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Invited speakers
Comunicações por convite

CC-01
X-CHROMOSOME: GENETIC FRAMING

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In order to discuss such a vast subject as the "genetic framing of the X-chromosome in humans" it is mandatory to approach several topics, starting with the time-frame of mammalian evolution. For many years little importance was attributed to the understanding of the evolution (divergence) of the dimorphic X and Y chromosomes, sex determination in heterogametic XY species, in species without sex chromosomes and the accurate characterization of Y and X chromosomes *per se*.

However, with the advent of cytogenetics and molecular techniques, great advances have been achieved in the knowledge of X-inactivation and gene dosage compensation in order to equalize the gene dosage between the sexes and, possibly, also between sex chromosomes and autosomes. In a relatively short time the molecular mechanisms involved in X-inactivation as an epigenetic process have been elucidated and have enabled the scientific and medical improvement of X-linked conditions, wether dominant or recessive. These achievements were followed by other scientific advances that are now routine diagnostic tools: study of the gene *XIST* and the chromosome distribution of 158 IQ-related genes, the effect of sex chromosome gene dosage on brain structure, the genetic defects and genetic-environmental interactions associated with Alzheimer's disease, fragile-X syndrome, X-linked genes and miRNA sexual dimorphism, hemophilia, Duchenne muscular dystrophy, Turner and Klinefelter syndromes.

CC-02
X-IMBALANCES BIG AND SMALL

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The X chromosome is fascinating, but the clinical interpretation of X-chromosomal aberrations are often a challenge, in particular because of (possible) mosaicism and X-inactivation.

Various abnormalities involving X will be addressed in this lecture, including whole chromosome numerical abnormalities, supernumerary marker chromosomes, X-autosome translocations as well as recurrent and non-recurrent copy number variations. For many indications, molecular techniques such as QF-PCR and genome wide array analysis are nowadays often used to test the patient samples in prenatal and postnatal genome diagnostics. For the correct interpretation of these data, however, cytogenetic knowledge is necessary and often routine cytogenetic analysis and /or Fluorescence In Situ Hybridisation (FISH) is required to further characterise the X-chromosomal abnormality.

After doing the tests, it is crucial for the clinical laboratory geneticist to not only correctly use the existing nomenclature in the test report, but also to include a clear and concise explanation of what the test result means. The requesting clinician needs to understand the meaning of the laboratory findings and the underlying genetic mechanisms in order to be able to properly counsel the patient and the parents with regard to prognosis and recurrence risk.

A variety of illustrative case examples will be presented to address the aforementioned aspects, but most likely, some questions will remain unanswered.