Comparative Genomic Hybridisation

Comparative Genomic Hybridisation (otherwise known as CGH) is a type of Fluorescence In Situ Hybridisation {FISH} technique that compares and measures differences in copy number changes between 2 DNA samples, the test and control sample, and also provides a map of chromosomal regions that are gained or lost

Advantages Of CGH

Comparative genomic hybridisation has allowed for:

- Visualisation of deletions and duplications in very small DNA segments (which is of high importance as these can occur in birth defect syndromes and in cancer)
- Searches of the whole genome without prior knowledge about the chromosomal aberration at hand
- Analysis without the need for specific probes
- The detection of the presence of amplified genes in cancer and map their location
- Unlike FISH, CGH is able to;

1. Identify the chromosome with the aberration 2. Identify the specific location from which the extra material originated

FISH is only able to identify the chromosome with the particular aberration

Disadvantages Of CGH

Some problems regarding the use of CGH have been found regarding :

- Inaccuracies in certain regions of chromosomes (in regions with high amounts of repeat sequences, centromeric regions of acrocentric chromosomes and in the telomeres of most chromosomes
- Copy number changes can only be spotted if more than 50% of cells analysed contain a chromosomal gain or loss
- Not been able to identify chromosomal abnormalities that are balanced
- Decreased sensitivity due to contamination of the test cells with normal cells

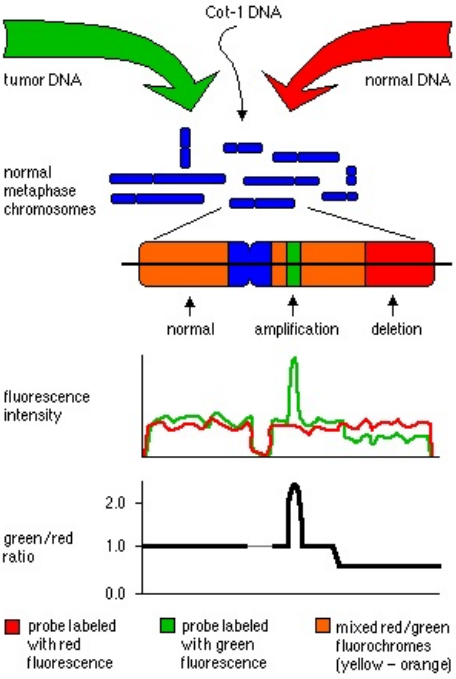
CGH Technique

1. **Preparation of Metaphase slides:** chromosomes in metaphase are used as the target DNA. Colchicine is then used to arrest cells in mitosis and the cells are then dropped onto slide in such a way that they are spread nicely and don’t overlap

2. **Extraction of Test and Reference DNA:** The test DNA is extracted from fresh/frozen bulk tissue or paraffin embedded tissue 3. **Labelling and Fragmentation Of Test and Reference DNA:** Is carried out by a process called Nick Translation where the Test and Reference DNA are labelled directly using different Fluorochromes -Test DNA produces a Green Fluorescence -Reference DNA produces a Red Fluorescence

4. **Hybridisation:** Equal amounts of the Test and Reference DNA labelled DNA compete to undergo complementary base pairing with specific sequences on metaphase spreads

5. **Use Of Fluorescence Microscopy & Digital Image Analysis:** The fluoresce ratio of Red – Green intensity is calculated in order to determine whether chromosomal Loss or Gain has occurred



Aplications Of CGH

CGH is currently being used in Cancer Research (as copy number alterations are of pathogenic importance in cancer) and in Clinical Genetics (to enhance diagnostic cytogenetics in diagnosing unbalanced chromosomal rearrangements)

Links

Related articles

[1] (http://en.wikipedia.org/wiki/Array_comparative_genomic_hybridization)

Bibliography

- Genetics In Medicine, Thompson & Thompson, 7th edition, Nussbaum, McInnes, Willard
- http://www.advalytix.com/advalytix/hybridization_330.htm
- http://www.sanger.ac.uk/about/press/2005/050404.html
- http://www.currentprotocols.com/protocol/hg0406
- http://www.nature.com/scitable/topicpage/microarray-based-comparative-genomic-hybridization-acgh-45432

Further reading

(Articles)

- Comparative Genomic Hybridisation, Contributed by Jane Bayani and Jeremy A. Squire,Princess Margaret Hospital and The Ontario Cancer Institute, University of Toronto,Toronto, Ontario, Canada
- Genome screening by comparative genomic hybridization, Farahnaz Forozan, Ritva Karhu,JuhaIA Kononen, Anne Kallioniemi, Olli-P Kallioniemi
- Cytogenetic analysis from DNA by comparative genomic hybridization, Gerard Tachdjian, Azzedine Aboura, Jean Michel Lapierre, Franck Viguie