CHRD 2021: Abstract & Poster Submission Form

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Research Category:

- ◉ Basic Science
- ○ Clinical
- ○ Community Health / Policy

What was your role in the project?

- ☐ Design
- ☐ Perform Experiments
- ☑ Analyze Data
- ☑ Write Abstract
- ☐

Presenter Status:

- ◉ Undergraduate Students
- ○ Masters Student
- ○ PhD Student
- ○ Post-Doctoral Fellows
- ○ Residents
- ○ Non-Trainee

Title

Genomics-Driven Drug Repurposing Analyses to Guide the Identification of Novel Treatments to Improve Reproductive Outcomes in Women with Polycystic Ovary Syndrome

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Background

Polycystic ovary syndrome (PCOS), which affects 5-10% of reproductive aged females, has been shown to be significantly influenced by genetics.

Objective

This project aims to identify heritable gene expression profiles that are associated with PCOS. These data analyses will be used to guide the identification of novel treatments to improve reproductive outcomes in women with PCOS.

Methods

We performed a transcriptome-wide association study (TWAS) to uncover heritable gene expression profiles that are associated with PCOS. After colocalization analyses, the lead variants associated with both gene expression and PCOS were included in a Phenome-wide association study (PheWAS) using the UK Biobank (UKBB) data. Drug repurposing using the data housed in CMap were performed to identify small molecules which induce gene expression changes that are significantly dissimilar to the PCOS-associated gene expression profiles.

Results

The TWAS analyses revealed that increased expression of ARL14EP in the reproductive organs was significantly associated with PCOS (P=1.6x10-6). Upon colocalization evaluation, rs4071559 was shown to be associated with both an increase in PCOS risk and ARL14EP expression. PheWAS analyses revealed that this genetic variant was associated with a number of traits of relevance to PCOS, including increased length of menstrual cycles (P=8.5x10-34), a key clinical feature of PCOS. The CMap analysis revealed a number of possible therapeutic candidates, including prednisone, which induces ovulation in patients with PCOS by reducing adrenal androgen production.

Conclusion

This TWAS of PCOS has provided evidence for the role of ARL14EP in PCOS disease mechanisms and has uncovered candidates for the treatment of PCOS. This study has generated knowledge that can be used to guide strategies to improve the efficiency and safety of therapeutics used in the treatment of PCOS. This information aims to improve reproductive and pregnancy outcomes in women with PCOS, and ultimately, the health of infants born to these mothers.

Authors

- For each author, please click "**[+] Add Item**" and provide the author's information

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