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Dna based diagnosis of genetic diseases pdf

A specialist using the ziasimphony, an automation platform for molecular diagnostic tests, Molecular Diagnostics is a set of methods used to analyze biological markers in the genome and proteome - the human genetic code and how their cells express their genes as proteins, applying molecular biology to medical testing. The technique is used to diagnose and monitor diseases, identify risk and decide which treatments will work best for individual patients. Analyzing the specifics of the patient and his illness, molecular diagnosis opens up the prospects of personalized medicine. These tests are useful in a number of medical specialties, including infectious diseases, oncology, human typing of the human white blood cell antigen (which investigates and predicts immune function), coagulation and pharmacogenomics - genetic prediction of which drugs will work best. They overlap with clinical chemistry (medical tests on bodily fluids). History Molecular Diagnostics uses techniques such as mass spectrometry and gene chips to capture the expression of genes and proteins The field of molecular biology grew in the late twentieth century, as did its clinical application. In 1980, Yuet Wai Kan et al. proposed a prenatal genetic test for thalassaemia, which relied not on DNA sequencing, but on infancy, but on enzyme limitations that cut out DNA, where they recognized specific short sequences, creating different lengths of strand DNA depending on what allele (genetic variation) the fruit possessed. In the 1980s, the phrase was used in the names of companies such as Molecular Diagnostics Incorporated and Bethesda Research Laboratories Molecular Diagnostics. In the 1990s, the identification of newly discovered genes and new DNA sequencing techniques led to a separate area of molecular and genomic laboratory medicine; in 1995, the Association of Molecular Pathology (AMP) was established to give it a structure. In 1999, AMP co-founded the Journal of Medical Diagnostics. In 2001, Informa Healthcare launched expert reviews in the field of medical diagnostics. Since 2002, the HapMap project has been aggregating information about single-forward genetic differences that are repeated in the human population - the only nucleotide polymorphism - and their links to the disease. In 2012, molecular diagnostic techniques of thalassaemia used genetic hybridization tests to identify specific single-aderous polymorphism that causes human disease. As the commercial application of molecular diagnostics becomes increasingly important, the debate on patenting genetic discovery is at the heart of the debate. In 1998, the European Union Directive 98/44/EC clarified that patents DNA sequences are valid. In 2010, in the United States, AMP sued Myriad Genetics to challenge the latter's patents against genes, BRCA1, BRCA2, which are associated with breast cancer. In 2013, the U.S. Supreme Court partially agreed with the decision that a naturally occurring gene sequence could not be patented. The methods of Affymetrix 5.0, a micro-array development chip from the research tools Industrialization of Molecular Biology tools have made it practical for their use in clinics. Miniaturization in a single portable device can bring medical diagnostics to the clinic and to the office or home. The clinical laboratory requires high standards of reliability; diagnosis may require accreditation or be subject to medical device rules. As of 2011, some U.S. clinical laboratories used tests sold for research only. Laboratory processes must comply with regulations such as the Clinical Laboratory Improvement Amendment, the Health Insurance Portability and Accountability Act, the Medical Laboratory Practice, and the specifications of the Food and Drug Administration in the United States. Information management lab systems help track these processes. The regulation applies to both staff and consumables. As of 2012, twelve U.S. states require the license of molecular pathologists; several boards such as the American Council of Medical Genetics and the American Pathology Council certify technologists, lab managers and directors. Automation and barcoding of samples maximize bandwidth and reduce the likelihood of error or contamination in manual processing and reporting of results. Individual devices for analysis from start to finish are now available. Analysis of the main articles: Analysis and biological analysis Of Molecular Diagnostics uses in vitro biological analyses such as PCR-ELISA or Fluorescence at the hybridization site. The analysis detects a molecule, often in low concentrations, that is a marker of disease or risk in a sample taken from the patient. Keeping the sample before analysis is crucial. Manual processing should be kept to a minimum. Fragile RNA molecule creates certain problems. As part of the cellular process of gene expression in the form of proteins, it offers a measure of gene expression, but it is vulnerable to hydrolysis and the breakdown of the constantly present enzymes of RANA. Samples can be frozen in liquid nitrogen or incubated in conservation agents. (h 39) Because molecular diagnostic techniques can detect sensitive markers, these tests are less intrusive than traditional biopsies. For example, since there are non-cell nucleic acids in human plasma, a simple blood sample may be sufficient to give genetic information

