DOWNLOAD PDF MOLECULAR MAKERS OF BRAIN TUMOR CELLS

Chapter 1 : - Molecular Makers of Brain Tumor Cells by Stuart E. Siegel

Childhood brain tumors are a diverse group of diseases characterized by the abnormal growth of tissue contained within the skull. Other than leukemia and lymphoma, brain tumors are the most common typ.

Fluorescent marker can help guide surgeons to remove dangerous brain tumor cells more accurately November 4, , National Cancer Research Institute The top picture pink shows fluorescence, the bottom picture is not fluorescing. Colin Watts A chemical that highlights tumour cells has been used by surgeons to help spot and safely remove brain cancer in a trial presented at the NCRI Cancer Conference. The research was carried out with patients who had suspected glioma, the disease that killed Dame Tessa Jowell, and the most common form of brain cancer. Treatment usually involves surgery to remove as much of the cancer as possible, but it can be challenging for surgeons to identify all of the cancer cells while avoiding healthy brain tissue. Researchers say that using the fluorescent marker helps surgeons to distinguish the most aggressive cancer cells from other brain tissue and they hope this will ultimately improve patient survival. The research was presented by Dr. Many patients are treated with surgery and the aim is to safely remove as much of the cancer as possible. And we can plan further treatment, such as radiotherapy or chemotherapy, based on that diagnosis. Previous research shows that, when consumed, 5-ALA accumulates in fast growing cancer cells and this means it can act as a fluorescent marker of high-grade cells. They were aged between 23 and 77 years, with an average median age of 59 years. Before surgery to remove their brain tumours , each patient was given a drink containing 5-ALA. A total of 99 patients received the 5-ALA marker and could be assessed for signs of fluorescence. During their operations, surgeons reported seeing fluorescence in 85 patients and 81 of these were subsequently confirmed by pathologists to have high-grade disease, one was found to have low-grade disease and three could not be assessed. In the 14 patients where surgeons did not see any fluorescence, only seven tumours could be subsequently evaluated by pathology but in all these cases, low-grade disease was confirmed. This is the first prospective trial to show the benefits of using 5-ALA to improve the accuracy of diagnosing high-grade glioma during surgery. These results show that the marker is very good at indicating the presence and location of high-grade cancer cells. They say that other types of markers may need to be tested for detecting low-grade glioma cells. Next steps could include testing the 5-ALA in children with brain tumours, or to help surgeons distinguish between tumour tissue and scar tissue in adult patients whose brain cancers have recurred following treatment. In treating cancer, we are trying to improve survival by tailoring treatments to each individual patient. This technique provides on-the-spot information to help surgeons tailor the operation according to the location, size and grade of the tumour. We know that patients who have near total removal of their tumour have better outcomes, so we are optimistic that, in the long term, these new data will help to increase survival times for glioma patients. National Cancer Research Institute 11 shares.

Chapter 2 : Fluorescent Marker Can Help Guide Surgeons to Remove Dangerous Brain Tumor Cells | Lab

Molecular Markers of Brain Tumor Cells and millions of other books are available for Amazon Kindle. Learn more Enter your mobile number or email address below and we'll send you a link to download the free Kindle App.

