ABSTRACTS COLLECTION

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P01

Reproductive Genetics

P01.002.B PPARG1 gene methylation in granulosa cells relation to hyperinsulinemia and hyperandrogenism in women with polycystic ovary syndrome

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Background/Objective: one of the most prevalence endocrine disorders in women is Polycystic Ovary Syndrome (PCOS). This syndrome is heterogeneous, and recent evidence suggested that epigenetic events could responsible for the occurrence of this syndrome. one of the most significant epigenetic modifications is DNA methylation, which could decrease gene expression. There is a close connection between energy metabolism and female fertility. PPARG gene plays an important role in lipid and glucose metabolism, and it shows significant role in the evolution of the reproductive system growth and development in embryonic stage. This study aimed to investigate the frequency PPARG1 gene methylation in granulosa cells in PCOS patients with hyperinsulinemia and hyperandrogenism.

Methods: The follicular fluid of 30 normal individuals, 25 women with polycystic ovary syndrome only, 20 PCO women with hyperandrogenism (HA), and 20 PCO women with insulin resistance (IR) were collected. After isolation of granulosa cells from follicular fluid, genomic DNA extracted and after bisulfite DNA treatment, CpG-rich region in PPARG1 gene promoter was selected and methylation-specific polymerase chain reaction (MS-PCR) was performed on bisulfite DNA.

Results: The results analysis revealed a significant difference between the methylation of the PPARG1 gene in four patient groups ($P < 0.005$), indicating that the PPARG1 gene promoter is hypermethylated more significantly in PCO-IR and PCO-HA patients.

Conclusion: The frequency of PPARG1 gene promoter methylation in PCO-IR and PCO-HA individuals were higher than in other groups. So higher methylation would decrease PPARG1 gene expression in ovary, which could cause PCO-IR and PCO-HA in women in reproductive age.

Conflict of Interest: None declared

P01.004.D Severe premature ovarian insufficiency: don't forget about men

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panel, we describe an analysis extension with star allele calling for CYP2D6 using Pangu and other PGx genes using PharmCAT.

Results: We describe a scalable analysis workflow for targeted sequencing panels on PacBio HiFi sequencing systems. We demonstrate this workflow for pharmacogenomics, going from DNA to star allele calling for 10 GeT-RM reference samples, with a public dataset included.

Conclusion: This demonstrative workflow supports the use of HiFi sequencing for the development of scalable pharmacogenomics and its implementation, streamlining translation of sequencing data into phenotype that can help drive clinical decision support for PGx.

Conflict of Interest: Sam Holt PacBio, PacBio, John Harting PacBio, PacBio, Tina Han Twist Bioscience, Twist Bioscience, Leonardo Arbiza Twist Bioscience, Twist Bioscience, Sarah Kingan PacBio, PacBio, Aurelie Souppe PacBio, PacBio, Siyuan Zhang PacBio, PacBio, primo baybayan PacBio, PacBio, christine lambert PacBio, PacBio, Heather Ferrao PacBio, PacBio, Binglan Li: None declared, Katrin Sangkuhl: None declared, Mark Woon: None declared, Ryan Whaley: None declared, Michelle Whirl-Carrillo: None declared, Yao Yang: None declared, Teri Klein PharmGKB, Stuart Scott In-kind sequencing consumables from PacBio, Nina Gonzaludo PacBio, PacBio

P19.057.A Two in one: Pharmacogenetic profiling from whole genomes

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Backgroud: Drugs are usually prescribed using a one-size-fits-all approach, although several frequent pharmacogenetic predispositions affecting drug efficacy and safety are well established. Recently, a large randomised study of the U-PGx project has confirmed the benefit of preemptive pharmacogenetic testing. Furthermore, the costs of whole genome sequencing (WGS) are decreasing, enabling and accelerating genome-scale genetic testing, including pharmacogenetic predispositions.

Methods: Using a bioinformatic pipeline, we extract pharmacogenetic relevant single nucleotide variants and structural variations of whole genomes (60× WGS, PCR-free, PE150) of our patients with rare (aortic) disorders. The results of every patient are interpreted according to the guidelines of the Dutch Pharmacogenetics Working Group (DPWG) used in the U-PGx Project.

Results: The results are presented on the Medication Safety Card (MSC), a personalized pharmacogenetic profile in credit card format. The MSC displays individual medication and dosing recommendations and may be presented to the treating physician or at a pharmacy. As novel findings are expected, the MSC contains a QR-code, providing online access to an up-to-date version of the report.

Conclusions: We developed a WGS-based approach for the implementation of pharmacogenetics by leveraging WGS data instead of requiring a dedicated test. The MSC allows accurate medication selection and dosing, enabling precision medicine. Our approach not only benefits the patients but also saves time and costs, showing novel possibilities for the future of healthcare and personalized medicine.

Conflict of Interest: None declared

P19.059.C Introducing breast cancer genetic risk-based stratified screening service. BRIGHT clinical study. Estonian experience

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Introduction: n Europe, mammographic screening of women aged 50-74 addresses approximately 58% of all breast cancer cases. It is cost-effective and reduces the breast cancer mortality by 20-40%. We introduce BRIGHT genetic risk-based service for addressing the higher risk population below 50 years that is commonly not screened. The risk model comprises of questionnaire for assessing the hereditary cancer risk and a polygenic risk score (PRS) testing.

Materials and Methods: the BRIGHT study will address 2250 women in three clinical centers in Estonia, Sweden and Portugal. In Estonia, the clinical study has been largely completed. In Estonia, several recruitment paths were tested - web-based, pharmacy, breast clinic, primary care.

A simple web-based self-reporting questionnaire was introduced to assess the eligibility for monogenic pathogenic variant testing.

AnteBC polygenic risk score test (Antegenes OÜ, Estonia) was used to assess the breast cancer polygenic risk for all participants.

Results: 12% of women recruited in Estonia were eligible for genetic counselling. 84% of those genetically counselled were referred for MPV testing. In a few cases, the family member was already tested for MPV.

16% of participants had 1.5-fold or a higher genetic risk. In 6% of participants, the risk was increased 2- to 3-fold.

Next steps: clinical follow-up and feedback data will be collected to assess the feasibility of stratified cancer screening.

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P20 Population Genetics and Evolutionary Genetics

P20.002.B Short-term effects of heated tobacco product (HTP) use on DNA methylation profiles and whole transcriptome profiles

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Abstract

Background/Objectives: Heated tobacco products (HTP) have rapidly increased in popularity since 2016, advertised as having