from tumors, transplants or future fetuses. Many but not all molecular diagnostic methods based on the detection of nucleic acids use polymerase chain reaction (PCR) to significantly increase the number of nucleic acid molecules, thereby strengthening the target sequence (s) in the Sample. PCR is a method that the DNA pattern is enhanced by synthetic primer, DNA polymerase, and dNTPs. The mixture cycled between at least 2 temperatures: a high temperature for the denaturation of double strands of DNA in single-jet molecules and low temperature for primer to hybridize the pattern and for polymerase to extend the primer. Each temperature cycle theoretically doubles the amount of target sequence. Detection of sequence variations using PCR usually involves the design and use of oligonucleotide reagents, which enhance the variant of interest more effectively than the sequence of wild type. PCR is now the most widely used method for detecting DNA sequences. The marker detection can be used by PCR in real time, direct sequencing, (ch 17) , micro-array chips - prefabricated chips that check many markers at the same time, (ch 24) or MALDI-TOF, the same principle applies to the proteom and genome. High-speed protein arrays can use additional DNA or antibodies to bind and therefore can detect many different proteins in parallel. Molecular diagnostic tests vary greatly in sensitivity, time, cost, scope and regulatory approval. They also vary in the level of verification used in the laboratories that use them. Thus, a robust local check-up is needed in accordance with regulatory requirements and the use of appropriate controls, especially where the result can be used to inform the patient treatment decision. The micro-array chip application contains additional DNA (cDNA) for many sequences of interest. CDNA fluoresce when it is hybridized with a corresponding DNA fragment in the sample. Prenatal See also: Category:Tests during pregnancy. Conventional prenatal tests for chromosomal abnormalities, such as Down syndrome, rely on analysis of the number and appearance of chromosomes - karyotype. Molecular diagnostic tests, such as micro-array comparative genomic hybridization dna sample testing, and because of cell-free DNA in plasma, may be less invasive, but according to 2013 data it is still an addition to conventional tests. Main treatment article: Pharmacogenomics Some of the only nucleotide polymorphisms of a patient - small differences in their DNA - can help predict how quickly they will metabolize specific drugs; it's called pharmacogenomics. For example, the enzyme CYP2C19 is absorbed by several drugs, such as the anti-clotting agent Clopidogrel, into their active forms. Some patients have polymorphisms in certain places on the 2C19 gene that make bad metabolizers of these drugs; Doctors can check for these and find out if the drugs will be fully effective for this patient. Advances in molecular biology have helped show that some syndromes that were previously classified as a single disease are actually multiple subtypes with fully causes and treatments. Molecular diagnostics can help diagnose subtypes such as infection and cancer, or genetic analysis of a disease with a hereditary component such as Silver-Russell syndrome. Infectious Diseases See also: Pathogenomics Molecular Diagnostics is used to detect infectious diseases such as chlamydia, influenza virus and tuberculosis; or specific strains such as the H1N1 virus. Genetic identification can be rapid; for example, a loop-ined isothermal amplification diagnoses the malaria parasite and is strong enough for developing countries. But despite these advances in genome analysis, infections are still more commonly identified by other means in 2013 - their proteome, bacteriophage or chromatographic profile. Molecular diagnostics are also used to understand a specific strain of the pathogen, for example, by identifying which genes of drug resistance it possesses, and therefore which treatments should be avoided. Disease Risk Management See also: Screening (medication) and genetic testing of the patient's genome may include an inherited or accidental mutation that affects the likelihood of developing the disease in the future. For example, Lynch syndrome is a genetic disease that predisposes patients to colorectal and other cancers; Early detection can lead to close monitoring, which increases the patient's chances of a good outcome. Cardiovascular risk is indicated by biological markers, and screening can measure the risk that a child will be born with a genetic condition such as cystic fibrosis. Genetic testing is ethically complex: patients may not want stress knowing their risk. In countries where there is no universal health care, a known risk can increase premiums. Cancer See also: Cancer cancer metaboloma cancer changes in cellular processes that cause the tumor to grow out of control. Cancer cells sometimes have mutations in oncogenes such as KRAS and CTNNB1 (K-catenin). Analysis of the molecular signature of cancer cells - DNA and its levels of