How to cite this article: Targeting cerebrospinal fluid for discovery of brain cancer biomarkers. J Cancer Metastasis Treat ;2: Abstract Central nervous system CNS cancer is a devastating illness with unmet therapeutic needs. Establishing biomarkers that have the potential to guide accurate CNS cancer diagnosis or are helpful in predicting disease progression or therapy response is of great interest. Cerebrospinal fluid CSF has been extensively targeted for the detection of molecules that might be useful markers for cancer detection. However, so far very few of such markers have found a standardized routine clinical application. This review examines the current scientific knowledge about the biochemical elements in the CSF that have been reported in the literature as brain cancer biomarkers and highlight reasons why the role of most markers is not yet established in the managment of CNS tumors. Cerebrospinal fluid; central nervous system cancers; cerebrospinal fluid cytology; biochemical markers Introduction Brain cancers are the leading cause of death by solid tumors in children and the cause of morbidity and mortality across a wide range of adult individuals. Blood analysis for novel biomarkers has facilitated the timely diagnosis for patients with several malignancies such as prostate and breast cancers. Cerebrospinal fluid CSF has thus been investigated in the search for brain tumor markers. CSF is a readily accessible body fluid that is reflective of the underlying pathological state of the CNS, hence it has been widely targeted for biomarker discovery for a variety of neurological disorders. The CSF is continuously produced and recycled much like blood or lymph. The rate of CSF production in humans is 0. Any cancer cells released by brain cancer bulk or molecules that are actively secreted or passively diffused by cancer cells are likely to disperse into the CSF and therefore can be detected. This review discusses potential and limitations of CSF analyses in brain cancer patients. Association between primary brain tumors localisation and LS incidence Click here to view CSF cytoanalysis CSF cytology, in which CSF is prepared and examined under a microscope to look for cells, is currently considered the gold standard for diagnosis of brain cancer with leptomeningeal spread and metastatic cancer to the brain. During the ThinPrep analysis, the CSF cells are collected through high-precision filtration driven by fluid mechanics and gently absorbed onto a glass slide by using electrochemical forces. The collected samples need to be added to 10 mL preservation solution, mixed and stood for 15 min. To start with it involves the pathological identification of abnormal cells in the CSF by Giemsa stain and clinicians must make judgments on the presence or absence of malignant cells. Hence, CSF cytological analysis is a pure qualitative test that bears no quantification and lacks validation. CSF specimens may, therefore, fail to capture malignant cells representing one of the major weaknesses of CSF cytology. It is therefore recommended that CSF analysis should be repeated if initially negative. Advantages and disadvantages of different methods for brain tumors biomarkers detection in the CSF Click here to view Flow cytometry analysis CSF fluid flow cytometry is a useful addition to CSF cytology. Cytology examines morphologic patterns, and flow cytometry has the potential to provide information about cell surface protein expression. It is an additional highly sensitive cytological technique capable of accurately detecting malignant CSF cells, especially in comparatively smaller CSF volume and in samples with very low cell counts when combined with multicolor fluorescent antibody labelling. However the cell count and the percentage of neoplastic cells reported in the CSF by both cytology and flow cytometry were significantly higher compared with those found to be positive by flow cytometry alone. Therefore before flow cytometry can be recommended in a routine CSF examination in combination with the conventional cytology, standardized protocols are needed to uniform definitions of positivity and procedure. This method is established to detect prognostic marker on different cancer cells circulating in the peripheral blood such as breast cancer and has recently attracted the interest of CSF cancer researcher. Other tools for cancer cell detection in the CSF Measuring the chromosomal content of cancer cells in the CSF, using DNA single cell cytometry techniques or fluorescence in-situ hybridization that detects genetic aberrations as a sign of malignancy, can also give additional diagnostic information to CSF analysis, but still has a low sensitivity

