more precise detection.
Results: A total of 252 cases (1.93%) showed these chromosomal alterations. Twenty one (0.16%) were inv(Y)(p11.2q11.2), fifteen (0.11%) inv(Y)(q11.2q12), one hundred thirty nine (1.06%) inv(9)(p11q12), forty four (0.34%) inv(3)(p11q11.2), nine (0.07%) inv(2)(p11.2q13), and twenty four (0.18%) inversions of other chromosomes.
Conclusion: Human inversion mutations occur at a low but detectable frequency. Although the number of inversions has been considered normal variants such as inv (9)(p11q12), we are trying to discuss the importance of this chromosomal rearrangement and its role on infertility or spontaneously abortions. Carriers of such inversions are at risk of producing abnormal gametes during meiosis that may lead to unbalanced offspring. Our data suggests that it's better for all couples with the same symptoms to have karyotype analysis on a parallel with their routine tests.

P03.034
Mosaic trisomy 1q and Fryns-like phenotype

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Fryns Syndrome is a lethal condition characterized by diaphragmatic hernia, coarse facial features, lung hypoplasia, cardiac defects, and the characteristic distal limb defects. Autosomal recessive inheritance has been suggested on the basis of occurrence in both sexes and recurrence in siblings with healthy parents. Cases with chromosomal abnormality have been reported with clinical findings very similar to Fryns syndrome. Duplication and or deletion of long arm of chromosome 1, and anomalies of chromosomes 15, 6 and 22 have been reported in cases with Fryns-like syndrome.
Herein, we reported a case of midtrimester fetus with multiple congenital anomalies. Prenatal ultra-sound at 21 weeks of gestation demonstrated congenital hernia of diaphragm and hydrocephaly. Pregnancy was terminated and fetus was sent for autopsy, karyotyping and aCGH. Autopsy examination showed microphthalmia of left eye, hydrocephaly, hypoplasia of corpus callosum, left optic nerve hypoplasia, congenital hernia of diaphragm, micrognathia, dysplastic ears, lung hypoplasia (left lung), malformed uterus and right club foot. Chromosomal study showed mosaic 46,XX/47,XX+1(q21-q41). Array comparative genomic hybridization (a-CGH) confirmed mosaic duplication of long arm of chromosome 1q21 to 1q41. Our fetus has many of the clinical features of Fryns syndrome. Our case gives further evidence that 1q duplications are associated with a Fryns-like phenotype including congenital hernia of diaphragm, pulmonary hypoplasia, micrognathia, long philtrum and joint contractures.

P03.035
Mosaic interstitial duplication of the long arm of chromosome 20 associated with vertebral malformations as the only major phenotypic manifestation

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Duplication of the long arm of chromosome 20 as the only chromosomal aberration is rarely described. Better known are reports on patients with a mosaic trisomy 20 or a rearranged chromosome 20 with additional imbalances.
We report on a girl born in the 35th week of gestation to a 31 year old mother. The patient is the second child of healthy parents. Birth weight, length and head circumference were within the normal range according to the gestational week. The girl presented with some mild dysmorphic features, e.g. low set and dysplastic ears, short nose with depressed nasal root, simple philtrum and thin lips. Ultrasounds of heart, abdomen and kidneys were normal while the corpus callosum was shortened and thicker than usually. Multiple vertebrae anomalies, e.g. hemi as well as cleft vertebrae and rip fusion were identified by radiography. Cytogenetic and molecular cytogenetic analysis revealed a mosaic female karyotype with a duplication of part of the long arm of chromosome 20 in 8% of blood cells. The karyotype is described as 46,XX,dup(20)(q11.2q13.3)/46,XX. ish dup(20)(D20S1157+,20QTEL14+,wcp20+). The parents have normal karyotypes.
Hemi and cleft vertebrae as well as rip fusion have been described in cases with duplication 20 associated with other chromosomal imbalances. The present case helps to further establish the correlation of these malformations with duplication of a part of the long arm of chromosome 20.

P03.036
Chromosome kissing in association with the ATR-X syndrome

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ATR-X (X-linked α-thalassemia / mental retardation) syndrome is one of the syndromes associated with abnormal epigenetic gene regulation, which appears males with X-linked mental retardation, HbH disease, skeletal abnormalities, and autistic behavior. ATR-X syndrome is caused by a mutation in the ATRX gene localized on the X chromosome (Xq21.1), which encodes ATRX protein, one of the chromatin-remodeling proteins. However, the details of molecular mechanism with symptoms of this syndrome are still unknown. Here to learn more about the relationships between nuclear architecture and failure of epigenetic regulation in the ATR-X syndrome, we examined characteristics of spatial positioning of following three chromosome arm specific regions by 3D-FISH technique; 1) Xq (ATRX gene has mapped on), 2) 16p (HBA has mapped on), and 3) 11p (HBB has mapped on). After image acquisition by confocal laser scaning microscope, analysis of relative spatial positioning of three painted regions was performed. The results showed that neighborhood association of particular two chromosome territory regions called as chromosome kissing was observed with high frequency between Xq and 16p and between 11p and 16p in cell nuclei from the ATR-X syndrome patients, respectively. The frequency of the same combination from the normal individual is approximately halves of them, respectively. Thus we considered that the spatial arrangement of nuclear architecture has been affected after one has been attacked with the ATR-X syndrome.

