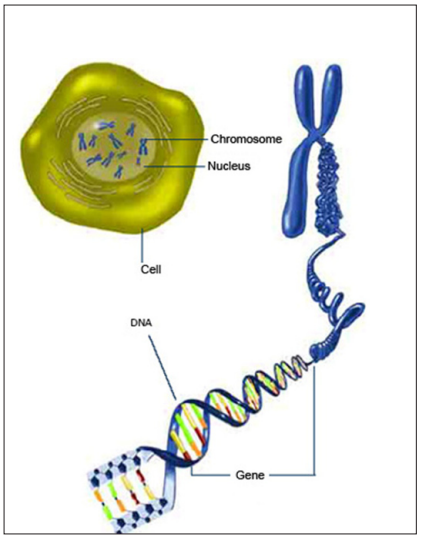
BCCGN
British Columbia Clinical Genomics Network

ARRAY COMPARATIVE GENOMIC HYBRIDIZATION

GENES 101

The 23 pairs of chromosomes in our genome contain approximately 30,000 genes. A gene is made up of a long molecule of double stranded DNA, which in turn is a nucleotide sequence consisting of a sugar molecule, a phosphate group and one of four bases (A=adenine, T=tyrosine, C=cytosine, or G=guanine). Each base pairs with its complementary base on the opposing strand. For example: A only pairs with T and G only pairs with C. Genes encode all the biological information that parents pass on to their children. Sometimes a mistake occurs that results in a large deletion, duplication or rearrangement of some of the genetic material such as a whole chromosome or part of a chromosome causing a genetic disorder. Often certain chromosomal regions are affected more than others.

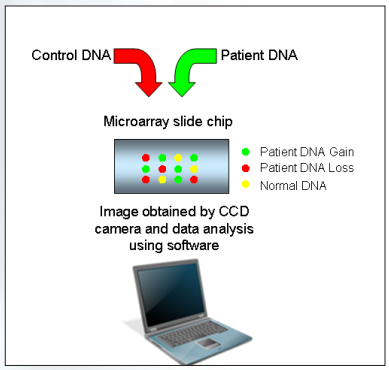


www./publications.nigms.nih.gov

WHAT IS ACGH?

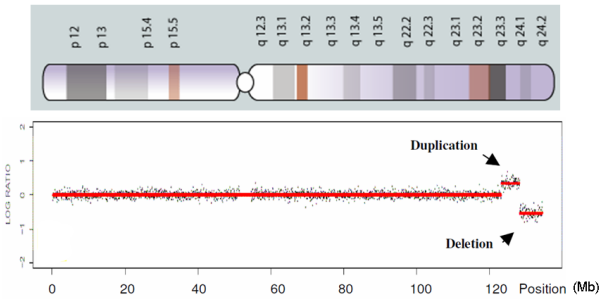
ACGH stands for Array Comparative Genomic Hybridization. This latest technological advance combines the technologies of DNA hybridization, high-throughput microarrays and advanced computing power to allow the detection of chromosome imbalances that are significantly smaller than those previously detected through routine microscopic analysis. Other names have also been used to describe this technology including "AGH" meaning Array Genomic Hybridization and "CMA" for Chromosomal Microarray Analysis.

HOW DOES IT WORK?



This technology is extremely versatile and can be used in a variety of ways. In general, a microarray slide or microchip is made containing thousands to millions of DNA fragments (or targets) covering the entire human genome. Alternatively, the array may be designed to probe specific regions in more detail and in this case DNA fragments from those regions would be enhanced on the chip. As a rule, the distance separating these fragments and their size and distribution in the genome, determines the resolution of the array. The more fragments there are tightly spaced across the genome or region, the higher the resolution of the microarray. Testing will only detect the loss (deletion) or gain (duplication) of chromosomal regions that are represented on the array.

Patient DNA and Control DNA are labelled separately with different coloured fluorescent dyes (red or green), then equal amounts are mixed together, applied onto the slide and allowed to combine (hybridize) with the attached DNA fragments. The amount of hybridization is measured by the amount and colour of light emitted from each spot. Computer analysis of the fluorescent signals allows us to read and interpret the findings. In the previous example, green fluorescence means there is a gain or excess of the patient's DNA fragment (green) relative to the control (red). Red fluorescence means there is a relative loss in the patient's DNA fragment. Yellow means there was the same amount of DNA in the fragments of both control and patient DNA samples and therefore no change in the copy number in the patient.
The figure on the right clearly shows a microdeletion and microduplication after analysis.



Data Source: Tyson, C. et al. Mol Cytogenet 2008 Nov 11;1(1):23

WHY IS IT SO USEFUL?

This method is highly sensitive to very small changes in genetic material. Using ACGH technology, we can detect microdeletions or microduplications 1/100th the size of those seen with conventional chromosomal analysis.

ACGH testing may be used to investigate microdeletions/microduplications in cases such as developmental delay/mental retardation, birth defects, autism and other conditions. Large scale studies have demonstrated that 10-20% of children with unexplained mental retardation, developmental delay, dysmorphic features or congenital anomalies/malformations have abnormalities detected through ACGH testing, a rate much higher than the 5-10% detectable by conventional cytogenetic analysis.

ACGH technology can be used to identify novel pathogenic changes in either a single affected family member or groups of unrelated individuals. Through research using this technology we can now identify the genetic basis for medical conditions that may be due to very subtle changes in genetic composition.

HOW CAN I GET INVOLVED?

If you are a clinician interested in genomic research please contact us for more information or visit our web site to submit a research proposal.

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