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MEETING ABSTRACTS

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E-P01 Reproductive Genetics/Prenatal Genetics

E-P01.01
Parent of origin in familial 22q11.2 deletions impacts full scale intelligence quotient scores

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Background: Familial 22q11.2 deletions are thought to have a negative impact on mean Full Scale IQ scores (MFSIQ) in affected offspring, however, parent of origin (PO) effect has not been examined.

Methods: We compared MFSIQ on children of affected parents from Philadelphia (N=26) and Leuven (N=26), assessed using the age appropriate Wechsler Intelligence Scale, in those with familial v. *de novo* deletions and maternally v. paternally inherited familial deletions. We then compared this data to *de novo* cases where research based PO studies were completed (N=57) in NY.

Results: MFSIQ (66.4) for familial deletions was statistically lower (p = .01) than for *de novo* deletions (N=399, MFSIQ=76.2). MFSIQ for children with maternally inherited deletions (63.7) was statistically lower (p = .03) than for paternally inherited deletions (72.0). As compared with the NY cohort where the MFSIQ for maternal deletions (N=37, MFSIQ=73.41) was no different (p = 0.67) than paternal deletions (N=20, MFSIQ=75.2).

Conclusions: Our findings confirm the association of lower FSIQ scores in familial versus *de novo* 22q11.2 deletions. We also observed the novel association of lower MFSIQ scores in maternally v. paternally inherited familial deletions in contrast to *de novo* deletions where no difference was observed based on PO. Thus, a maternally inherited familial deletion is a significant risk factor for poorer cognitive outcome. Confounding factors could include maternal comorbidities, mitochondrial effects, epigenetics, assortative mating, socioeconomics, grandparental engagement, etc. to explain this finding. Regardless, this data serves as an important adjunct to traditional genetic counseling for women with 22q11.2DS in the prenatal and preconception setting.

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Laboratory evaluation of patients with developmental delay/ intellectual disability, congenital anomalies, dismorphic features and autistic disorders has changed significantly in the last years with the introduction of microarray technologies. Structural aberrations of chromosomes are associates with various syndromes, although there are a lot of chomosomal gains and losses that are not yet associated with a specific syndrome. Most of the cases are the novo, few cases are due to unbalanced rearraments and others are inherents. We present a three years-old boy derived from neuropediatric for genetics studies due to global developmental delay. He was bom at 38 gestation week from no consanguineous healthy parents. Karyotype in leucocites was normal (46;XY). Comparative Genomic Hybridization (CGH-Array) with the Nimblegen CGX Cytogenetic Microarrays platform, suplied by PerkinElmer, was performed for the patient and parents. The CGH- Array was normal en both parents, but the patient presented a delecction of 2,40 Mb in 18q22.1-q22.3 chromosomical region (arr[hg19] 18q22.1-q22.3 (66,375,444-68,773,023)x1 Abnormal Male). The duplication is "de novo" and no previously described. These delection have 11 genes included (5 OMIM) and then with a high pathologic probability. . Chromosomic aberrations detected "de novo" and no previously described can be dificult to determine his pathologic potential, and it is necesary to have in mind the patient pathology and genes involved in the delecction/ duplication . In our case we believe that the chromosomal alteration detected, alone or in conjuntion with another chromosomal or enviromental cause will be responsible of the patient pathology.

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E-P11.36
Distribution of the Common TERT and TP53 Variants in Down Syndrome Children

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Introduction: The phenotype spectrum of Down syndrome (DS) related with the trisomy of chromosome 21 has a multi system associated features, but the exact mechanism of these abnormalities are not fully explained to date. To understand the role of common variants of TERT and TP53 genes on the diversity of DS phenotype, the frequency of these two variants was aimed to be investigated. The TERT gene rs2736100 A-C intronic variant is known with its association with various morbidities. The TP53 gene codon 72 Arg>Pro variant is related with altered TP53 protein functions. Allele distributions of these common variants were assessed between DS and control children.

Materials and Methods: DS (n:80) and control (n:32) subjects were included in this study. TERT gene rs2736100 A-C intronic variant and TP53 gene p.Arg72Pro (c.C215G) variant was determined with melting analysis of hybridization probes.

Results: The allele frequency of TERT and TP53 variants were not different between DS and control groups, however allele frequencies were higher than that of the highest population level. The TERT variant distribution was similar in the control group of children with homozygous Pro72 variant or Arg72 variant carriers. The variant distribution of TERT, however, was significantly lower in DS group of children with homozygous Pro72 variant compared to Arg72 variant carriers.

Conclusion: Similar distribution of the common variants of TERT and TP53 genes are implying that these variants may contribute to DS phenotype by more complex associations.

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E-P11.37
Enamel-renal syndrome: identification of two novel non-consanguinous families with mutations in *FAM20A* gene

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Amelogenesis imperfecta forms a group of inherited conditions having in common a defect in dental enamel formation on primary and/or secondary dentitions. It can be isolated or syndromic. When associated with nephrocalcinosis, the condition is designated as « enamel-renal syndrome » or « amelogenesis imperfecta type IG » (OMIM 204690), and is consecutive to biallelic mutations of *FAM20A* gene. The encoding protein is involved in the manufacture and maturation of enamel. However, the mechanism explaining the renal damage remains unclear. Rare, this autosomal recessive condition is often observed in consanguineous families. We report on 2 new patients from distinct and non-consanguineous families. The first, 14-year-old, had amelogenesis imperfecta and nephrocalcinosis without impact on renal function, accidentally