Table 2. PCR can also establish cancer diagnosis when cytology is inconclusive, but the genetic alteration of the neoplasia must be known for it to be amplified with this technique, and this is generally not the case. Recent studies have shown that specific proteomic patterns can differentiate subtypes or grades of human brain tumors. However, the majority of these markers exhibited limited value in a clinical setting, justifying the need for the exploration of more clinically relevant sampling sources. For example the CSF level of carcinoembryonic antigen CEA , is a protein tumor marker that is commonly increased in several human malignances, was found recently to play an important role in differential diagnosis of primary and metastatic brain tumors[34 , 35] and useful auxiliary marker in diagnosis of meningeal carcinomas. The most significant example of how analysis of CSF proteins has impacted the clinical management of CNS cancer is in the case of intracranial malignant germ cell tumors. Germ cell tumors retain the molecular characteristics of their primordial lineage as they maintain the expression of embryonic proteins, such as beta human chorionic gonadotropin bHCG and alpha-fetoprotein AFP. AFP is elevated in wide range of cancers, including colon adenocarcinoma, liver and gastric cancers while bHCG and AFP were found to be markedly elevated in the CSF of intracranial malignant germ cell tumor patients. Moreover, the verification of bHCG and AFP levels prior to surgical resection provides a reference point that can be used to assess recurrence during follow-up however their absence does not rule out a germ cell tumor. Additional CSF protein markers such as placental alkaline phosphatase PLAP and lactate dehydrogenase isoenzymes have been shown to be clinically useful in the diagnosis and monitoring of pediatric intracranial germinomas, however such markers are less specific. Gliomas are the most common primary brain tumors in adults. Glioblastoma multiforme GBM is the deadliest glioma with a median survival of only 14 months despite the recent advances in intensive therapeutic strategies. Fang Shen et al. Further functional assessments revealed several important protein networks e. On the same theme, Khwaja et al. By performing retrospective analyses on 60 samples derived from astrocytomas WHO grade II, III, and IV, schwannomas, metastastic brain tumors, inflammatory samples, and non-neoplastic controls, the group identified potential tumor-specific markers of which 20 were high-grade astrocytoma-specific. The levels of VEGF were significantly higher in high-grade astrocytomas than in nonastrocytic tumors indicating that detection of VEGF in CSF could be a potential marker for differentiating astrocytic from nonastrocytic tumors. They were specific C-terminal fragments of alphaantichymotrypsin, osteopontin, and transthyretin as well as N-terminal residue of albumin. To detect biomarkers in high-grade astrocytomas, Ohnishi et al. The authors found that the expression of gelsolin protein is decreased with histological grade. To examine whether gelsolin is a useful indicator of tumor aggressiveness the group further analysed the gelsolin expression in 41FFPE astrocytomas. Gelsolin expression was found to be significantly lower in high-grade than in low-grade astrocytomas. Moreover the overall survival of patients in the low-gelsolin expression was significantly poorer than in the high expression group highlighting the usefulness of gelsolin as a potential prognostic factor in astrocytoma. Diffuse intrinsic pontine glioma DIPG is not surgically resectable, resulting in a paucity of tissue available for molecular studies and, currently, there are no effective treatments. Protein profiling was generated by mass spectrometry. Protein expression was further validated with Western blot analysis and immunohistochemical assays using CSF and brain tissue as well as in blood samples from DIPG. Primary central nervous system lymphoma PCNSL is another highly aggressive tumor that can lead to quick death if not diagnosed in time. It relies on histopathology of brain biopsies to the same extent as most brain tumors, while less invasive tests to detect early tumor pathogens with sufficient diagnostic accuracy are not available yet. ATIII levels higher than 1. However and on the contrary a recent study from Finland, by Kuusisto et al. Their result demonstrated that elevated CXCL13 concentration in CSF is a highly specific marker for the detection of CNS lymphoma and can be helpful as an adjunctive diagnostic test and response to treatment assessment. Medulloblastoma MB is the most common malignant brain tumor in children. It includes various subtypes with group 3 and 4 subtypes being clinically distinct with regard to metastasis and prognosis, which may also manifest in a difference in their proteomic spectra. In their study levels of prostaglandin D2 synthase PGD2S were found to be six-fold significantly decreased in the CSF of tumor samples most likely representing a host response to the presence of the tumor. On the other hand it has to be said that while negative biomarkers are potentially useful, their relationship to tumor biology is less

direct and more highly complex in comparison to proteins that are over-expressed in tumor associated samples. In their study the CSF proteomics demonstrated the potential biomarker role of the hemoglobin subunit beta fragments peptides LVV- and VV-hemorphin-7 in posterior cranial fossa pediatric brain tumors. Their data suggest that analysis in post-surgery CSF could be used to predict patient prognosis. Finally levels of polysialic-neural cell adhesion molecule PSANCAM , considered a marker of developing neuron, were found to be significantly higher in CSF from MB patients that are refractory to treatment or those who relapsed, than patients in remission. Clinical studies identified OPN as a potential diagnostic marker in ovarian, breast, colon, prostate, and lung cancers. MiRNAs have been found to stably coexist in several body fluids including CSF which can be collected with minimal invasiveness and permit following the disease over time. While Teplyuk et al. The paucity of biomarkers represents a sizable gap in improving the clinical management of these patients. An earlier work by Baraniskin et al. In the same theme, Scott et al. Twenty three studies with a total of CNS cancer patients and controls were analyzed by Wei et al. However, further validation based on a larger sample of patients and controls is still required. Interestingly, three metastasis-associated miRNAs were over-represented in culture-medium of metastasis-related MB cell lines were found to be significantly enriched in the CSF of the MB patient. Although more samples are required to fully verify these results, our work presented the first evidence for the presence of miRNAs excreted extracellularly by MB cells and raises the possibility that investigations, using larger sets of MB samples, could lead in the near future to the discovery of CSF-derived miRNA markers, with diagnostic and prognostic significance. How near are we to using CSF molecular markers for brain cancer diagnosis in the clinic? The promise of CSF biochemical markers Table 3, such as proteins and miRNA, to detect and monitor brain cancer has swept through the oncology research area in recent years leading to ample publications. However, most putative markers did not progress beyond their initial discovery. A striking discrepancy exists between the effort directed toward CSF biomarker, whether it is protein or miRNA, discovery and the number of markers that made it into clinical practice. One of the confounding issues that participate in the failure of potential markers to reach the clinic is the lack of reproducibility between similar studies or low correlation of results. No wonder there is often a low correlation of results obtained from different platforms or even from the same labs using kits and reagents from different vendors. Yet there are no universally implemented guidelines. Hence standardization of these assays including CSF handling collection, storage and preparation is a challenge for the near future. Together with low sample numbers that usually result in inadequate statistical power is another general weakness and might explain why not many of these markers have been validated for clinical use. Finally there are some other limitations to the interpretation of CSF cancer related molecules studies as biomarker. It is easily accessible by minimally-invasive standard clinical methods and can provide the necessary biological information for the diagnosis of neurological diseases. Biochemical molecules secreted by brain cancers to the CSF hold great promise as diagnostic markers for a wide range of brain malignancies owing to the significant differences that have been reported between their expression profiles in healthy individuals and those of patients. However, significant concerns remain. Despite the sizeable published number of potential diagnostic and prognostic CSF biochemical markers their reproducibility between studies is unclear, and none have been validated for clinical use. The reported sample size in the literature is small. Most data were generated by a limited number of research groups using different protocols or technologies. No universally implemented guidelines are available yet for the CSF sample collection and preparation or for protein profiling or miRNA extraction from CSF and importantly for data analysis. It is therefore premature to make specific recommendations for their clinical implementation. The road from CSF biomarker discovery, validation, until the translation into the clinical setting could be long and difficult however, the reward for patients, clinicians and scientists could be rather significant. Financial support and sponsorship.

