GOOD CLINICAL PRACTICE RECOMMENDATIONS

CHROMOSOME, FISH & MOLECULAR KARYOTYPING / MICROARRAY ANALYSIS FOR CONSTITUTIONAL INVESTIGATIONS (POSTNATAL, PRENATAL, MISCARRIAGE)

(BeSHG Workgroup on Clinical Genetics, September 2011)

1. POSTNATAL CONSTITUTIONAL

Standard karyotyping (chromosome analysis)

- Clinically 'clear-cut' chromosomal disorders eg Down syndrome, Turner syndrome, Klinefelter syndrome, …
- Couples with recurrent miscarriages, Couples with idiopathic infertility/subfertility
- Gamete donors
- Parents (when prenatal karyotype is abnormal)
- Known chromosomal aberration in family/suspicion of a balanced translocation
- Aberration detected with molecular karyotyping, for which a standard karyotype could shed more light on the nature of the aberration eg marker chromosome, unbalanced translocation, …
- Suspicion of mosaïcism in an individual

Molecular karyotyping (various platforms; also known as micro-arrays)

- Intellectual disability/ autism/ dysmorphism/ Congenital Abnormalities/ neuropsychiatric disorders/neurology/
- Parents of individual with aberration detected with molecular karyotyping
- Refinement of an abnormal karyotype (eg. marker chromosome, deletion, (un)balanced translocation)

FISH (fluorescence *in situ* hybridization)

- Suspected mosaïcism in individual (Turner, Klinefelter, Pallister-Killian, …)
- Parental preparation for Pre-Implantation Genetic Diagnosis (PGD) for chromosome aberration
- Rapid analysis in a neonate with ambiguous genitalia, with suspicion of Down syndrome, trisomy 13/ 18, etc, …
- Clinically recognizable microdeletion disorders eg VCFS, Williams syndrome, ..
- As an additional tool to (molecular) karyotyping for confirmation and/or further delineation of a chromosomal aberration/ Testing of parents for balanced translocation

Chromosome breakage analysis

Suspected breakage disorderEg.Bloom, Fanconi, Nijmegen, ICF, Roberts, AT

Commenté [G1]: Should be more precisely defined for the guidelines

Mis en forme : Surlignage

Commenté [G2]: Is this not a separate item?

2. PRENATAL

Standard karyotyping + rapid screening (FISH/MLPA/QF-PCR)

- Elevated chromosomal aberration risk on 1st / 2nd trimester maternal blood screening
- Elevated chromosomal aberration risk on combined screening (nuchal translucency, soft markers,+blood)
- Advanced maternal age (≥35y)
- Chromosomal aberration in parent
- Previous pregnancy with chromosomal aberration
- A fetal abnormality on ultrasound
- ICSI pregnancies

Comment: Analysis on amniocytes is preferable to chorionic villi since there is a relative high risk for (confined) placental mosaicism in CVS samples. A chorionic villus sampling is recommended in high risk pregnancies eg echographic fetal abnormality, a parent with chromosome aberration or when molecular/ DNA diagnosis is planned.

Molecular karyotyping

- fetal abnormalities detected on ultrasound
- Refinement of a *de novo* structural chromosome aberration detected on standard karyotype (eg deletion, translocation, inversion, marker chromosome, additional chromosome material)
- Structural (cryptic) chromosomal aberration in sibling/parent

3. PREIMPLANTATION GENETIC DIAGNOSIS (PGD)

FISH or molecular karyotyping

- on blastomeres for chromosome aberration or sex-linked disorder in the parents

4. MISCARRIAGE/*MORS IN UTERO* MATERIAL

- Molecular karyotyping , or
- Standard karyotyping or
- MLPA/FISH

Commenté [G3]: Rather vague for a guideline…

5. REFERENCES

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