European Journal of Human Genetics

Volume 24 E-Supplement 1 May 2016 www.nature.com/ejhg

European Human Genetics Conference 2016

May 21-24, 2016
Barcelona, Spain

Abstracts

nature publishing group npg

AZF region including sY81, sY84 and sY86 for AZFa; sY121, sY124, sY127 and sY134 for AZFb; and sY242, sY239, sY254 and sY255 for AZFc were investigated using multiplex polymerase chain reaction (M-PCR). Existence of possible mutations in exon 7 of Stag3 gene was also investigated using multitemperature single strand conformation polymorphism (MSSCP) method. One hundred fertile men were also studied as control group.
Results: Thirteen (10.66%) patients showed Y chromosome microdeletions and among these, deletion in AZFc region was the most frequent. However, no mutation was detected in the Stag domain coded by exon 7 of the STAG3 gene.
Conclusion: According to the results, in the studied population, the main causing factor in developing azoospermia was Y chromosome microdeletions. Therefore, we did not suggest STAG3 gene as a strong candidate gene in non-obstructive azoospermia.

E-P01.79
The case of der(5)t(5;14)mat caused by adjacent I meiotic segregation in prenatal diagnosis

D. Yuksel[1], *O. Izci Ay*[1], *E. M. Ay*[1], *O. Tezol*[2], *G. Dogru*[1], *K. Cevik*[1], *U. Karakas*[1], *F. Cayan*[3], *I. Buran*[1], *E. M. Erdal*[1];
[1]*Mersin University, Faculty of Medicine, Departmant of Medical Biology, Mersin, Turkey,* [2]*Mersin University,Faculty of Medicine,Pediatrics Clinic, Mersin, Turkey,* [3]*Mersin University,Faculty of Medicine,Departmant of Gynecology and Obstetrics, Mersin, Turkey.*

Introduction: Genetic material exchange between homologous chromosomes occurs in somatic and germ cells. This type of exchanges in certain cases may occur in non-allelic chromosomal regions resulting in structural chromosomal anomalies in form of translocations. Translocations are categorized in two general types namely balanced and unbalanced. Balanced reciprocal translocations can risk the pregnancy as it may produce unbalanced gametes.
Materials and Methods: The amniotic fluid (20ml) belonged to a 27 years old female patient in 18th week of her pregnancy who was admitted to the Polyclinic of Gynecology and Obstetrics at Faculty of Medicine in Mersin University was sent to laboratory for cytogenetic analysis. Parents were not consanguinity. Amniotic material was processed using the in-situ culture method and GTG banding technique. 39 metaphase plates (20 colonies) were obtained and cytogenetic analyses performed on these plates.
Results: As a result of the cytogenetic analysis, the fetus was determined to be 46,XX,der(5)t(5;14)(p13;p11)mat karyotype. The cytogenetic analysis that was performed on peripheral blood samples taken from the parents showed that the finding was not de novo but of maternal origin.
Conclusions: Incidence of reciprocal translocations in the amniocentesis is 0.06%. Balanced reciprocal translocations do not change the amount of chromosomes and genetic materials. However they may cause unbalanced chromosomal rearrangement in the gametes of these carriers. Although the reciprocal translocation in our case is unbalanced. Upon family's request, the pregnancy was sustained. The 28-month case with Cri du Chat symptoms are being monitored by the Department of Pediatrics, Mersin University Faculty of Medicine.

E-P02 Sensory disorders (eye, ear, pain)

E-P02.01
Novel mutation in the CHST6 gene causes macular corneal dystrophy in a black South African family

N. Carstens[1], *S. Williams*[2], *T. Carmichael*[2], *M. Cheung*[3], *S. Büchmann-Møller*[3], *M. Sultan*[3], ***F. Staedtler***[3], *C. Zou*[4], *P. Swart*[5], *D. S. Rice*[5], *A. Lacoste*[5], *K. Paes*[5], *M. Ramsay*[1];
[1]*Sydney Brenner Institute for Molecular Bioscience, University of the Witwatersrand, Johannesburg, South Africa,* [2]*Division of Ophthalmology, Department of Neurosciences, University of the Witwatersrand, Johannesburg, South Africa,* [3]*Biomarker Development, Novartis Institutes for BioMedical Research, Basel, Switzerland,* [4]*4Center for Proteomic Chemistry, Novartis Institutes for BioMedical Research, Basel, Switzerland,* [5]*Novartis Institutes for Biomedical Research, Cambridge, MA, United States.*

Macular corneal dystrophy (MCD) is a rare autosomal recessive disorder that is characterized by progressive corneal opacity that starts in early childhood and ultimately progresses to blindness in early adulthood. The aim of this study was to identify the cause of type I MCD in a black South African Sotho-speaking family with two affected sisters using whole exome sequencing. Variant filtering to identify the MCD-causal mutation included the inheritance pattern, variant minor allele frequency and potential functional impact. Ophthalmologic evaluation of the cases revealed a typical MCD phenotype and none of the other family members were affected. Variant filtering identified a homozygous E71Q mutation in CHST6, a previously identified MCD-causing gene encoding corneal N-acetyl glucosamine-6-O-sulfotransferase, as the MCD-causal mutation in this family. This E71Q mutation results in a non-conservative amino acid change in a highly conserved functional domain of the human CHST6 that is essential for enzyme activity. This is the first description of MCD in a black Sub-Saharan African family and therefore contributes valuable insights into the genetic aetiology of this disease, while improving genetic counselling for this and potentially other MCD families.

