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We present an ADOA Italian family with four related affected females. The purpose of this study was 2-fold: to determine the types and frequency of matations in OPA1 which caused ADOA in our family, and to determine whether a second condition, Leber's hereditary optic neuropathy with a similar pathology to ADOA, could also be caused by mutations in OPA1.
For this, initially we screened the proband and the family members for the 3460A, 11778A, and 14484C LHON mutations by PCR amplification followed by mutation-specific restriction endonuclease digestion, but this search was negative. The analysis of the entire coding region of the OPA1 gene by direct sequencing of PCR- amplified exons in all familial cases revealed four polymorphisms described previuosly : 473G in exon 4, 2109T in exon 21, +51G, and +25A. The molecular analysis of other asymptomatic members of family confirmed the same polymorphisms.
These data suggest that OPA1 gene is not involved in ADOA in our family.
Further studies are required to identify the causative ADOA gene in this family and to delineate the role of this locus.

P0102. The meiotic stage of chromosome 21 nondisjunction as indicated by STR polymorphic markers among Down Syndromes in Iran

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Down syndrome is one of the main causes of mental and growth retardation mainly happened due to chromosome 21 nondisjunction. This is the first study in Iran categorizing cases of Down syndromes by parental origin and stage of meiotic error of chromosome 21. We studied 224 families having a child with Down syndrome using conventional cytogenetic analysis and chromosome 21 specific STR markers (D21S11, D21S1414, D21S1440, D21S1411, D21S1412). Parental origin and stage of meiotic error were studied using five STR markers. Meiotic nondisjunction of chromosome 21 was studied in 202 cases with free chromosome 21. The parental origin and the meiotic stage of chromosome 21 nondisjunction were detected in 190 of cases. Parental origin of nondisjunctions were derived as 167 (88%) maternal and 23 (12%) paternal. In maternally derived cases, meiotic I nondisjunction was observed in 121 (64%) and meiosis II in 46 (24%) of cases whereas in paternally derived cases meiosis I was detected in 13 (7%) and meiosis II in 10 (5%) cases. There was no significant difference in the distribution of maternal ages between maternal meiosis I error versus maternal meiosis II error. It is unexpected that a nondisjunction at especial of maternal ages between maternal meiosis I error against maternal II error, related significantly to the rising incidence of Down syndrome with advancing maternal age. This data is usable in analysis of maternal and paternal genetic or environmental risk factors to understand better the cause of chromosome 21 trisomy.

P0103. The partial trisomy for the distal short arm of chromosome 6 (region pter→p21) in a girl with psychomotor development delay and dysmorphic features

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We report a girl presenting a de novo partial trisomy for the distal short arm of the chromosome 6. Our patient is a two-year-old girl, first child of healthy non consanguineous parents from complicated pregnancy with symptoms of miscarriage. The dysmorphic features were seen from the birth of this girl. Facial dysmorphism is characterized by a microcephaly, craniosynostosis, facial asymmetry, high, prominent forehead with depressed frontal bone on the right size, ocular hypertelorism, blepharophimosis/short palpebral fissures, ptosis, flat nasal root, very short nose, long philtrum, thin lips, small mouth, high arched palate, simple, low-set pinnae with poorly developed lobes and small chin. Unusual dermatoglyphic changes are identified on the girl's palms. The nipples are hypoplastic and abnormally placed from each other. There are expressed hirsutism on the pubic bone area. The short stature attends this partial trisomy.
Clinical follow-up showed these clinical findings: CT scan showed mild hydrocephaly, X-ray - dysplastic ribs with partially accretion. Cardiac ultrasonography showed stenosis of a. pulmonalis, dilatation right size of the heart. Renal abnormalities have included hypoplastic kidney with renal dysfunction.
In our patient we detected a de novo duplication of the short arm of chromosome 6 identified on a 400 band chromosomal analysis. Cytogenetic analysis was performed from GTG banded metaphases. The girl's karyotype was 46, XX, dup(6)(pter→p21). Parental karyotypes were normal.

P0104. Dystrophic epidermolysis bullosa pruriginosa in Italy: molecular characterization and pathogenetic aspects

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Dystrophic epidermolysis bullosa pruriginosa (DEB-Pr) is a rare variant of DEB due to COL7A1 dominant and recessive mutations which is characterized by severe itching and lichenoid or nodular prurigo-like lesions mainly involving the extremities. Less than 20 patients have been described showing variable disease expression and, frequently, delayed age of onset. We report the clinical and molecular characterization of 7 Italian DEB-Pr patients, 3 with recessive DEB-Pr (RDEB-Pr) and 4 with dominant DEB-Pr (DDEB-Pr). In all patients the signs were typical of a mild DEB phenotype, until the pruritus onset, after which the distinctive skin lesions of DEB-Pr appeared. Nine mutations were disclosed in COL7A1, 5 recessive and 4 dominant. These mutations allowed in all patients the production of a given amount of partially functional type VII collagen (COLLVII), detected at the dermal-epidermal junction (DEJ). Three mutations were novel, and one arose *de novo*. Furthermore, 2 unrelated RDEB-Pr patients were carrying the recurrent c.7344G>A Italian mutation and 2 unrelated DDEB-Pr patients were carrying 2 different mutations in intron 87, leading to the in frame skipping of exon 87. In order to find factors involved in the pathogenesis of DEB-Pr, we analysed the patients skin for the presence of Igs by direct immunofluorescence. In a patient IgG and C3 linear deposits along the DEJ were present, in another IgM deposits were detected in the same location. These results underline for the first time the possible involvement of immunological factors, likely an antibody-mediated autoimmune reaction, at least in some DEB-Pr patients.

P0105. The genetic causes of early onset hereditary hearing loss among Estonian children

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During last 6 years (2000-2005) 119 children with early onset hearing loss, as a main complaint, have been referred to genetic counseling. Eighty five percent of them had moderate to profound and 9% mild bilateral hearing loss (sensorineural, conductive or mixed); 6% of patients had unspecified hearing loss.
Careful clinical investigation was performed in all of them for excluding syndromic hereditary impaired hearing (HIH). Since 1999 we have investigated 35delG mutation in *GJB2* gene, which encodes the gap junction protein connexin-26. Since 2005 we have investigated the genotype of the children with HIH by arrayed primer extension (APEX) method, which covers 201 mutations in 8 genes (6 nuclear genes: *GJB2,* Connexin-30, Connexin-31, Connexin-43, Prestin and Pendrin gene, and 2 mitochondrial genes: 12S-ribonuclear-RNA and the transfer RNA for serine gene).
Thirty eight patients (32%) were homozygous for 35delG mutation in *GJB2* gene, 15 (13%) were heterozygous for 35delG mutation, and in 9 of them the mutation in the second allele has already been identified (35delG/R143W, 35delG/167delT, 35delG/M34T, 35delG/