P03.037
Use of customised array CGH to investigate the sequence composition around the breakpoints of *de novo* CNVs according to their parental origin

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Among a large series of *de novo* CNVs identified by array CGH, we found the proportion of LCR-mediated imbalances (formed by non-allelic homologous recombination) to be significantly higher among maternally- compared to paternally-derived CNVs. To investigate the contribution of repetitive sequences other than LCRs to the formation of CNVs, we refined the breakpoint intervals (BPIs) of 37 patients with *de novo* non-LCR mediated CNVs (18 maternal and 19 paternal) using an Oxford Gene Technology customised oligonucleotide array and screened the BPIs for the presence of homologous and/or repetitive sequences. Twelve BPIs (in 10 patients) could not be refined further due to the high repetitive sequence content. For the remaining BPI the average size was reduced from 113kb (range 14 - 391kb) to 2.6kb (121bp - 34kb). At least 17/36 maternal and 18/38 paternal breakpoints occurred within the intron of a gene. The majority (76%) of BPI contained at least one repetitive sequence element and for 8/18 maternal CNVs and 5/19 paternal CNVs, the same or similar repetitive sequence element was present at both BPI. However, for those CNVs where both breakpoints were mapped to intervals below 1kb, only 1/9 showed significant homology between the BPI. Therefore, although we have demonstrated the utility of large scale breakpoint mapping using customised array CGH, further work to try and determine the exact breakpoint site by junction fragment cloning will be required to assess the contribution of repetitive sequences other than LCRs to the formation of CNVs.

P03.038
A case of *de novo* complex chromosomal abnormality involving a t(8;10) and an interstitial deletion 5q(q33.1→q34) characterized by GTG banding, FISH and cCGH

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Interstitial deletions of the long arm of chromosome 5 involving the region 5q33.1→q34 are rare occurrences. The clinical features of patients carrying similar deletions include dysmorphic facial features, such as epicanthus, retrognatia, protruding left ear and asymmetric mouth, high-arched palate, four finger lines and clinodactyly of digits II and V on both hands.
We report on a female child aged 13 presenting with development delay, agenesis of the corpus callosum, hallux diverted into, clinodactyly of 3rd, 4th and 5th fingers, obesity, hepatic steatosis, vesicular lithyasis and bilateral macular changes. Classical karyotyping using high resolution GTG banding revealed a *de novo* complex rearrangement including three abnormal chromosomes: 5, 8 and 10; apparently there was an inversion in the long arm

of chromosome 5 and a t(8;10). FISH whole chromosome painting probes confirmed an apparently balanced t(8;10), a deleted chromosome 5 and confirmed the inexistence of any other chromosomal involvement.
To define the deletion breakpoints and the extent of the deletion, cCGH techniques were performed and revealed an interstitial deletion 5(q33.1→q34). The final karyotype was: 46,XX,der(5)inv(5)(q21q33.1)del(5)(q33.1q34) t(8;10)(q13;q21.2)dn. ish cgh del(5)(q33.1q34).
The authors enhance the importance of using high resolution banding combined with molecular cytogenetic techniques for more precise definition of complex chromosomal rearrangements in patients with uncharacteristic phenotypic features and compare the present case findings with previously published data.

P03.039
A de novo complex chromosomal rearrangement involving four chromosomes in an infertile male with oligospermia: Case report

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Purpose: Complex chromosomal rearrangements (CCR) are rare events involving more than two chromosomes and more than two breakpoints. They are usually associated with infertility or sub fertility in male carriers. We examined a 29 year oligosperm man with a history of Varicocelectomy, normal testes size and normal endocrinology profile,who referred for chromosome analysis to genetic laboratory of Royan infertility institute.
Method: Chromosomal analysis was performed from peripheral blood lymphocyte cultures and analyzed by GTG banding. Additional tests such as C-banding and multicolor fluorescence in situ hybridization (FISH) procedure for each of the involved chromosomes were performed to determine the patterns of the segregations. Y chromosome micro deletions in the azoospermia factor (AZF) region were analyzed with multiplex polymerase chain reaction. To identify the history and origin of this CCR, all the family members were analyzed.
Result: The case was a complex chromosomal translocation; 46,XY,t(13;16;14;18) (q31.2;p13.2;q24.2;q21.2). No micro deletion in Y chromosome was detected. Just his monozygous twin brother has the same de novo reciprocal exchanges. The other siblings and parents were normal.
Conclusion: CCR are associated with male infertility as a result of the disruption of spermatogenesis due to complex meiotic configurations and the production of chromosomally abnormal sperm. In other words, it is likely that these chromosomal rearrangements might have influence in decreasing the number of sperms. To have a chance of healthy offspring**,** preimplantation genetic diagnosis (PGD) method is suggested.

