dation study, we sequenced a target of 500 kb (Agilent SureSelect capture, Illumina HiSeq sequencing) in 475 CAVS cases. The 500-kb target contained exonic regions of candidate genes from our exome sequencing project (69 genes) or the literature (31 genes), and regulatory regions. After applying standard frequency and quality filters, we performed burden tests to identify CAVS disease genes.
The identification of rare genetic variants within this project could lead to the possibility of alternative patient management for a disease that represents a major public health problem in the ageing population.

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P04.09

Homozygous mutation in the Myosin-Binding Protein C gene leading to an early onset of HCM with mild hypertrophy and severe arrhythmias.

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Introduction ~ Heterozygous mutations in the myosin-binding protein (MYBPC3) genes are the most frequent genetic causes of hypertrophic cardiomyopathy (HCM). Patients with MYBPC3 mutations generally have late onset disease and a relative good prognosis. Homozygous or compound heterozygous MYBPC3 mutations have been associated with early onset disease with severe hypertrophy and heart failure.
We will describe here the clinical features of a family with a homozygous mutation (p.Cys566Arg) in MYBPC3.
Case ~ The index patient (an 8 year old girl) presented with a cardiac arrest due to ventricular fibrillation at the age of 8 years. After resuscitation she underwent cardiac evaluation. The electrocardiogram (ECG) showed significant left ventricular hypertrophy (LVH) but echocardiogram and Magnetic Resonance Imaging (MRI) revealed only mild LVH. She fully recovered and underwent ICD implantation. During one year follow-up she had two appropriate ICD shocks for ventricular arrhythmias. The asymptomatic brother of the index patient (age 11 years) showed a similar typical ECG with only mild LVH on echo and MRI. Genetic testing of both the index patient and her brother showed a homozygous mutation (p.Cys566Arg) in the MYBPC3-gene. Both asymptomatic parents were heterozygous carriers of this mutation and their cardiac assessments revealed no abnormalities.
Conclusion ~ Homozygous mutations in the Myosin-Binding Protein C gene could lead to an early onset of HCM with mild hypertrophy and severe ventricular arrhythmias.

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P04.10

Steroid 21-hydroxylase genetic analysis of 50 Tunisian patients

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Congenital adrenal hyperplasia (CAH) is an autosomal recessive disease of steroid biosynthesis in humans. More than 90% of all CAH cases are caused by mutations of the 21-hydroxylase gene (CYP21A2), and approximately 75% of the defective CYP21A2 genes are generated through an intergenic recombination with the neighboring CYP21A1P pseudogene.
In this study, the CYP21A2 gene was genotyped in 50 patients in Tunisia with the clinical diagnosis of 21-hydroxylase deficiency. CYP21A2 mutations were identified in 87% of the alleles. The most common point mutation in our population was the pseudogene specific variant p.Q318X (26%). Three novel single nucleotide polymorphism (SNP) loci were identified in the CYP21A2 gene which seems to be specific for the Tunisian population. The overall concordance between genotype and phenotype was 98%.
With this study the molecular basis of CAH has been characterized, providing useful results for clinicians in terms of prediction of disease severity, genetic and prenatal counseling.

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P04.11

Association of single nucleotide polymorphisms with microalbuminuria in essential hypertension

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Objectives: Microalbuminuria (Malb) is an early marker for cardiovascular diseases and renal risk in hypertension. Several studies have identified different loci and genetic markers for the risk of developing hypertension in Malb, but the genetic basis of Malb is little known. Therefore, the objectives were the identification of genetic variations involved in the development of Malb in essential hypertension.
Methodology: we have designed an experiment which studies 1536 SNPs, selected in based results of prior GWAS, in 960 samples of hypertension Spanish population with a Custom Golden Gate Genotyping Assay of Illumina. Linear regression analysis of quantitative variables and logistic regression analysis of qualitative ones were performed using PLINK v1.07. We adjusted by age, sex, body mass index and systolic blood pressure for all analysis.
Results: we obtained an association between rs12322500(ERC1 gene) and log_UAE, 0.3253(0.1413-0.5093) and OR for Malb presence of 2.657(1.373-5.144); the AA genotype had higher value for UAE than AG/GG genotypes. Other SNP with a significant association was rs1746048(CXCL12 gene) that had for log_UAE 0.7362(0.2441-1.228), an OR for Malb presence of 28.53(3.237-251.4); the AA genotype has higher value for UAE than AG/GG genotypes. Finally, SNP rs12260555(WDFY4 gene) had log_UAE of 0.1367(0.0354-0.2381) and OR for Malb presence of 1.798(1.2-2.694); with the highest levels of UAE in the AC genotype.
Conclusions: this study shows three SNPs strongly associated with UAE and presence of Malb in hypertensive patients. These SNPs are located in genes involved in renal damaged in hypertension. Further functional studies will be necessary to confirm these results.

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P04.12

Introducing a multiplex panel of markers for genetic testing of familial hypertrophic cardiomyopathy based on linkage analysis

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Aims: Familial hypertrophic cardiomyopathy (HCM) is caused by mutations in genes encoding cardiac sarcomere proteins. Nowadays genetic testing of HCM plays an important role in clinical practice by contributing to the diagnosis, prognosis, and screening of high risk individuals. The aim of this study was developing a reliable testing strategy for HCM based on linkage analysis and appropriate for Iranian population.
Methods and Results: six panels of four microsatellite markers surrounding MYH7, MYBPC3, TNNT2, TNNI3, TPM1, and MYL2 genes (24 markers in total) were selected for multiplex PCR and fragment length analysis. Characteristics of markers and informativeness of the panels were evaluated in 50 unrelated Iranians. The efficacy of the strategy was verified in a family with HCM. all markers were highly polymorphic. The panels were informati-