tools were used together with intuitive filtering and
segregation analysis to narrow down the candidate gene
lists.

Results: In one family, we were able to narrow down the
variants from over 80,000 to 4 variants in 4 novel
candidate genes. Analysis on the other families will
further add to the identification of new genes for CMT and
to the knowledge of the pathogenic pathways involved.

Conclusion: Next generation sequencing technology has
enabled us to further characterise our CMT families which
would otherwise be classified as genetically unknown
cases. In the case of identification of novel genes,
functional work will be performed to validate the
pathogenicity of the mutations.

Disclosure of Interest: None Declared

P068
CBS GENE MUTATIONS DETECTED IN A FILIPINO
INDIVIDUAL WITH HOMOCYSTINURIA
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Objectives: Classical Homocystinuria due to cystathionine
β-synthase (CBS) deficiency is an autosomal recessive
disorder of sulfur metabolism. Clinical manifestations
include mental retardation, dislocation of the optic lens
(ectopia lentis), skeletal abnormalities and a tendency to
thromboembolic episodes. We present the first
mutational analysis of the CBS gene in a Filipino with
Classic Homocystinuria.

Methods: Genomic DNA was extracted from peripheral
blood collected from a diagnosed Filipino patient with
Classical Homocystinuria. The entire coding region of the
CBS gene (17 exons) was PCR amplified and bidirectionally
sequenced using standard protocols.

Results: The patient was found to be compound
heterozygous for two novel mutations. Four known single
nucleotide polymorphisms were also detected in the CBS
gene of the patient. The patient is heterozygous for all the
identified alleles.

Conclusion: This is the first mutational analysis of the CBS
gene done in a Filipino with Classical Homocystinuria who
presented with a novel duplication mutation and a novel
missense mutation. This study suggests that
Homocystinuria due CBS deficiency is a heterogeneous
disorder at the molecular level.

Disclosure of Interest: None Declared

P069
CHARACTERIZATION OF MUTATIONS THROUGH WHOLE
GENE SEQUENCING OF THE GLUCOSE-6-PHOSPHATE
DEHYDROGENASE GENE AMONG FILIPINO CHILDREN
WITH G6PD DEFICIENCY

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Objectives: Glucose-6-phosphate dehydrogenase (G6PD)
deficiency has a high prevalence among Filipinos. This
study aims to characterize the mutations and
polymorphisms in the G6PD gene among Filipino children
aged 0-12 months old with G6PD deficiency and to
document the mean enzyme activity associated with each
of the variants, and to establish a database of G6PD
variants in the Filipino population.

Methods: Patients aged 0-12 months confirmed with
G6PD deficiency through an enzyme assay were recruited.
Whole gene sequencing was performed through PCR
amplification of 12 protein-encoding exons of the G6PD
gene. Sequence variations were classified as mutations,
benign variants unrelated to disease, or variations of
unknown clinical significance.

Results: A total of 113 participants were recruited and
only 101 patients were confirmed to have G6PD
deficiency. Thirty of the G6PD deficient participants were
female while 71 were male. Preliminary results show that
majority of the patients (~67%) had the Viangchan
mutation followed by the Chatham (14%) and Union (8%)
variants. There are also less common variants in the G6PD
gene in the other cases. One male patient was not found
to have a pathogenic variant. All these variants identified
cause an amino acid substitution and have likewise been
reported in other Southeast Asian populations.

Conclusion: Among Filipino newborns confirmed with
G6PD deficiency by enzyme assay, majority of the patients
have the Viangchan mutation.

Disclosure of Interest: None Declared

P070
COMBINED PITUITARY HORMONE DEFICIENCY:
MUTATION ANALYSIS OF POU1F1 AND PROP1 GENES IN
A COHORT OF MALAYSIAN PATIENTS
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Objectives: Combined Pituitary Hormone Deficiency
(CPHD) is a genetic disorder characterized by the
deficiencies of growth hormone (GH) and at least another
one of the other five anterior pituitary hormones (APH).
Many of the CPHD patients are sporadic cases, although
familial cases with autosomal dominant, autosomal
recessive and X-linked forms have been reported. Ten
genes have been reported to cause CPHD (POU1F1,
PROP1, HESX1, LHX3, LHX4, SIX6, OTX2, PTX2, GLI2 and
SOX3), and these genes encode signaling proteins or
transcription factors that are crucial for pituitary
development/organogenesis. Mutations in PROP1 gene is
the most prevalent cause of CPHD, particularly among the
familial cases. Despite the identification of the ten causative genes, the etiology for the majority of CPHD cases is unknown, including some of the familial cases, and this highlights the significance of further analysis to uncover the genetic basis of the disease. To our knowledge, there has not been any report of CPHD mutation analysis from the South East Asian region. This study performed the mutation screening of all coding exons of POUIF1 (CPHD1, MIM#613038) and PROP1 (CPHD2, MIM#262600) in a Malaysian cohort of 12 sporadic cases of CPHD (3 Malays, 5 Chinese and 4 Indians).