Chapter 3 : Immunosignaturing Can Detect Products from Molecular Markers in Brain Cancer

Childhood brain tumors are a diverse group of diseases characterized by the abnormal growth of tissue contained within the skull. Other than leukemia and lymphoma, brain tumors are the most common type of neoplasms that occur in children.

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 4 : Brain tumor - Wikipedia

The discovery of these molecular "fingerprints" or markers over the last two decades has generated renewed interest in the classification of brain tumors. In , revisions to the classification system of brain tumors incorporated molecular findings in brain tumor diagnosis.

Colin Watts A chemical that highlights tumor cells has been used by surgeons to help spot and safely remove brain cancer in a trial presented at the NCRI Cancer Conference. The research was carried out with patients who had suspected glioma, the disease that killed Dame Tessa Jowell, and the most common form of brain cancer. Treatment usually involves surgery to remove as much of the cancer as possible, but it can be challenging for surgeons to identify all of the cancer cells while avoiding healthy brain tissue. Researchers say that using the fluorescent marker helps surgeons to distinguish the most aggressive cancer cells from other brain tissue and they hope this will ultimately improve patient survival. Many patients are treated with surgery and the aim is to safely remove as much of the cancer as possible. And we can plan further treatment, such as radiotherapy or chemotherapy, based on that diagnosis. Previous research shows that, when consumed, 5-ALA accumulates in fast growing cancer cells and this means it can act as a fluorescent marker of high-grade cells. They were aged between 23 and 77 years, with an average median age of 59 years. Before surgery to remove their brain tumors, each patient was given a drink containing 5-ALA. A total of 99 patients received the 5-ALA marker and could be assessed for signs of fluorescence. During their operations, surgeons reported seeing fluorescence in 85 patients and 81 of these were subsequently confirmed by pathologists to have high-grade disease, one was found to have low-grade disease and three could not be assessed. In the 14 patients where surgeons did not see any fluorescence, only seven tumors could be subsequently evaluated by pathology but in all these cases, low-grade disease was confirmed. This is the first prospective trial to show the benefits of using 5-ALA to improve the accuracy of diagnosing high-grade glioma during surgery. These results show that the marker is very good at indicating the presence and location of high-grade cancer cells. They say that other types of markers may need to be tested for detecting low-grade glioma cells. Next steps could include testing the 5-ALA in children with brain tumors, or to help surgeons distinguish between tumor tissue and scar tissue in adult patients whose brain cancers have recurred following treatment. In treating cancer, we are trying to improve survival by tailoring treatments to each individual patient. This technique provides on-the-spot information to help surgeons tailor the operation according to the location, size, and grade of the tumor. We know that patients who have near total removal of their tumor have better outcomes, so we are optimistic that, in the long term, these new data will help to increase survival times for glioma patients. Click here to subscribe to free newsletters from Lab Manager.

