2nd announcement

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CNVs and the gene CNTN4 (contactin 4). The protein encoded by CNTN4 is a member of the immunoglobulin superfamily that may play a role in the formation of axon connections in the developing nervous system.

Case 2: a 9 year-old boy presenting with tetralogy of Fallot, hypotonia, and mild dysmorphism. We identified a small interstitial duplication of 270 kb in the long arm of chromosome 22 (22q11.2–q12.1). This region (from bp 23,931,520-24,197,568) includes many CNVs, the gene IGLL3 (immunoglobulin lambda-like polypeptide 3), and two members of a gene cluster CRYBB2 and CRYBB3 (crystallin, beta B2 and beta B3). The Crystallin genes may play a role in eye development.

Currently we investigate the parents of these two patients. A pathogenetic function of these duplications will become even more likely if the parents do not carry these duplications.

2.2-P

Microsatellite Null Alleles in paternity testing

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2.3-P

Idiopathic Silver-Russell syndrome patients should be tested for (sub)microscopic chromosomal aberrations

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Silver-Russell syndrome (SRS) is a clinically and genetically heterogeneous disorder. The phenotype is characterized by intrauterine and postnatal growth restriction and additional morphologic abnormalities including a typical triangular face, relative macrocephaly and asymmetry. In about 50% of SRS cases (epi)genetic alterations can be detected: >38% show a hypomethylation in 11p15, a further 10% carry a UPD (7)mat. In several cases, conventional cytogenetic aberrations have been reported, but often the clinical picture was ambiguous. Furthermore, a uniform aberration pattern was not obvious. Due to the recent identification of two cases with submicroscopic duplications in 11p15 we decided to screen a cohort of 20 SRS patients without 11p15 epimutation or UPD(7)mat for submicroscopic imbalances by genomic microarray analysis using the Affymetrix GeneChip® Human Mapping 500K Array Set. The detected imbalances were surveyed in respect to their gene coverage and overlaps with registered copy number variations (CNVs) by online databases queries. Apart from numerous apathogenic CNVs we identified 13 so far unregistered copy number alterations (CNAs) in 10 patients. We classified the majority of them as apathogenic because they were either detectable in one parent or because they did not affect genes. However, in one SRS patient with normal intellectual capacities we detected a de-novo 1 Mb deletion in 12q14 for which recently a new microdeletion syndrome has been described; one of the 12q14 microdeletion carriers showed SRS features, however all patients were mentally retarded. In an additional patient from routine diagnostic screening for the 11p15 epimutation we detected a cytogenetically invisible 11p15 duplication by MLPA which was retrospectively diagnosed as a 11;15 translocation by FISH. In conclusion, our findings show that a significant number of 11p15 epimutation and UPD(7)mat negative patients carry chromosomal abnormalities. We therefore suggest to routinely test idiopathic SRS(-like) patients for submicroscopic chromosomal aberrations.

2.4-P

The crucial role of mdr1 (ABCB1) gene polymorphisim in abdominal aortic aneurysm: preliminary results of a pilot study

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Summary
Objective: The aim of this study was to assess the influence of multidrug resistance (MDR1) gene polymorphisms on Turkish patients with abdominal aortic aneurysm(AAA). METHODS: The comman polymorphic G2677T/A region in MDR1 was determined by PCR based StripAssay revers hybridisation thecnique in a total of 116 individuals(58 patients with AAA, mean age 62.94±6.59 and 58 healthy controls, mean age 58.82±11.60).RESULTS: The G2677T/A polymorphism of MDR1 gene was significantly higher in patients with AAA when compared to the control group individiuals (X^2= 11.47; P<0.0001 for homozygous and X^2=5.80; p= 0,016 for heterozygous mutations), (p<0,05). CONCLUSION: The preliminary results of current pilot study demonstrated that the G2677T/A single nucleotide polymorphism in MDR1 gene is associated with AAA. These gene polymorphism may play an curicial role in initiation and/or progression aneurysm in human with combine effetcs of other ethiological parameters.

Key words: AAA, MDR1 gene polymorphism

2.5-P

Screening for Genomic Imbalances in Autism Spectrum Disorders (ASDs) using Array-based Comparative Genomic Hybridization (array-CGH)

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Autism spectrum disorders (ASDs) are characterized by impairments in communication and social interaction, accompanied by stereotyped behaviors and interests. It's a highly heritable and heterogeneous group of disorders with a complex genetic etiology. Until recently, G-banded karyoptyping was the standard method for the detection of cytogenetic aberrations in patients with developmental disorders. The development of whole-genome screening methodologies such as array-CGH has enabled screening of the whole genome at much higher resolution than provided by karyotyping, leading to the identification of novel microdeletion- and microduplication syndromes. In our present ongoing study, we use array-CGH to screen for genomic imbalances in ASD patients in order to identify genetic aberrations and genes that cause or increase susceptibility for autism. So far ~200 patients have been screened and clinically significant imbalances have been identified in 18 cases (~9%). Some of these aberrations are recognized as recently identified recurrent aberrations associated with autism. We also observed that duplications seem more frequent in ASD patients than in patients with mental retardation where deletions are more frequently observed. An identified genetic cause gives the family and the patient an explanation of the disorder. In hereditary cases, genetic counseling and prenatal diagnosis is also possible.

2.6-P

MLPA: A new tool for detection of delection in FVIII gene

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Haemophilia A is an X-linked bleeding disorder caused by mutations widespread in the human coagulation FVIII gene. Most of the mutations in the FVIII gene are detectable by routinely screening methods such as sequencing analysis or DHPLC. However, large deletions or deletion encompassing the entire gene F8 can go undetected. Moreover, in heterozygous females the diagnosis proves difficult as the presence of a normal allele does not recognize the partial or complete loss of the F8 gene.

In this study we analyzed 25 patients, affected by haemophilia A which resulted mutation negative after complete sequencing of F8 gene. However, PCR failed to amplify one or more exons in some of these patients. This work aimed to confirm the conjectured deletions and the diagnosis of carriers thanks to the Multiplex Ligation-dependent Probe Amplification (MLPA) Test. Recently, MLPA has been broadly applied to detect mutation as deletions and duplications, especially in X-linked disease (Duchenne/