**Methods:** All of the patients included in this study have GH deficiency, and deficiency in at least one of the other APH. Four of the cases had small pituitary as revealed by MRI. All of the coding exons, including the intron-exon boundaries for the two genes were PCR-amplified and screened using a combination of SSCP and heteroduplex (HD) analysis. Sanger sequencing was carried out if aberrant bands/HD-shift was detected.

**Results:** We detected four genomic sequence changes in PROP1: c.27T>C [p.(=),[exon 1]; (c.424G>A, p.A142T) [exon 3]; IVS1+13insG [intron 1] and IVS1+3 A>G [intron 1] .These are non-pathogenic variants which have been reported in other studies. We did not detect any sequence change in POUIF1.

**Conclusion:** This study shows a similar finding as of other studies: PROP1 mutation is rare among sporadic cases of CPHD. Whole genome sequencing or exome sequencing might provide better approaches to detect disease causing variants for the unresolved cases.

**Disclosure of Interest:** None Declared

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**P071**

**A PATIENT WITH AORTIC DISSECTION AS A RESULT OF MUTATIONS IN TGFBR2 AND ACTA2 GENES**

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**Objectives:** Thoracic aortic aneurysms and dissections (TAAD) are among the most common and serious chronic diseases of the aorta and severe life-threatening conditions. TAAD affects all parts of the thoracic aorta - ascending aorta, aortic arch, descending aorta and thoracoabdominal area of aorta. TAAD is a genetically heterogeneous group of thoracic aorta disability with reduced penetrance and variable expressivity. TAAD is categorized into 2 broad groups: syndromic such as Marfan syndrome, Loeys-Dietz syndrome, Ehlers-Danlos syndrome type IV and arterial tortuosity syndrome (associated with abnormalities of the other organ system); and non-syndromic (with manifestation restricted to the aorta). Non-syndromic is divided into familial TAAD (FTAAD) and isolated or sporadic form. We detected 2 mutations in 2 different genes (TGFBR2 and ACTA2), which are responsible for FTAAD in a patient with aortic aneurysm dissection during pregnancy and with TAAD positive family history (two first-degree and one second-degree relatives died of aortic aneurysm dissection).

**Methods:** DNA was isolated from peripheral blood. The main FTAAD genes TGFBR2, TGFBR1, ACTA2, SMAD3 and TGFBR2 were analyzed. The DNA analysis of the TGFBR2 and TGFBR1 genes included MLPA, separation of PCR products of all 9 exons by SSCP and direct sequencing of abnormal migrating patterns. ACTA2 and other genes were analyzed by direct sequencing. Newly detected sequence variant was subjected to *in silico* predictions (for its effect on protein function).

**Results:** On the basis of different migration shift in SSCP analysis of TGFBR2 gene, one previously described change, c.383delA (p.Lys128SerfsTer35), was found in patient’s DNA. This deletion is described as a somatic mutation in esophageal and colorectal cancer, but not as germline mutation and not with aortic aneurysm phenotype. Direct sequencing of the ACTA2 gene revealed one novel nucleotide change in exon 3, c.143G>A (p.Gly48Glu). *In silico* analysis performed by prediction software (PMut, PolyPhen-2) indicates this change as pathogenic.

**Conclusion:** We wanted to analyze DNA of all family members to assess the genotype-phenotype correlations. We analyzed DNA from patient’s asymptomatic daughter who has not proved the presence of either mutation, because all symptomatic family members have already died. There is no incidence of any cancer in family history and so we assumed that one of these mutations is responsible for FTAAD in this family.

**Disclosure of Interest:** None Declared

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**P072**

**POPULATION STUDY OF A CLASSICAL MENDELIAN GENETIC MARKER FOR A TASTE SENSITIVITY TO PHENYLTHIOCARBAMIDE IN UKRAINE**

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**Objectives:** The taste sensitivity to phenylthiocarbamide (PTC) is one of the classical genetic markers of a human. PTC is a synthetic compound, which is felt bitter in some individuals (tasters) and tasteless in other (non-tasters). The molecular genetic nature of PTC was determined when describing the gene of the sensitivity receptor to a bitter taste hTAS2R38. PTC is of great interest from the medical point of view since a number of associations of the taster status with human diseases has been found. The aim of this study was to analyze distribution of the sensitivity to PTC in the sample of the population of Ukraine presented by residents of Kharkov and some other populations of Ukraine.

**Methods:** The study involved 255 people (47 males and 208 females) aged from 16 to 20. The PTC solution in the