Chapter 5 : Targeting cerebrospinal fluid for discovery of brain cancer biomarkers

Molecular Markers of Brain Tumor Cells Implications for Diagnosis, Prognosis and Anti-Neoplastic Biological Therapy by Bela Bodey Department of Pathology and Laboratory Medicine.

Published online Jul Coons Find articles by Stephen W. Conceived the principal of immunosignaturing: Received Feb 15; Accepted Jun 6. Copyright Hughes et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are properly credited. This article has been cited by other articles in PMC. Abstract Immunosignaturing shows promise as a general approach to diagnosis. Here we test whether immunosignatures correspond to clinical classifications of disease using samples from people with brain tumors. Because samples were taken prior to adjuvant therapy, they are unlikely to be perturbed by non-cancer related affects. The immunosignaturing platform distinguished not only brain cancer from controls, but also pathologically important features about the tumor including type, grade, and the presence or absence of O6-methyl-guanine-DNA methyltransferase methylation promoter MGMT , an important biomarker that predicts response to temozolomide in Glioblastoma multiformae patients. Introduction The identification of biomarkers for presymptomatic detection of disease and classification of existing disease states could provide a rapid and inexpensive adjunct to standard pathological diagnosis. Researchers continue to search for blood-borne protein biomarker s for detection of cancer, but sensitivity remains stubbornly low [1] , [2]. Immune surveillance, however, occurs continuously and is quite sensitive to changes antigen profiles [3] , [4] , [5] , [6] , [7]. It has been demonstrated that cancer cells elicit a detectable humoral immune response [6] , [7]. Antibodies make excellent biomarkers because they are stable in serum, have high specificity and affinity to their cognate antigen, are abundant, and enable retrospective studies. Antibody-based biomarkers avoid the dilution problem seen with proteomic biomarkers [13] , [14] and in are not only highly abundant but can be physically captured at nano- and picomolar affinities. Further, unpurified antibodies are stable, allowing archival samples to be used for testing where RNA or proteins may have degraded [15]. The major impediment to using antibodies as biomarkers has been our inability to deconvolve the dense information contained in antibodies as they exist in a complex milieu [16]. Fingerprinting cancer antibodies has worked in the past [17] , [18] but this has been an onerous task. We introduced immunosignaturing as a simple and very inexpensive approach to diagnostics. Here we address whether immunosignatures are correlated to biological or clinical classifications. Cancer cells may elicit the production of antibodies against self-antigens or against neo-antigens [3] , [18] , [19] , [20] , [21] , [22] , [23] , [24]. We have no a priori way to determine exactly what profile of antigens will be presented by a cancer cell although analysis of EST libraries may suggest candidates. Thus, creating an epitope or protein microarray capable of detecting cancer-specific antigens would be difficult. Although phage display has been shown to detect antibodies specific to cancer [17] , [18] , [25] , for a number of technical and practical reasons panning is not amenable as a diagnostic tool. We created a single-use microarray composed of 10, different random-sequence peptides. We use 20mer peptides that incorporate all possible amino acids, except cysteine which we use as a linker. These 20mers can contain at least 7 typical-sized epitopes. Phage display and epitope microarrays tend to use shorter peptides to prevent cross-talk and maintain specificity; in our case, longer peptides allow us to extend the complexity of our microarray which has comparatively few features. Also, the arrays exhibit extremely high reproducibility so that even small differences in binding between antibody and peptide can be significant. The peptides are printed at very high density, an important consideration when using random peptides to detect antibodies that bind at micromolar or even millimolar affinities [26]. The density of these random-sequence peptides on the surface of the microarray creates an avidity-like affect where the off-rate is slowed by several orders of magnitude, enhancing the weak but reproducible interactions between antibody and the peptide. Patterns become detectable, and are so reproducible that sub-classification of diseases is feasible. Although the array has an effective many-to-many relationship between antibody and peptide, the patterns produced are by no means monotonic; in fact they are quite distinguishable from disease to disease.