expression using RNA messenger - allows doctors to characterize cancer and choose the best therapy for their patients. By 2010, the analyses, which include many antibodies against specific protein marker molecules, are a new technology; There are hopes for these multiplex analyses that could measure many markers at once. Other potential future biomarkers include microRNS molecules, which cancer cells express more than healthy ones. Cancer is a disease with excessive molecular causes and constant evolution. There's also the heterogeneity of the disease even in humans. Molecular studies of cancer have proven the importance of driver mutations in tumor growth and metastases. Many technologies for detection sequences have been developed for cancer cancer These technologies can usually be grouped into three approaches: polymerase chain reaction (PCR), hybridization and next-generation sequencing (NGS). Currently, many PCR and hybridization tests have been approved by the FDA as an in vitro diagnosis. However, NGS tests are still in the early stages of clinical diagnosis. To make a molecular diagnostic test for cancer, one of the important problems is the detection of variations in DNA sequence. Tumor biopsy samples used for diagnosis always contain only 5% of the target variant compared to the wild-type sequence. In addition, for non-invasive applications from peripheral blood or urine, the DNA test should be specific enough to detect mutations on the allele frequency variant of less than 0.1%. Currently, by optimizing traditional PCR, there is a new invention, the fire-resistant mutation system (ARMS) is a method for detecting VARIANTS of DNA sequence in cancer. Arms principle is that the enzymatic activity of dna polymerase enlargement is very sensitive to inconsistencies near the 3rd end of the primer. Many companies have developed diagnostic tests based on ARMS PCR primers. For example, Iagen therascreen, Roche cobas and Biomerieux THxID have developed FDA-approved PCR tests to detect lung, colon and metastatic melanoma mutations in the KRAS, EGFR and BRAF genes. Their IVD kits were mostly tested on genomic DNA extracted from FFPE tissue. There's also microarrays that use the hybridization mechanism to diagnose cancer. More than a million different probes can be synthesized on an array with Affymetrix's Genechip technology, with a detection limit of one to ten copies of mRNA per well. Optimized micro-arrays are generally considered to be a repeatable relative quantifying of different targets. Currently, the FDA has already approved a number of diagnostic tests using micro-array: Agendia's MammaPrint analyses can report the risk of breast cancer recurrence by profiling the expression of 70 genes associated with breast cancer; The analysis of ingetomics INFNITI CYP2C19 can profiling genetic polymorphisms, the effect of which on the therapeutic response to antidepressants is great; Affymetrix's CytoScan Dx can assess intellectual impairment and congenital disorders by analyzing chromosomal mutations. In the future, cancer diagnostic tools are likely to focus on next-generation sequencing (NGS). Using DNA and RNA sequencing to diagnose cancer, molecular diagnostic technologies will develop better. Although the bandwidth and price of NGS have dropped dramatically over the past 10 years by about 100 times, we are still at least 6 orders more from performing deep sequencing on the whole genome. Ion Torrent has now developed several ngS-based panels AmpliSeq, for example, OncoPrint Comprehensive Analysis. They focus on using deep sequencing of cancer-related genes to detect rare sequence variants. The molecular diagnostic tool can be used to assess cancer risk. For example, a BRCA1/2 test from Myriad Genetics rates women at lifetime risk of breast cancer. In addition, some cancers are not always used with obvious symptoms. It is useful to analyze people when they do not show obvious symptoms and thus can detect cancer at an early stage. For example, the ColoGuard test can be used to test people over 55 years of age for colorectal cancer. Cancer is a long-standing disease with various progression steps, molecular diagnostic tools can be used to predict the progression of cancer. For example, The OncoType Dx test from Genomic Health may assess the risk of breast cancer. Their technology can inform patients to seek chemotherapy when needed by studying levels of RNA expression in breast cancer biopsy tissue. With increased government support for molecular DNA diagnostics, an increasing number of DNA dna tests for cancer are expected to emerge soon. Currently, research into cancer diagnostics is developing rapidly with goals to reduce cost, less consumption time and simpler methods for doctors and patients. See also The Biology Portal Technology Portal Medicine Portal Molecular Medicine (wider field of molecular understanding of the disease) Molecular Pathology Laboratory developed pathogenesis test pathogenomics Pathology Precision Medicine Personalized Medicine Links - b c Poste G (May 2001). Molecular Diagnostics: A powerful new component of the health value chain. Expert review of molecular diagnostics. 1 (1): 1–5. doi:10.1586/14737159.1.1.1. 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