= Molecular diagnostics =

Molecular diagnostics is a collection of techniques used to analyse biological markers in the genome and proteome ? the individual 's genetic code and how their cells express their genes as proteins ? by applying molecular biology to medical testing . The technique is used to diagnose and monitor disease , detect risk , and decide which therapies will work best for individual patients .

By analysing the specifics of the patient and their disease , molecular diagnostics offers the prospect of personalised medicine .

These tests are useful in a range of medical specialisms , including infectious disease , oncology , human leukocyte antigen typing (which investigates and predicts immune function) , coagulation , and pharmacogenomics ? the genetic prediction of which drugs will work best . They overlap with clinical chemistry (medical tests on bodily fluids) .

= = History = =

The field of molecular biology grew in the late twentieth century , as did its clinical application . In 1980 , Yuet Wai Kan et al. suggested a prenatal genetic test for Thalassemia that did not rely upon DNA sequencing ? then in its infancy ? but on restriction enzymes that cut DNA where they recognised specific short sequences , creating different lengths of DNA strand depending on which allele (genetic variation) the fetus possessed . In the 1980s , the phrase was used in the names of companies such asMolecular Diagnostics Incorporated and Bethseda Research Laboraties Molecular Diagnostics .

During the 1990s , the identification of newly discovered genes and new techniques for DNA sequencing led to the appearance of a distinct field of molecular and genomic laboratory medicine ; in 1995 , the Association for Molecular Pathology (AMP) was formed to give it structure . In 1999 , the AMP co @-@ founded The Journal of Medical Diagnostics . Informa Healthcare launched Expert Reviews in Medical Diagnostics in 2001 . From 2002 onwards , the HapMap Project aggregated information on the one @-@ letter genetic differences that recur in the human population ? the single nucleotide polymorphisms ? and their relationship with disease . In 2012 , molecular diagnostic techniques for Thalassemia use genetic hybridization tests to identify the specific single nucleotide polymorphism causing an individual 's disease .

As the commercial application of molecular diagnostics has become more important , so has the debate about patenting of the genetic discoveries at its heart . In 1998 , the European Union 's Directive 98 / 44 / ECclarified that patents on DNA sequences were allowable . In 2010 in the US , AMP sued Myriad Genetics to challenge the latter 's patents regarding two genes , BRCA1 , BRCA2 , which are associated with breast cancer . In 2013 , the U.S. Supreme Court partially agreed , ruling that a naturally occurring gene sequence could not be patented .

= = Techniques = =

= = = Development from research tools = = =

The industrialisation of molecular biology assay tools has made it practical to use them in clinics . Miniaturisation into a single handheld device can bring medical diagnostics into the clinic and into the office or home . The clinical laboratory requires high standards of reliability ; diagnostics may require accreditation or fall under medical device regulations . As of 2011 , some US clinical laboratories nevertheless used assays sold for " research use only " .

Laboratory processes need to adhere to regulations , for example Clinical Laboratory Improvement Amendments , Health Insurance Portability and Accountability Act , Good Laboratory Practice , and Food and Drug Administration specifications in the United States . Laboratory Information Management Systems help by tracking these processes . Regulation applies to both staff and supplies . As of 2012 , twelve US states require molecular pathologists to be licensed ; several

boards such as the American Board of Medical Genetics and the American Board of Pathology certify technologists , supervisors , and laboratory directors .

Automation maximises throughput and reduces the possibility of error or contamination during manual handling . Single devices to do the assay from beginning to end are now available .

= = = Assays = = =

Molecular diagnostics uses biological assays such as PCR @-@ ELISA or Fluorescence in situ hybridization . The assay detects a molecule , often in low concentrations , that is a marker of disease or risk in a sample taken from a patient . Preservation of the sample before analysis is critical . Manual handling should be minimised . The fragile RNA molecule poses certain challenges . As part of the cellular process of expressing genes as proteins , it offers a measure of gene expression but it is vulnerable to hydrolysis and breakdown by ever @-@ present RNAse enzymes . Samples can be snap @-@ frozen in liquid nitrogen or incubated in preservation agents .

Because molecular diagnostics can detect slighter markers , it is less intrusive than a biopsy . For example , because cell @-@ free nucleic acids exist in human plasma , a simple blood sample can be enough to sample genetic information from tumours , transplants or an unborn fetus . Molecular diagnostics based on nucleic acids use polymerase chain reaction (PCR) to vastly increase the number of nucleic acid molecules and amplify the target . The detection of the marker might use real time PCR , direct sequencing , or microarray chips ? prefabricated chips that test many markers at once . The same principle applies to the proteome and the genome . High @-@ throughput protein arrays can use complementary DNA or antibodies to bind and hence can detect many different proteins in parallel .

= = Applications = =

= = = Prenatal = = =

Conventional prenatal tests for chromosomal abnormalities such as Down Syndrome rely on analysing the number and appearance of the chromosomes ? the karyotype . Molecular diagnostics tests such as microarray comparative genomic hybridisation test a sample of DNA instead , and because of cell @-@ free DNA in plasma , could be less invasive , but as of 2013 it is still an adjunct to the conventional tests .

= = = Treatment = = =

Some of a patient 's single nucleotide polymorphisms ? slight differences in their DNA ? can help predict how quickly they will metabolise particular drugs ; this is called pharmacogenomics . For example , the enzyme CYP2C19 metabolises several drugs , such as the anti @-@ clotting agent Clopidogrel , into their active forms . Some patients possess polymorphisms in specific places on the 2C19 gene that make poor metabolisers of those drugs ; physicians can test for these polymorphisms and find out whether the drugs will be fully effective for that patient . Advances in molecular biology have helped show that some syndromes that were previously classed as a single disease are actually multiple subtypes with entirely different causes and treatments . Molecular diagnostics can help diagnose the subtype ? for example of infections and cancers ? or the genetic analysis of a disease with an inherited component , such as Silver @-@ Russell syndrome .

= = = Infectious disease = = =

Molecular diagnostics are used to identify infectious diseases such as chlamydia , influenza virus and tuberculosis ; or specific strains such as H1N1 virus . Genetic identification can be swift ; for example a loop @-@ mediated isothermal amplification test diagnoses the malaria parasite and is

rugged enough for developing countries . But despite these advances in genome analysis , in 2013 infections are still more often identified by other means ? their proteome , bacteriophage , or chromatographic profile . Molecular diagnostics are also used to understand the specific strain of the pathogen ? for example by detecting which drug resistance genes it possesses ? and hence which therapies to avoid .

= = = Disease risk management = = =

A patient 's genome may include an inherited or random mutation which affects the probability of developing a 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 that improves 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 disease such as Cystic fibrosis . Genetic testing is ethically complex : patients may not want the stress of knowing their risk . In countries without universal healthcare , a known risk may raise insurance premiums .

= = = Cancer = = =

Cancer is a change in the cellular processes that cause a tumour to grow out of control . Cancerous cells sometimes have mutations in oncogenes , such as KRAS and CTNNB1 (? @-@ catenin) . Analysing the molecular signature of cancerous cells ? the DNA and its levels of expression via messenger RNA ? enables physicians to characterise the cancer and to choose the best therapy for their patients . As of 2010 , assays that incorporate an array of antibodies against specific protein marker molecules are an emerging technology ; there are hopes for these multiplex assays that could measure many markers at once . Other potential future biomarkers include micro RNA molecules , which cancerous cells express more of than healthy ones .