors, talk with your doctor about ways you can lower your risk and about screening for breast cancer. The risk for breast cancer increases with age; most breast cancers are diagnosed after age Women who have inherited these genetic changes are at higher risk of breast and ovarian cancer. Early menstrual periods before age 12 and starting menopause after age 55 expose women to hormones longer, raising their risk of getting breast cancer. Dense breasts have more connective tissue than fatty tissue, which can sometimes make it hard to see tumors on a mammogram. Women with dense breasts are more likely to get breast cancer. Personal history of breast cancer or certain non-cancerous breast diseases. Women who have had breast cancer are more likely to get breast cancer a second time. Some non-cancerous breast diseases such as atypical hyperplasia or lobular carcinoma in situ are associated with a higher risk of getting breast cancer. Family history of breast cancer. Previous treatment using radiation therapy. Women who took the drug diethylstilbestrol DES , which was given to some pregnant women in the United States between and to prevent miscarriage, have a higher risk. Women whose mothers took DES while pregnant with them are also at risk. Women who are not physically active have a higher risk of getting breast cancer. Being overweight or obese after menopause. Older women who are overweight or obese have a higher risk of getting breast cancer than those at a normal weight. Some forms of hormone replacement therapy those that include both estrogen and progesterone taken during menopause can raise risk for breast cancer when taken for more than five years. Certain oral contraceptives birth control pills also have been found to raise breast cancer risk. Having the first pregnancy after age 30, not breastfeeding, and never having a full-term pregnancy can raise breast cancer risk. Research suggests that other factors such as smoking, being exposed to chemicals that can cause cancer, and changes in other hormones due to night shift working also may increase breast cancer risk.

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Chapter 4 : Breast cancer - Wikipedia

Here, we use newly developed bioinformatic algorithms (Greenman et al.,) to reconstruct the genomic history of 21 breast cancers. Borrowing the concept of a "most-recent common ancestor" from population genetics, we can divide somatic mutations into those acquired before the last complete selective sweep (and thus shared by all cancer.

See other articles in PMC that cite the published article. SUMMARY Cancer evolves dynamically as clonal expansions supersede one another driven by shifting selective pressures, mutational processes, and disrupted cancer genes. We developed algorithms to decipher this narrative and applied them to 21 breast cancers. Subclonal diversification is prominent, and most mutations are found in just a fraction of tumor cells. Minimal expansion of these subclones occurs until many hundreds to thousands of mutations have accumulated, implying the existence of long-lived, quiescent cell lineages capable of substantial proliferation upon acquisition of enabling genomic changes. Classic mathematical models of tumor development developed by Armitage and Doll Armitage and Doll, ; Hornsby et al. Since these studies were performed in the s, we have learnt much about the biological and genetic basis of cancer. Somatic mutation is the fundamental mechanism by which cancer cells suborn these pathways Stratton et al. Whole-cancer genomes sequenced to date carry thousands to tens of thousands of somatic mutations Chapman et al. The accumulation of mutations in cancerous and precancerous cells over time is increasingly recognized as a complex, dynamic process. Carcinogenic exposures and DNA repair defects can lead to sustained elevations in mutation rate; telomere attrition and chromothripsis can drive massive genomic rearrangement in catastrophic bursts Bignell et al. In the classic view of cancer development, those somatic mutations conferring a selective advantage on the cell drive successive waves of clonal expansion, with the fittest clone coming to dominate the cellular compartment. Increasingly, however, cancers are recognized to be mixtures of competing subclones, based on analyses of cancers sampled within a patient at different times Ding et al. Although these studies imply the existence of genetic heterogeneity within a tumor, fundamental questions remain about the dynamics of Darwinian evolution in cancer, the biological relevance of subclonal genetic variation and the relationship between mutational processes and clonal expansion. Here, we use newly developed bioinformatic algorithms Greenman et al. We study the early genomic evolution of the eventual cancer clone, quantify the extent and dynamics of subclonal variation within the cancer sample sequenced and explore changes in mutation signatures over time. These findings have important implications for our understanding of how breast cancers develop over the decades between breast organogenesis and diagnosis in the adult. As described in the companion paper to this Nik-Zainal et al. To develop the reasoning that underpins this paper, we start with the tumor sequenced to fold depth, PDa. At the chromosomal scale, the cancer genome is hypodiploid, with relatively few copy number changes Figure 1A. To exploit the considerable sequencing depth available for this tumor, we modified the parameters of our somatic substitution algorithm in order to identify subclonal mutations; those found in only a fraction of tumor cells.

Chapter 5 : Understanding Your Risk of Developing Secondary Cancers

Cancer evolves dynamically as clonal expansions supersede one another driven by shifting selective pressures, mutational processes, and disrupted cancer genes. These processes mark the genome, such that a cancer's life history is encrypted in the.

Chapter 6 : RePub, Erasmus University Repository: The life history of 21 breast cancers

Cancer evolves dynamically as clonal expansions supersede one another driven by shifting selective pressures, mutational processes, and disrupted cancer genes. These processes mark the genome, such that a cancer's life history is encrypted in the somatic mutations present. We developed algorithms to.

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Chapter 7 : The Life History of 21 Breast Cancers

INTRODUCTION. Age-incidence curves of most common epithelial cancers show rapidly increasing rates after the 4 th -5 th decades of life. Classic mathematical models of tumor development developed by Armitage and Doll (Armitage and Doll, ; Hornsby et al.,) suggested that rate-limiting events are required to generate such incidence patterns.

Chapter 8 : The Life History of 21 Breast Cancers - Europe PMC Article - Europe PMC

title = "The life history of 21 breast cancers", abstract = "Cancer evolves dynamically as clonal expansions supersede one another driven by shifting selective pressures, mutational processes, and disrupted cancer genes.

Chapter 9 : CDC - What Are the Risk Factors for Breast Cancer?

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