morphogenesis. Their prevalence is estimated between 0.4 and 0.6% of live births. CHD is essentially multifactorial. Among the genetic causes, chromosomal aberrations are involved in congenital heart disease. Indeed, among patients who carry chromosomal abnormalities, 30% have cardiovascular problems. 22q11.2 microdeletion is the most common cause.

The purpose of this study was to determine whether subtle chromosomal anomalies previously undetected by conventional cytogenetic banding methods could be identified by array-CGH in children with isolated CHD. We reported 30 unrelated newborns recruited from Neonatology service for genetic exploration.

Genetic investigations are essentially based on the techniques of cytogenetics and molecular cytogenetics. At first intension banded karyotyping was performed followed by fluorescent in situ hybridization (FISH) using gene-specific probe TUPLE1 in 22q11.2. As a last resort comparative genomic hybridization CGH-array 44K (Agilent® Technology) has been performed for 4 patients.

FISH showed normal hybridization to the DiGeorge syndrome critical region for all patients and no copy number variations was detected by array-CGH.

Our analysis was limited by a small and heterogenous study population. Also Increasing resolution arrays are needed to detect cryptic rearrangements.

We propose this strategy to explore a wider group of patients to identify new genetic factors involved in the development of cardiac malformations. The identification of genetic etiologies for CHD is important to provide genetic counseling and to establish a report genotype phenotype for every type of heart disorder.

738 MOLECULAR CHARACTERIZATION OF DER (8) (QTERQ21.13: PTERP23.3) *DN* IN A CHILD ASSOCIATING PSYCHOMOTOR RETARDATION, HYDROCEPHALUS AND FACIAL DYSMORPHISM

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Complex but balanced chromosomal rearrangements can give rise, through recombination during meiosis, to complex unbalanced rearrangements. Here, we report on the case of a 21 months old child associating a 8q21.13 duplication and 8p23.3 microdeletion. The proposita was referred to our lab for cytogenetic exploration of a hydrocephalus associated with facial dysmorphism. He had also psychomotor retardation and microcephaly. The patient R-banding karyotype revealed a partial trisomy 8q captured by the p telomere of the same chromosome, whereas the parents' karyotypes were normal. CGH-array technique characterized breakpoints and estimated its size to 61.8 Mb. Interestingly, an additional cryptic loss of 260 Kb in 8(p23.3-pter) was also identified by the same technique. These anomalies were confirmed by FISH technique.

The partial deletion of a chromosome arm in combination with partial duplication of the other was evocative of a recombinant chromosome deriving from a parental pericentric inversion. We suggest, therefore that a parental pericentric prezygotic 8(p23.3–q 21.13) inversion resulted in the complex unbalanced rearrangement of chromosome 8 in our patient. The clinical picture including hydrocephalus, inguinal hernia, long-term fever and psychomotor retardation, was described in patients with pure 8q2-qter duplication. However, the 8p23.3 microdeletion may contribute to the psychomotor retardation, microcephaly and some minor dysmorphic features. Here we emphasize the fact that the 8p microdeletion would be cytogenetically undetectable in the absence of CGH-array technique underlining the need of entire genome high-resolution analysis in patients with idiopathic mental retardation and/or birth defects even in abnormal conventional karyotype cases.

739 18Q22 MONOSOMY: GENOTYPE-PHENOTYPE CORRELATION AND THERAPEUTIC IMPACT

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The deletion of the long arm of chromosome 18 causes a contiguous gene deletion syndrome with a highly variable phenotype, usually related to the extent of the deleted region. The most commonly reported clinical features include: mental disabilities, decreased growth, microcephaly and facial abnormalities.

We report on a case with partial monosomy 18q22 derived from a maternal reciprocal translocation t(8; 18). The patient was 7 months old referred for genetic exploration of neurodevelopmental delay, craniofacial dysmorphism, post natal growth retardation, choanal atresia, club foot and congenital hip dislocation.

Chromosome analysis from peripheral blood showed a 46, XY, der (18). Array CGH was performed and revealed a partial monosomy 18q21.33q22.31 of 15.3MB associated with partial trisomy 8q24.12q24.23 of 22.7MB region. These results were confirmed by FISH using telomeric 18q probe.

Choanal atresia and skeletal malformation are in agreement with the monosomy 18q. Interestingly, the deletion includes *GALR1* gene in 18q23 witch encodes galanine receptor. Galanine is a neuromodulator that stimulates growth hormone secretion. *MBP,* and adjacent genes, are implicated in myelination process and haploinsufficiency explains partially developmental delay. Otherwise, the haploinsufficiency of the 18q22.3-q23 gene region is suggested to be a critical region for the immunoglobuline A deficiency which is significantly associated to celiac disease. Our patient has not until now immunological desorders.

The association deletion 18q22- GH deficiency and decreased myelinisation is now well estabilished. The real therapeutic impact of GH treatment is discussed.

740 DUPLICATION OF THE SOX3 GENE IN A SRY NEGATIVE 46, XX MALE

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Case presentation An 11 old patient with hypoplasia of the right kidney and hypospadias was found to be SRY negative, 46, XX. His parents and younger sister were healthy. His intelligence was normal (IQ 92) and he had no other anomalies. The behavior, growth and development were all normal. His testes were >4ml and the penis was 5 cm. Ultrasound and MRI did not show internal female genitals, while confirming right kidney hypoplasia (as did the DMSA scan).

ACTH test showed normal basal and stimulated 17OH-progesterone excluding a form of 46XX DSD due to 21-hydroxylase deficiency. 11-DOC and 11S were normal at both baseline and after ACTH stimulation, excluding 11-hydroxylase deficiency. Cortisol levels were in the mid normal range at baseline and responded to stimulation, excluding primary adrenal insufficiency. Androstenedione,

The hCG test found testosterone in the low normal range for male sex and age at baseline. It rised up to 146 ng/mL indicating the presence of functional Leydig cells targeted by hCG. The stimulated ratio T:DHT was 5.6, not supporting 5 alpha-reductase deficiency.