

PRENATAL DIAGNOSIS – MICROARRAY CGH

Worldwide, millions of individuals are affected by dominant or recessive genetic mutations. In order to avoid the transmission of severe pathogenic genetic variants and to enable early detection of genetic disorders, prenatal testing is offered.

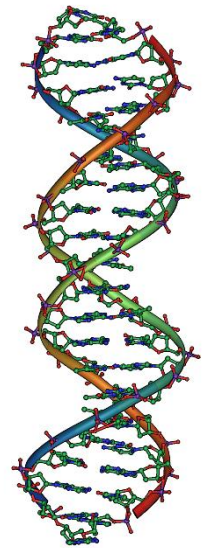
Parents who carry a genetic disease and who have a high risk of passing it on their child can decide consciously whether they want to carry on, or not, thanks to the prenatal tests.

There are many several prenatal techniques that can be used to discover to see whether there is a genetic disease or not.



Thanks to common screening procedures such as routine ultrasounds, blood tests and blood pressure measurement problems could be found among a large population.

Prenatal diagnosis is used to look whether there are genetic mutations or diseases or it could focus on pursuing additional detailed information once a particular problem has been found.



These are divided into two categories: Non-invasive or Invasive techniques

Non-invasive

Non-invasive procedures are used to detect general disease or deformations and don't have particular risk of abortions. The most popular ones are Rh safe and prenatal safe.

Rh safe is a blood test that will be used to determine the blood type and Rh factor, which determines the compatibility with the mother and her growing fetus. The blood can be either Rh-positive or Rh-negative, if a mother is found to be Rh-negative, her body will produce antibodies that will affect any subsequent pregnancies. When there's an Rh incompatibility, most women will be given a shot of Rh-immune globulin.

Prenatal safe is a recent technique that takes the DNA of free fetal cells (cffDNA) that are circulating in a very little amount in the mother's blood. During pregnancy the placenta leaks baby's DNA into the mother's bloodstream. As a result, the mother's blood contains a mixture of baby's and mother's DNA. This technique could be very useful because it doesn't create any risk of abortion but nowadays there are many difficulties to find and isolate them because the levels in the blood is too low.

Invasive techniques:

Common diagnosis procedures include amniocentesis and chorionic villus sampling.

Amniocentesis is an invasive method that extract some **amniotic fluid from the uterus and it** can be done between the 14th and 20th weeks gestation

Chorionic villus sampling, take a sample of the chorionic villus and it can be done earlier (between 9 and 12 weeks gestation)

The invasive techniques has 1% risk of causing abortion, but it's still recommended in particular to women over the age of 35 and women who have previously had premature babies or babies with a birth defect.

HOW CAN SCIENTISTS ANALYSIS THE FETAL DNA?

In order to analysis the fetal DNA several technologies have been invented and now are being developed. There are general or specific analysis that can use fast methods, so the result would be ready sooner, or slow methods which are very precise so microdeletions and micro mutations can be detected.



We can divide these techniques into:

- Traditional genetic ones: karyotyping
- Molecular genetic ones: Genetic screening such as microarray CGH and FISH

Now we want to examine what are microarrays and how do they work.

ARRAY CGH

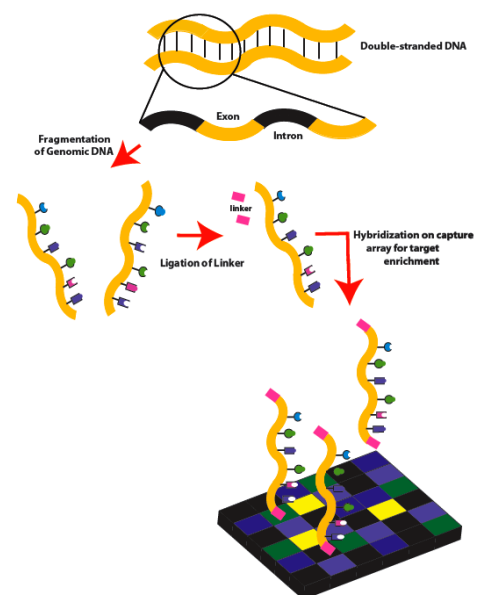
What is it?

Array CGH is a significant advance in technology that allows detection of chromosomes imbalances that are too small to be detected by looking down the microscope. Karyotyping is only as good as the resolution of a microscope and is not able to detect subtle chromosomes changes. These smaller alternations, often called submicroscopic alterations because they cannot be seen down the microscope, can still disrupt growth and development. These very small changes are often called microdeletions and micro-duplications. It compares the fetus DNA with a control DNA sample and identifies differences between the two sets of DNA. In this way deletions and duplications can be identified.