We asked whether antibodies raised against cancer cells might be related to, or serve as a proxy for, clinically useful disease biomarkers. To answer the question, we focused on malignant brain tumors. Although the incidence of brain cancer is relatively low compared to other cancers like breast and lung, Glioblastoma multiformae GBM is one of the most deadly and aggressive tumors with peaks of incidence in both younger and older populations [31] , [32]. Malignant tumors may also arise from the oligodendrocytes and are considered low grade oligodendroglioma grade II and anaplastic oligodendroglioma grade III. There are also mixed oligoastrocytomas low grade and anaplastic. Menigiomas arise from the arachnoid cells that cover the brain and are typically benign, but can recur. A small percentage of these may progress to higher grades that are more invasive. In fact, patients with any of the tumor types mentioned may present with a high grade tumor initially, or they may progress over time. While the diagnosis of some of these tumors may be relatively straightforward, such is not always the case [33] , [34]. Neuropathologists are faced with the challenge of making consistent calls â€” a non-subjective biomarker panel that can distinguish between these different types and grades of brain tumors would be very useful in eliminating lab-to-lab variance. In this paper we present data that illustrates the performance of our immunosignaturing platform for identifying a variety of brain tumor types and subtypes. First, we tested the hypothesis that an autoimmune response occurs in patients suffering from brain cancer. After controlling for the false discovery rate, no significant reactivity to any protein on the ProtoArray was seen, either for the healthy controls or the cancer patients. Given this, we asked whether cancer was detectable at all on our peptide microarray, and whether different cancer types produced distinct patterns of binding. We conclude that the GBM brain cancer samples have immunosignature patterns distinguishable from other diseases.

Chapter 6 : At Brain Tumor Diagnosis: Glossary

Add tags for "Molecular markers of brain tumor cells: implications for diagnosis, prognosis and anti-neoplastic biological therapy". Be the first. Similar Items.

These two types are equally numerous in the brain as a whole, although glial cells outnumber neurons roughly 4 to 1 in the cerebral cortex. Glia come in several types, which perform a number of critical functions, including structural support, metabolic support, insulation, and guidance of development. Primary tumors of the glial cells are called gliomas and often are malignant by the time they are diagnosed. Spinal cord and other tissues[edit] The pons in the brainstem is a specific region that consists of myelinated axons much like the spinal cord. The thalamus and hypothalamus of the diencephalon also consist of neuron and glial cell tissue with the hypophysis pituitary gland and pineal gland which is glandular tissue attached at the bottom; tumors of the pituitary and pineal gland are often benign. The medulla oblongata is at the start of the spinal cord and is composed mainly of neuron tissue enveloped in oligodendrocytes and meninges tissue. The spinal cord is made up of bundles of these axons. Glial cells such as Schwann cells in the periphery or, within the cord itself, oligodendrocytes , wrap themselves around the axon, thus promoting faster transmission of electrical signals and also providing for general maintenance of the environment surrounding the cord, in part by shuttling different compounds around in response to injury or other stimulus. Diagnosis[edit] A posterior fossa tumor leading to mass effect and midline shift Most of the brain is separated from the blood by the blood-brain barrier BBB , which exerts a restrictive control as to which substances are allowed to pass. Therefore, many tracers that reach tumors in the body very easily would only reach brain tumors once there is a disruption of the BBB. Thus the disruption of the BBB, which can be detected by MRI and CT, is regarded as the main diagnostic indicator for malignant gliomas, meningiomas, and brain metastases. Brain tumors have similar characteristics and obstacles when it comes to diagnosis and therapy with tumors located elsewhere in the body. However, they create specific issues that follow closely to the properties of the organ they are in. Clinical and laboratory investigations will serve to exclude infections as the cause of the symptoms. Examinations in this stage may include the eyes, otolaryngological or ENT and electrophysiological exams. The use of electroencephalography EEG often plays a role in the diagnosis of brain tumors. Swelling or obstruction of the passage of cerebrospinal fluid CSF from the brain may cause early signs of increased intracranial pressure which translates clinically into headaches , vomiting , or an altered state of consciousness , and in children changes to the diameter of the skull and bulging of the fontanelles. More complex symptoms such as endocrine dysfunctions should alarm doctors not to exclude brain tumors. A bilateral temporal visual field defect due to compression of the optic chiasm or dilation of the pupil, and the occurrence of either slowly evolving or the sudden onset of focal neurologic symptoms , such as cognitive and behavioral impairment including impaired judgment, memory loss, lack of recognition, spatial orientation disorders , personality or emotional changes, hemiparesis , hypoesthesia , aphasia , ataxia , visual field impairment, impaired sense of smell, impaired hearing, facial paralysis , double vision , or more severe symptoms such as tremors , paralysis on one side of the body hemiplegia , or epileptic seizures in a patient with a negative history for epilepsy, should raise the possibility of a brain tumor. Imaging[edit] CT scan of a brain tumor, with its diameters marked as an X. There is hypoattenuating dark peritumoral edema in the surrounding white matter, with a "finger-like" spread. Medical imaging plays a central role in the diagnosis of brain tumors. Neoplasms will often show as differently colored masses also referred to as processes in CT or MRI results. Benign brain tumors often show up as hypodense darker than brain tissue mass lesions on CT scans. On MRI, they appear either hypodense or isointense same intensity as brain tissue on T1-weighted scans, or hyperintense brighter than brain tissue on T2-weighted MRI, although the appearance is variable. Contrast agent uptake, sometimes in characteristic patterns, can be demonstrated on either CT or MRI scans in most malignant primary and metastatic brain tumors. Pressure areas where the brain tissue has been compressed by a tumor also appear hyperintense on T2-weighted scans and might indicate the presence a diffuse neoplasm due to an unclear outline. Swelling around the tumor known as peritumoral edema can also show a similar result. This is