P03.040
Complex translocation involving 13, 15 and 16 chromosomes: a case report

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Complex chromosomal rearrangements (CCR) occurring in phenotypically normal persons are rare. CCR are usually considered to include severe reproductive impairment by disturbing the meiotic process and producing unbalanced gametes responsible for high reproductive risk. Most of CCR are reported to be de novo.
We report a case of a complex translocation in a 38 years old female with menopause praecox and sterility. Conventional chromosomal analysis revealed an apparently balanced translocation involving 13, 15 and 16 chromosomes. This balanced complex translocation (BCT) involves three chromosomes and three different breakpoints. Molecular cytogenetic analysis with whole chromosome probes , centromeric and locus specific FISH probes showed breaks at 13q21.2, 15q26 and 16q23. Carriers of balanced complex translocation have a high risk of having spontaneous abortions or a child with an unbalanced karyotype. Our patient was informed by genetic counsellor.

P03.041
High frequency of copy number abnormalities in adult patients with mental disabilities and psychiatric disorders

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Background: Copy number variants (CNV) are associated with a significance increased risk of diseases for the individual and/or their family members. They are contributing to the development of congenital anomalies, intellectual disabilities, spectrum autism disorder and other psychiatric disorders. It is known that the prevalence of psychiatric disorders among adults with intellectual disability is higher than in control population.
Methods: We analyzed a cohort of 100 adult patients affected by mild/moderate intellectual disability associated with psychiatric disorders and minor dysmorphic features. Genetic analysis included array comparative genomic hybridization (aCGH) (Agilent 400K), performed in 45 cases at present.
Results: We detected 89 rare and potentially pathogenic CNVs in 37 cases, with an average of 2,4 CNV/case (1-8). These CNVs include 184 genes (2,07 genes/CNV). At present, we can correlate known CNVs with intellectual disability and/or psychiatric disorders in 13 patients (31,1%). Deletions and duplications found in these cases are: del2p12, del2p16.3, dup3q29, del12p12.1, dup15q11q13, del15q13.1q13.3, dup15q25.2, del15q26.2, dup15qter, dup17q24.1q24.2, del22qter, and dupXq22.1. Genes responsible of psychiatric disorders and some of them also with intellectual disability are: *CTNNA2, NRXN1, PAK2, SOX5, GABRB3, CHRNA7, ADAMTSL3, MCTP2, APOH* and *SHANK3.* Del2p16.3 is present in three patients and is the only recurrent CNV associated with psychiatric disorders. *NRXN1* gene is related with susceptibility to autism, schizophrenia and mental retardation.
Conclusion: We most emphasise the high frequency of rare CNVs associated specially with psychiatric disorder in patients with mild/moderate intellectual disability.
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P03.042
Detection of cryptic chromosome rearrangements by BAC Genome Array-CGH in five patients, with normal and/or abnormal karyotypes, associated with Mental Retardation, Autism and/or Epilepsy: new insights for genotype/phenotype correlation

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We re-examined ten patients with normal and/or abnormal karyotypes and dysmorphic features, associated with Mental Retardation, Autism and/or Epilepsy. We applied a fast BAC Genome Array- CGH platform (Cytochips Blue-gnome, Techno-genetics - Bouty). Cyto-Chips are high quality BAC microarrays (4898 BAC Clones spotted in quadruplicate 0.6 Mb). This approach led us to discover further cryptic chromosomal rearrangements, previously undetected by conventional cytogenetic procedures. We identified two genes: **SLC8A3** (human gene for member 3 of solute carrier family 8), a sodium-calcium exchanger electively expressed in the brain, and a possible candidate gene for Epilepsy (Nucaro et al 2010) and the **CSMD1** gene (Cub and sushi multiple domains 1) a candidate gene for Autism associated with Mental Retardation (MR) and Epilepsy (Nucaro et al 2011). This approach allows us to better delineate the genotype/phenotype correlation in our patients. Our experience shows the validity of the BAC platform as a reliable method for genome-wide screening of chromosomal aberrations, as well as oligonucleotide-based Array CGH, in patients with idiopathic Mental Retardation and/or in association with Autism and Epilepsy.

P03.043
A de novo interstitial deletion at 1p36.11 in a patient presenting with severe psychomotor delay, sensoneural hearing loss, congenital heart defect and dysmorphic features

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We report on a patient with severe psychomotor delay, sensoneural hearing loss, absent speech, hydrocephaly, congenital heart defect, broad thumbs, dysmorphic features (flat nasal bridge, pointed chin, low-set, abnormal ears) and *de novo* interstitial deletion at 1p36.11 detected by arrayCGH (400K). The deleted segment at 1p36.11 is 1 Mb in size and involves 20 protein coding genes. Based on the clinical and molecular data analysis we suspect *PIGV* gene as one of the strongest candidate genes responsible for severe psychomotor delay, deafness and limb anomalies in our patient. Horn et al. (2011) reported two cases with homozygous and compound heterozygous missense mutations of *PIGV* and intelectual disability, hearing loss, muscular hypotonia and dysmorphic features, which are observed in our patient