CAD. The effects of the CC and CT genotypes of the MTHFR 677C > T rs1801133 variant on the model are statistically marginal.

Conclusion: The investigated gene variants have a potential in clinical prediction of the risk for developing coronary artery disease.

Conflict of Interest: Marina Stratrova Genomika Medical, Skopje, Hristo Pejkov University Clinic of Cardiology, Medical Faculty, Ss. Cyril and Methodius University in Skopje, Macedonia, Zan Zimbakov University Clinic of Cardiology, Medical Faculty, Ss. Cyril and Methodius University in Skopje, Macedonia, Slavica Josifovska Laboratory for Molecular Biology, Faculty of Natural Sciences and Mathematics, Ss. Cyril and Methodius University in Skopje, Sasho Panov Laboratory for Molecular Biology, Faculty of Natural Sciences and Mathematics, Ss. Cyril and Methodius University in Skopje.

EP06.010 Rapid exome sequencing for children with acute cardiomyopathy in the PICU – a case series

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Background: Rapid exome sequencing (ES) is increasingly being utilized as an efficient diagnostic tool in the critical care setting with high diagnostic yield. Acutely presenting cardiomyopathy (CM) can often require critical care and has numerous possible etiologies including various genetic disorders, particularly in children.

Here we describe a brief series of pediatric patients hospitalized in the intensive care unit (ICU) with acute cardiomyopathy of unknown cause. Rapid ES provided a timely diagnosis and informed clinical decisions including eligibility for extracorporeal membrane oxygenation ECMO or heart transplant.

Methods: ES was performed for 5 unrelated patients ages 8 days to 10 years with acute cardiomyopathy hospitalized in the ICU. Turnaround time was 5 to 60 days

Results: ES was diagnostic in 3/5 cases including a likely pathogenic variant in *ACTC1*,c.664G>A, in a 6 year old boy with left ventricular non-compaction and a homozygous pathogenic variant in *NRAP*,p.Gln1113Hisfs*40, in a 10 year old boy with dilated CM. In both cases, as results confirmed isolated cardiac involvement, the patients were eligible for transplant and received bridging therapies.

A homozygous pathogenic variant in *MYBPC3* :c.3491-2A > C was detected in a neonate confirming the diagnosis of fatal neonatal CM. Results were delivered within 5 days precluding ECMO.

In two cases, a variant of unknown significant was identified in genes, related to broader phenotypes These results prompted further investigation and extended metabolic workup.

Discussion and conclusion: Rapid ES for pediatric patients with acute CM had a high diagnostic yield and a significant impact on patient care.

Conflict of Interest: None declared.

EP06.011 A homozygous rare TTR variant of transthyretin amyloidosis

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Background/Objectives: Hereditary transthyretin amyloidosis (ATTRv) is a rare autosomal dominantly inherited disease caused by mutations in the transthyretin (*TTR*) gene. More than 140 *TTR* gene variants have been reported in ATTRv. Few cases have been described in which the rare *TTR* variant c.302C>T, p.(Ala101Val) was mostly associated with cardiac ATTRv.

Methods: We present a 45-years-old patient with diagnosed sensomotor polyneuropathy of the upper and lower extremities and pronounced tetraparesis. Cardiac involvement (amyloidosis) was suspected only 4 years later. Cardiac MRI was performed showing asymmetric LV hypertrophy with a suspicion of hypertrophic cardiomyopathy. Haematological analysis for AL amyloidosis were negative. 99mTc-PYP bone scintigraphy showed no myocardial uptake (Grade 0). Endomyocardial biopsy was performed for differential diagnosis. Amyloid deposits were found, but immunohistochemistry showed a likely non-specific reaction to transthyretin. Mass spectrometry was not available.

Results: Next-generation sequencing revealed a likely pathogenic homozygous variant of the *TTR* gene NM_000371.3:c.302C>T, NP_000362.1:p.(Ala101Val). As parental testing was not available, real-time PCR analysis was performed and no heterozygous deletion of exon 3 of the *TTR* gene was detected. This variant in the homozygous state was not described in the literature before. The same c.302C>T *TTR* variant in the heterozygous state was also found in 3 other unrelated probands (2 females and 1 male) with predominant cardiac involvement at our centre. Their ages at diagnosis were 57, 74 and 77.

Conclusion: The homozygous c.302C>T *TTR* variant is associated with earlier disease onset and neurological involvement compared to the heterozygote state.

Conflict of Interest: Dovile Zebrauskiene Created a presentation about ATTR cardiomyopathy which was funded by Pfizer., Egle Sadauskiene: None declared, Sigita Aidietiene: None declared, Agnė Šiaudinienė: None declared, Valdas Pečeliūnas: None declared, Jurate Barysiene: None declared, Egle Preiksaitiene: None declared.

EP06.012 Generation of antibodies against α-Klotho protein using canarian camels

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Cardiovascular disease (CVD) is the leading cause of death worldwide. Atherosclerosis is the substrate responsible for the vast majority of cardiovascular events. Reductions in α-Klotho protein levels have been related with the pathophysiology of CVD, particularly in chronic kidney disease patients.

The main objective of our project is to obtain mini- and nanoantibodies (nanobodies) from Canarian camels to be employed in the detection of human α-Klotho protein in different tissues, and serum and urine samples.