because these tumors disrupt the normal functioning of the BBB and lead to an increase in its permeability. However, it is not possible to diagnose high- versus low-grade gliomas based on enhancement pattern alone. The definitive diagnosis of brain tumor can only be confirmed by histological examination of tumor tissue samples obtained either by means of brain biopsy or open surgery. The histological examination is essential for determining the appropriate treatment and the correct prognosis. This examination, performed by a pathologist , typically has three stages: Micrograph of an oligodendroglioma , a type of brain cancer. Tumors have characteristics that allow determination of malignancy and how they will evolve, and determining these characteristics will allow the medical team to determine the management plan. Anaplastic cells have lost total control of their normal functions and many have deteriorated cell structures. Anaplastic cells often have abnormally high nuclear-to-cytoplasmic ratios, and many are multinucleated. Additionally, the nuclei of anaplastic cells are usually unnaturally shaped or oversized. Cells can become anaplastic in two ways: Significance of the abnormality is highly dependent on context. As such, neoplasia is not problematic but its consequences are: Increased intracranial pressure ICP may be attributable to the direct mass effect of the tumor, increased blood volume, or increased cerebrospinal fluid CSF volume, which may, in turn, have secondary symptoms. Necrotic cells send the wrong chemical signals which prevent phagocytes from disposing of the dead cells, leading to a buildup of dead tissue, cell debris and toxins at or near the site of the necrotic cells [27] Arterial and venous hypoxia , or the deprivation of adequate oxygen supply to certain areas of the brain, occurs when a tumor makes use of nearby blood vessels for its supply of blood and the neoplasm enters into competition for nutrients with the surrounding brain tissue. More generally a neoplasm may cause release of metabolic end products e. Classification[edit] Secondary brain tumors[edit] Secondary tumors of the brain are metastatic and have invaded the brain from cancers originating in other organs. This means that a cancerous neoplasm has developed in another organ elsewhere in the body and that cancer cells have leaked from that primary tumor and then entered the lymphatic system and blood vessels. They then circulate through the bloodstream, and are deposited in the brain. Secondary tumors of the brain are very common in the terminal phases of patients with an incurable metastasized cancer; the most common types of cancers that bring about secondary tumors of the brain are lung cancer , breast cancer , malignant melanoma , kidney cancer , and colon cancer in decreasing order of frequency. Secondary brain tumors are more common than primary ones; in the United States there are about , new cases every year. Secondary brain tumors are the most common cause of tumors in the intracranial cavity. The skull bone structure can also be subject to a neoplasm that by its very nature reduces the volume of the intracranial cavity, and can damage the brain. However, the definitions of malignant or benign neoplasms differ from those commonly used in other types of cancerous or non-cancerous neoplasms in the body. In cancers elsewhere in the body, three malignant properties differentiate benign tumors from malignant forms of cancer: Characteristics of malignant tumors include: Anaplastic cells display marked pleomorphism. The cell nuclei are characteristically extremely hyperchromatic darkly stained and enlarged; the nucleus might have the same size as the cytoplasm of the cell nuclear-cytoplasmic ratio may approach 1: Giant cells â€” considerably larger than their neighbors â€” may form and possess either one enormous nucleus or several nuclei syncytia. Anaplastic nuclei are variable and bizarre in size and shape. However, for clarity, the articles that follow adhere to a convention that they mean slightly different things; this convention is not followed outside these articles: Invasion or invasiveness is the spatial expansion of the tumor through uncontrolled mitosis, in the sense that the neoplasm invades the space occupied by adjacent tissue, thereby pushing the other tissue aside and eventually compressing the tissue. Often these tumors are associated with clearly outlined tumors in imaging. Infiltration is the behavior of the tumor either to grow microscopic tentacles that push into the surrounding tissue often making the outline of the tumor undefined or diffuse or to have tumor cells "seeded" into the tissue beyond the circumference of the tumorous mass; this does not mean that an infiltrative tumor does not take up space or does not compress the surrounding tissue as it grows, but an infiltrating neoplasm makes it difficult to say where the tumor ends and the healthy tissue starts. Of the above malignant characteristics, some elements do not apply to primary neoplasms of the brain: Primary brain tumors rarely metastasize to other organs; some forms of primary brain tumors can metastasize but will not spread outside the intracranial cavity or the central spinal canal. Due to the

