Special Article

Role of Molecular Cytogenetics in Obstetrics

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Cytogenetics has become an important part of obstetric daily practice since prenatal diagnosis became feasible a few decades ago. Information of chromosome constitution of the fetus can be obtained through the prenatal diagnosis procedure. This consists of a collection of fetal samples such as chorion, amniocytes, or fetal blood and the laboratory analysis of chromosomes. However, this usually takes time for cell culture so that cells in metaphase are available for analysis and routine chromosome banding has limitation in resolution.

Molecular cytogenetics has lately been developed as a result of tremendous improvement in molecular genetics both in knowledge and laboratory technology. The first one to develop was probably FISH (fluorescent in situ hybridization). This technology has subsequently been modified to several techniques for more applications or better quality of chromosome analysis.

FISH involves hybridization of segment (s) of DNA of interest onto the sample[1-3]. The aforementioned DNA segment is named "probe". Probes are made to be specific for particular parts of particular chromosomes. They are then labeled with fluorescent dyes. When they are placed with the samples in certain conditions, they will hybridize to those particular parts of chromosomes. Signals from the labeled fluorescent dyes are then visualized under fluorescent microscope. If hybridized on to interphase cells, the number of signals of a particular probe can be count for number of DNA segment the probe represents in each cell. This allows for rapid diagnosis of numerical aberration of the studied chromosome in interphase cells as the sample can be analyzed without culture. This also has a tremendous benefit on preimplantation genetic diagnosis as the cell (s) biopsied from an embryo is in interphase. However, FISH has a drawback that not all chromosomes can be analyzed and structural anomalies will be missed. A full karyotyping is needed later if feasible[4-7].

Chromosome painting. Another modification of in situ hybridization technique is to identify a chromosome of interest on a sample. Sometimes parts of chromosome rearrangements are difficult to identified using conventional chromosome banding. The altered position of chromosomes in question can be determined using chromosome painting. Probes for the whole particular chromosomes are hybridized on to sample cells in metaphase to locate parts of the rearranged chromosomes.

Comparative Genomic Hybridization (CGH). All the previous techniques have a drawback of limited number of chromosomes that can be analyzed in a procedure due to limitation of fluorescent colors that can be used. CGH is one of the techniques that try to circumvent this limitation. Instead of probe labeling, the sample genome is labeled with a fluorescent color and a normal genome is labeled with another (for example, red against green). Both genomes are then hybridized to a standard metaphase and the ratio of the fluorescent intensity of both genomes from each chromosome can be analyzed using a computer program to see if there is any deletion or duplication of a chromosome or parts of chromosomes.

M-FISH, spectral karyotyping (SKY), multicolor FISH[8-9]. All these are analysis of all chromosomes simultaneously using different combination of available fluorescent dyes. The analysis needs a special computer program to visualize the subtle difference among each chromosome probe. The objective is to be able to analyze all chromosomes simultaneously, especially to identify chromosomes involved in chromosome rearrangement.

Therefore, molecular cytogenetics helps in some situations in obstetrics as follow:

1. in cases where rapid diagnosis for common trisomies is needed as a screening investigation such as in late prenatal diagnosis[10,11].

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2. in cases where parts of chromosomes or a chromosome marker could not be identified using conventional banding[10,12,13].

3. in cases of microdeletions or microduplications of chromosomes[10,12,14].

4. in cases where metaphase cannot be obtained such as in preimplantation genetic diagnosis[12].

However, as these techniques are very expensive and need expertise in the laboratory procedure, they are still not available as routine service and most are still in research refinement. Hopefully, with further development in other areas of prenatal sampling such as fetal cells in maternal circulation and preimplantation genetic diagnosis along with the laboratory technology, molecular cytogenetics will be more beneficial to obstetrics in the future.

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