Nanobodies are variable domains of heavy chain-only antibodies (HCAbs) that can be isolated from camelids. In spite of their single domain structure, nanobodies display many unique features, such as small size, high stability, and cryptic epitopes accessibility, which make them ideal for sophisticated applications in plants and animals.

We carried out immunizations in camels with the different regions of the protein to detect the different forms in which the protein is presented. We isolated lymphocytes from camel blood in order to clone the DNA regions codifying for antibodies against α-Klotho, that will be further expressed in bacteria. Effectiveness and sensitivity of these new generation antibodies are being tested in clinical samples and cell lines that express α-Klotho through different approaches, e.g. western blot, ELISA and immunohistochemistry assays. These mini- and nanobodies will allow us to use α-Klotho as a biomarker with clinical applicability.

This work is supported by Cabildo de Tenerife, Tenerife 2030, FDCAN, MEDI, in the Agustín de Betancourt programme and PIFIISC21/23 from Fundación Canaria Instituto de Investigación Sanitaria de Canarias (FIISC).

Conflict of Interest: None declared.

EP06.013 Clinical and laboratory characteristics of congenital heart defects, caused by microdeletion of 22q11.2

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Introduction: Isolated congenital heart defects (CHD) are the most frequent among all congenital defects (CD). Their frequency among live births of Kyiv is 8-9:1000 (2019-2021). Microdeletion of 22q11.2 and trisomy of chromosome 21 are the most common causes of CHD.

Materials and methods: Prospective genetic counseling and examination of 77 children, aged 1 day to 12 years from different regions of Ukraine for the last 10 years was undergone at the Center of Medical Genetics of Children's Hospital "OKHMATDYT" (hospital cohort). All cases of CHD were confirmed by pediatric cardiologist. Cytogenetic examination included G-banding karyotyping according to the standard protocol. The FISH using loci-specific microdeletion of 22q11.2 DNA-probes was applied to verify the microdeletion.

Results: Sixty-seven full-term children (87%) were born via physiological delivery, with body weight more than 2,5 kg (81%). Prenatally diagnosed CHD before 22 week of pregnancy were in 16 women (21%), invasive prenatal diagnostics took place in 12% of cases. Phenotype of probands: presence of stigmas was in 51 children (66%), hypo- and aplasia of thymus were in 50 children (65%), other CD - 27%, among them – multiple CD in 8 cases (38%), polydactyly in 4 cases (19%). Four probands (5%) with microdeletion of 22q11.2 did not have any CHD. Conotruncal defects were in 55% of all CHD, critical CHD were in 14%. Microdeletion of 22q11.2 was confirmed in all probands.

Conclusion: With the aim of study the etiology and differential diagnostics of CHD in children, applying of whole range of molecular studies are recommended.

Conflict of Interest: Nikita Pozhar full, Vira Galagan full, Valentyna Kurakova full, Andrii Kurkevych full, Yuliia Dudierina full, Maryna Tsyhankova full, Yurii Hryshuk full, Diana Mykhailova full.

EP06.014 Time to downgrade genetic testing? Review of pathogenic variants in cardiogenetic

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The financial and societal impact of hereditary cardiac diseases (HCD) is widely acknowledged. One of the most prevalent of these conditions is hypertrophic cardiomyopathy – it affects 1:200 to 1:500 people – where is reported that in half of cases it is found a pathogenic mutation. In 2022 it was published international "Expert Consensus Statement on the state of genetic testing for cardiac diseases".

We reviewed the results of genetic testing performed for HCD in our laboratory between January 2019 and January 2023. A total of 675 genetic analysis were carried out for, confirmed or suspected: hypertrophic cardiomyopathy (HCM N = 243), dilated cardiomyopathy (DCM N = 215), arrhythmogenic cardiomyopathy (ACM N = 38), among others.

We found pathogenic or likely pathogenic variants in 130 samples with genetic diagnostic rates for:

HCM 22,2% (N = 54) – with pathogenic (P) or likely pathogenic (LP) variants on *ACTN2, ALPK3, FHOD3, MYBPC3, MYH7, MYL2, PRKAG2, RBM20, RYR2, SLC25A4, TNNI3, TNNT2, TPM1;*
DCM 21.4% (N = 46) *–DSP, FLNC, GLA, LMNA, MYBPC3, MYH7, PKP2, RBM20, RYR2, SCN5A, TNNT2, TPM1, TTN;*
ACM 31,6% (N = 12) – *DSP, GLA, HAMP, KCNJ2, MYBPC3, PKP2, RYR2*.

Currently, the evident benefits of genetic testing in HCD is widely accepted, namely for early disease detection and management. In our cohort it was found P/LP variants on genes with clinical implications for medical management of patients, not included in the 2022 international recommendations. This work aims to contribute to the ongoing discussion of potential benefits of expanded genetic testing in HCD, namely the possibility of reverse phenotyping on cases of clinical uncertainty.

Conflict of Interest: Diana Antunes Genomed Part-time

Chulc/santa marta full time, Ana Coutinho full-time, Yuri Chiodo full-time, Brigida Meireles full-time, Sofia Pérez CHULC/Estefânia Hospital, Maria Carmo-Fonseca IMM full time, Genomed

EP06.015 Prognostic value of microRNA-126-3p for cardiovascular events in a Spaninsh general population

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Background and objectives: Measurement of circulating levels of microRNAs (miRNAs) is emerging as potential biomarkers for cardiovascular disease. Here we estimate the predictive value of a