BBB, cancerous cells of a primary neoplasm cannot enter the bloodstream and get carried to another location in the body. Occasional isolated case reports suggest spread of certain brain tumors outside the central nervous system, e. Of numerous grading systems in use for the classification of tumor of the central nervous system, the World Health Organization WHO grading system is commonly used for astrocytoma. Established in in an effort to eliminate confusion regarding diagnoses, the WHO system established a four-tiered histologic grading guideline for astrocytomas that assigns a grade from 1 to 4, with 1 being the least aggressive and 4 being the most aggressive. Types[edit] Tumors can be benign or malignant , can occur in different parts of the brain, and may be primary or secondary. A primary tumor is one that has started in the brain, as opposed to a metastatic tumor, which is something that has spread to the brain from another part of the body. The most common primary brain tumors are:

Chapter 7 : Fluorescent marker can help guide surgeons to remove dangerous brain tumor cells more accu

Molecular Markers Of Brain Tumor Cells (Hb) by Bodey B.. HARDCOVER. New. We Do not Ship APO FPO AND PO BOX.. Printing in English calendrierdelascience.com CD AND ACCESS CODE.

The top picture pink shows fluorescence, the bottom picture is not fluorescing. Colin Watts Glasgow, UK: A chemical that highlights tumour cells has been used by surgeons to help spot and safely remove brain cancer in a trial presented at the NCRI Cancer Conference. The research was carried out with patients who had suspected glioma, the disease that killed Dame Tessa Jowell, and the most common form of brain cancer. Treatment usually involves surgery to remove as much of the cancer as possible, but it can be challenging for surgeons to identify all of the cancer cells while avoiding healthy brain tissue. Researchers say that using the fluorescent marker helps surgeons to distinguish the most aggressive cancer cells from other brain tissue and they hope this will ultimately improve patient survival. Many patients are treated with surgery and the aim is to safely remove as much of the cancer as possible. And we can plan further treatment, such as radiotherapy or chemotherapy, based on that diagnosis. Previous research shows that, when consumed, 5-ALA accumulates in fast growing cancer cells and this means it can act as a fluorescent marker of high-grade cells. They were aged between 23 and 77 years, with an average median age of 59 years. Before surgery to remove their brain tumours, each patient was given a drink containing 5-ALA. A total of 99 patients received the 5-ALA marker and could be assessed for signs of fluorescence. During their operations, surgeons reported seeing fluorescence in 85 patients and 81 of these were subsequently confirmed by pathologists to have high-grade disease, one was found to have low-grade disease and three could not be assessed. In the 14 patients where surgeons did not see any fluorescence, only seven tumours could be subsequently evaluated by pathology but in all these cases, low-grade disease was confirmed. This is the first prospective trial to show the benefits of using 5-ALA to improve the accuracy of diagnosing high-grade glioma during surgery. These results show that the marker is very good at indicating the presence and location of high-grade cancer cells. They say that other types of markers may need to be tested for detecting low-grade glioma cells. Next steps could include testing the 5-ALA in children with brain tumours, or to help surgeons distinguish between tumour tissue and scar tissue in adult patients whose brain cancers have recurred following treatment. In treating cancer, we are trying to improve survival by tailoring treatments to each individual patient. This technique provides on-the-spot information to help surgeons tailor the operation according to the location, size and grade of the tumour. We know that patients who have near total removal of their tumour have better outcomes, so we are optimistic that, in the long term, these new data will help to increase survival times for glioma patients.