E-P02.02
A novel FOXC1 mutation in an Axenfeld-Rieger patient with childhood glaucoma

S. Carmona[1,2], *M. Freitas*[3], *H. Froufe*[1], *M. Simões*[1], *M. Sampaio*[4], *E. Silva*[5], *C. Egas*[1,6];
[1]*Next-Gen Sequencing Unit, UC-Biotech, Cantanhede, Portugal,* [2]*Faculty of Medicine, University of Coimbra, Coimbra, Portugal,* [3]*Department of Ophthalmology, Hospital da Arrábida, Porto, Portugal,* [4]*Department of Paediatric, Hospital CUF, Porto, Portugal,* [5]*Vision Psychophysiology Unit, Faculty of Medicine, University of Coimbra, Coimbra, Portugal,* [6]*Center for Neuroscience and Cell Biology, University of Coimbra, Coimbra, Portugal.*

Axenfeld-Rieger syndrome (ARS) is a rare dominant, autosomal developmental disorder characterized by anterior segment abnormalities of the eye. Posterior embryotoxon with iridocorneal adhesions are always present and iris stromal thinning or atrophy, corectopia, iris holes and iris ectropion are common. Approximately half of the ARS patients develop glaucoma. Systemic anomalies like craniofacial anomalies and cardiovascular can also be present. Mutations and CNV in FOXC1 and PITX2 have been previously reported in ARS patients.
A DNA sample of a 14-month-old male with bilateral glaucoma, posterior embryotoxon with extension of the peripheral iris to Schwalbe's line, short stature, hypertelorism, frontal prominence, broad flat nasal root, maxillary hypoplasia and unilateral testicular atrophy was sequenced for the whole exome with the Ion Proton sequencer. Rare variants with functional impact were selected to identify the disease-causing variant. Sanger sequencing was performed to validate the mutation in the patient and to study the parents.
A novel heterozygous nonsense variant Y64X (c.192 C>G) was found in the FOXC1 gene. This de novo mutation leads to the loss of 88.6% of the protein, including the functional FHD domain.
The presence of de novo FOXC1 mutation confirms the ARS diagnosis. This result is consonant with previous studies that report a positive association between FOXC1 mutations and ARS patients with glaucoma. Further studies will be needed to understand the pathogenic mechanism of this mutation.
S. Carmona was supported by a doctoral fellowship from Fundação para a Ciência e Tecnologia (SFRH/BD/90445/2012), Programa Operacional Potencial Humano / Fundo Social Europeu (POPH/FSE).

E-P02.03
Novel BMP4 mutation causing coloboma in a Jewish Ashkenazi kindred

Y. Yogev[1], *O. Wormser*[1], *D. Halperin*[1], *Y. Perez*[1], *M. Volordarsky*[1], *L. Gradstein*[2], *O. S. Birk*[3,1];
[1]*Morris Kahn Laboratory of Human Genetics, National Institute for Biotechnology in the Negev (NIBN), Ben-Gurion University of the Negev, Be'er Sheva, Israel,* [2]*Department of Ophthalmology, Soroka University Medical Center, Be'er Sheva, Israel,* [3]*Institute of Genetics, Soroka University Medical Center, Be'er Sheva, Israel.*

An Israeli family of Jewish Ashkenazi descent presented with a phenotype of bilateral coloboma affecting several generations in an apparent dominant mode of inheritance. Whole exome sequencing data of an affected individual were analyzed and filtered for known benign variants using our in-house databases along with open access databases (1000 genomes, NHLBI ESP, ExAC etc.). The analysis yielded several candidate variants in genes which were previously associated with various ocular disorders. Candidate variants were further analyzed using Sanger sequencing and restriction analysis. Only a single heterozygous c.392A>G missense mutation in BMP4, resulting in a p.H121R substitution, showed full segregation within the family and was not found in 100 healthy Ashkenazi controls. In-silico analysis of the novel p.H121R variant showed that it is likely to have a deleterious effect on the mature protein. Mutations in BMP4 were previously described as causative for various conditions such as anophthalmia-microphthalmia, coloboma, retinal dystrophy, myopia, cleft lip, cleft palate and brain- digital abnormalities. Our data suggest that the novel BMP4 heterozygous mutation is the cause for the dominantly inherited isolated coloboma in this kindred, possibly through a dominant negative effect, in line with the known function of BMP4 as a homodimer.