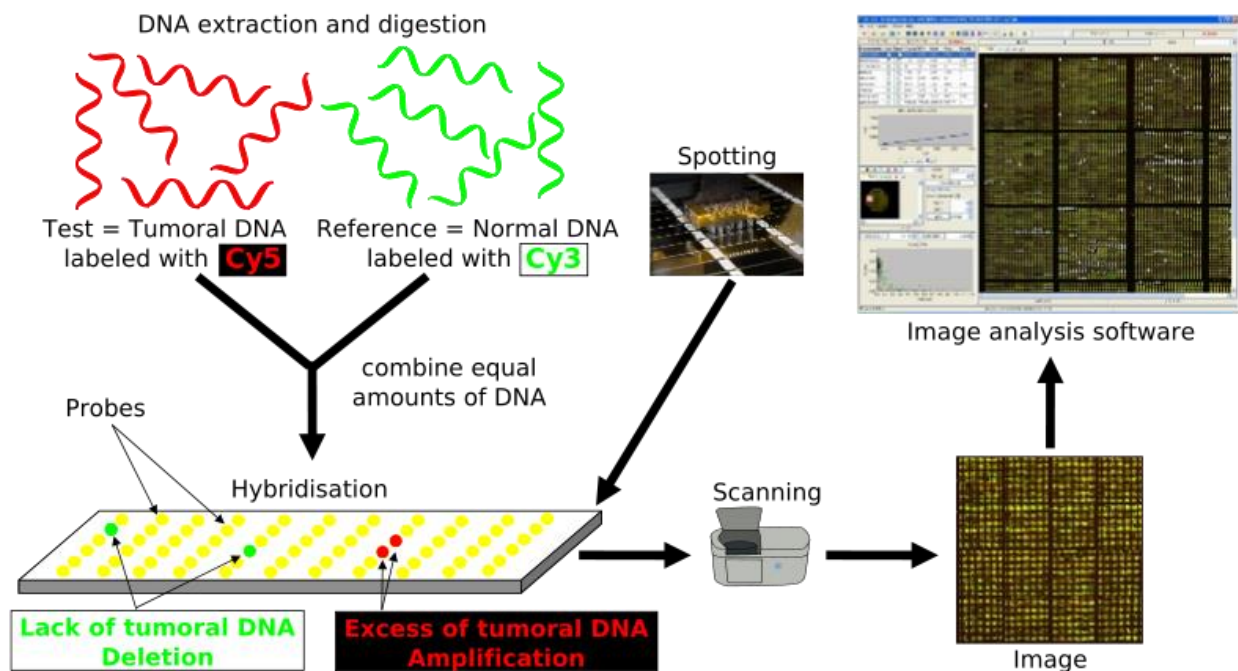
How does it work ?

A microarray works by exploiting the ability of a DNA molecule or strand to bind specifically to or hybridize to, another DNA molecule.

The microarray comprises tens of thousands of short sequences of DNA arranged in a precise grid on a glass slide called a chip. DNA from the patient is "digested" (chopped up into short lengths or fragments), then these fragments are labeled with a colored fluorescent dye. Reference DNA, from a person, or pool of people, with no genetic abnormalities, is labeled with a different colored fluorescent dye. The fluorescent dyes commonly used are red and green. Reference and patient samples are mixed together and applied to the chip and hybridization takes place- the fragments of DNA hybridize with their matching probes on the array. The chip is then scanned in a machine called a microarray scanner which measures the amount of red and green fluorescence on each probe.



The microarray scanner, together with computer analytical software, calculates the ratio of the red to green fluorescent dyes to determine whether, for the piece of DNA represented by each probe. The patient sample has the correct amount of DNA (shown as yellow), too much DNA (a duplication) which would be shown by too much red, or too little DNA (a deletion) shown by too much green.



CONCLUSION

ADVANTAGES:

- Ability to explore all 46 chromosomes in a single test and to detect any DNA imbalance including extra or missing chromosomes and loss or gain of chromosomes material.
- It may avoid your child having to undergo many other tests in order to discover a reason for your child's difficulties.
- Helps to predict what to expect as your child gets older
- When a specific chromosomes imbalance is diagnosed, the parents (and other family members) can be tested to see if they are carriers of changes in their DNA that put them at risk of having more children with a chromosome change.

LIMITATIONS:

- Balanced translocations and inversions (where chromosomes are inverted or reversed), will not be identified using array CGH.
- Genetic conditions are caused not only by chromosomes imbalances, but may also be caused by point(single base pair) changes, which it cannot detect these tiny changes.
- May identify chromosomes changes that are unrelated to your child's problems at the time of testing.

SOURCES:

<https://en.wikipedia.org/>

<https://www.healthline.com/health/pregnancy/prenatal-testing#first-trimester>

(sources from university genetics lessons)

<https://www.samaa.tv/health/2016/10/babies-should-sleep-in-parents-room-first-year-us-doctors/>

(picture 3)

<http://seeyourbaby4d.com/leftie-or-rightie-its-all-determined-in-the-womb/> (picture2)

https://commons.wikimedia.org/wiki/File:DNA_Overview_landscape_orientation.png (picture 1)

https://www.google.nl/imgres?imgurl=https%3A%2F%2Fupload.wikimedia.org%2Fwikipedia%2Fcommons%2Fthumb%2Fd%2Fd%2FArray-CGH_protocol.svg%2F2000px-Array-CGH_protocol.svg.png&imgrefurl=https%3A%2F%2Fcommons.wikimedia.org%2Fwiki%2FFile%3AArray-CGH_protocol.svg&docid=DaLljZD5gH75qM&tbnid=WWwGyoaCw0EbZM%3A&vet=10ahUKEwiRpp2085XZAhVDbVAKHcf8AfsQMwg9KAAwAA..i&w=2000&h=1069&bih=794&biw=1440&q=array%20cgh&ved=0ahUKEwiRpp2085XZAhVDbVAKHcf8AfsQMwg9KAAwAA&iact=mrc&uact=8

(picture 5)

https://commons.wikimedia.org/wiki/File:Exome_Sequencing_Workflow_1a.png (picture 4)