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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Background/Objectives: The exponential growth of unlabeled medical data in the last two decades presents a challenge in the accurate labeling of complex medical data such as syndromic faces. We propose a novel approach that uses a convolutional neural network (CNN) to automatically label syndromic faces with their respective Human Phenotype Ontology (HPO)-terms and predict the patients' disorders. This approach not only helps clinicians with their diagnosis and administration but also facilitates users in the GestaltMatcher DataBase (GMDB) when adding new patient photos or supplementing old ones with more information.

Methods and Results: Our CNN-based approach leverages the tree-like data structure of HPO to allow for multiple levels of abstraction, known as HPO-levels, which help us address the data scarcity of underrepresented cases in the GMDB. This approach also provides new explainable artificial intelligence (XAI) insights into the decision-making process of the black box CNN, as we condition the feature space on both HPO and disorder classification. With the HPO-classifier, we can infer the regions of interest and consider the spatial and descriptive information of the predicted HPO terms to justify the disorder classification.

Conclusion: Our proposed approach for combining HPO and disorder classification for automatic labeling and diagnosis of syndromic faces is another step forward in the field of bioinformatics in genetics. The use of HPO terms in our model inherently makes the process more explainable than most other diagnostic tools. Additionally, it will help to reduce the labor-intensive labeling process and enable clinicians to work more efficiently.

Conflict of Interest: None declared

P18.089.A Orphadata : Orphanet data and tools to power rare disease knowledge generation

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Orphadata (www.orphadata.com) is a platform dedicated to providing downloadable, computable and re-usable aggregated datasets and services derived from the Orphanet rare disease knowledge base (www.orpha.net). Orphadata services aim to help health professionals, academic researchers, industry researchers, policy makers, software editors, advocacy organisations and the biotech/pharma industry better understand rare diseases (RD) and the RD landscape.

Users can access through Orphadata.com Orphadata Science, an open data suite (CC-BY 4.0 licence) derived from the Orphanet knowledge base and recognised as an ELIXIR Core Data Resource and a Global Core Biodata Resource: this includes the Orphanet nomenclature pack for coding of RD in 9 languages, datasets from the Orphanet scientific knowledge base (terminology alignments, classifications, genes associated with rare diseases, clinical signs and symptoms in RD, epidemiology, natural history and functional consequences), and the Orphanet Ontology of Rare Diseases (ORDO) and HPO-ORDO Ontological Module, all updated twice a year. The ORPHAcodes API is also made available to aid the implementation of ORPHAcodes in health information systems and third-party tools so as to improve data interoperability. These products were downloaded over 420 000 times in 2022.

Users can also access Orphanet's textual information, orphan drug and designations, and directories of expert centres, networks of expert centres, medical laboratories and diagnostic tests, patient organisations, and research activities through Orphadata after signature of a Data Transfer Agreement or a service contract depending on their status.

Orphadata will be offering additional APIs and services in 2023 in order to help users make the most of Orphanet data.

Conflict of Interest: David Lagorce Fulltime INSERM US14 - Orphanet, collaborator OD4RD2; EJP RD, ELIXIR-FR; Solve-RD; TEHDaS JA, Valerie Serriere-Lanneau INSERM, US14-Orphanet: Full time, collaborator: EJP-RD, OD4RD2, Marc Hanauer Full-time INSERM, US14 - Orphanet, collaborator OD4RD2; EJP RD, ELIXIR-FR; Solve-RD; EHDS Pilot 2; TEHDaS JA;, advisory board: Scientific Advisory board national support group "Aide aux Jeunes Diabétiques", Support group Chairman (Association ENT'RED-paris, réseau enfance diabète), Charlotte Rodwell Part time (90% FTE) INSERM, US14 - Orphanet No other employment., Collaborator: EJP RD; Solve-RD, Advisory board: Maladies Rares Info Services, Ana Rath Full-time, PI OD4RD2; collaborator: EJP RD; Solve-RD; EHDS Pilot 2; TEHDaS JA; (tu as besin des tous les numéros de contrats? Sylvie peut te le donner, advisory board: ERN-LUNG; ERN-BOND; Share4Rare

P18.090.B The dark side of Moon and other commercial genome analysis or interpretation tools

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Background/Objectives: Genome diagnostics requires software tools that are not only accurate and fast but also available over a reasonable time. Sudden unavailability of such tools can severely impact established pipelines. Current example is the recent discontinuation of the in-2017-launched fast and reliable variant interpretation platform Moon outside of the USA. Since Moon is a cloud-based artificial intelligence engine, after its discontinuation no further use is possible, e.g. local for temporary life cycle extension. Here, we address the disappearance of innovative genome analysis tools, suggesting potential solutions.

Methods: Considering "make vs. buy" and software life cycle management in (bio-)informatics, we explored various options for replacing discontinued genome analysis tools, such as developing new software in-house or through (open-source) collaborations and acquiring (long-term) commercial solutions.

Results: Short term, "buy" an on-site tool is clearly preferred. Long term, "make" an open-source tool, like Linux/Firefox/OpenOffice, would be the solution to reduce the risk of a Moon-like complete loss of access. Software for Oxford-Nanopore-Technologies sequencers and NCBI BLAST search are well-known examples of powerful open-source solutions for genome analysis. The residual risk of open-source projects being abandoned, leading to non-update scenarios is acceptable, since in life cycle management it is still much better than the worst-case scenario of a commercial (cloud-based) tool, where the software is suddenly inaccessible.

Conclusions: To deal with the sudden disappearance of software, we propose that the genomics community support each other by redirecting resources from various in-house developments towards a few open-source genome analysis tools accessible for long-term usage.

Conflict of Interest: None declared

P18.091.C Assessment of sequencing coverage uniformity for two whole-exome enrichment capture solutions

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