SNP ANALYSIS OF lncRNA GENES ASSOCIATED WITH POLYCYSTIC OVARY SYNDROME USING GWAS CATALOG AND THE 1000 GENOMES PROJECT

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**Introduction:** According to WHO, around 8-13% of women of reproductive age suffer from polycystic ovary syndrome (PCOS), while up to 70% of women worldwide with PCOS remain undiagnosed. PCOS is the most common cause of anovulation and the main cause of infertility. Previously, scientists have observed a large number of ncRNAs with altered levels in the plasma, serum or other specimens from patients with PCOS (Han, J., e.a., 2019; Liangshan Mu, e.a., 2021; ElMonier, A. A., 2023). LncRNAs have been identified that regulate the response of androgen, estrogen and progesterone receptors, suggesting that lncRNAs play a role in the hormone regulatory system in PCOS (Zhao X, e.a., 2004; Nabi, M.,e.a.,2023). One of the reasons for impaired expression of reporter genes could be SNP alleles of lncRNA genes (Ali, R. M., e.a. 2022; Gonzalez-Moro, I.,2023, Li, Y. K.,2023).

**Methods:** For testing this hypothesis, we examined 10 Genome-Wide Association Studies comprising a total of 48881 cases and 837947 controls from four populations: European, Chinese, African, American (https://www.ebi.ac.uk/gwas/efotraits/EFO\_0000660). From these GWA studies we obtained 17 significant SNPs in 11 lncRNA mapped genes: *ARL14EP-DT, CASC22, IRF1-AS1, KAZN-AS1, LINC01060, LINC01229, LINC01826, LINC02055, LINC02529, MAFTRR, SSTR5-AS1.* Then we explored the gene expression of abovementioned lncRNA genes in NCBI Gene database (https://www.ncbi.nlm.nih.gov/gene).

**Results:** The table shows the allele frequences of 17 significant polymorphic loci associated with PCOS in various populations of the world (according to the 3rd phase of the 1000 Genomes project).

The frequencies of polymorphic loci of long non-coding RNAs associated with PCOS in various populations of the world according to The 1000 Genomes Project.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **SNP and its allele** | **Mapped gene**  **(Reference assembly: hg38)** | **Allele frequency in African population** | **Allele frequency in American population** | **Allele frequency in East Asian population** | **Allele frequency in European population** |
| rs10835638-T | *ARL14EP-DT* | 0.047 | 0.117 | 0.032 | 0.143 |
| rs11031002-A | *ARL14EP-DT* | 0.045 | 0.095 | 0.031 | 0.121 |
| rs11031005-T | *ARL14EP-DT* | 0.983 | 0.906 | 0.969 | 0.860 |
| rs11031006-A | *ARL14EP-DT* | 0.047 | 0.097 | 0.032 | 0.141 |
| rs4784165-G | *CASC22* | 0.435 | 0.330 | 0.359 | 0.260 |
| rs8043701-A | *CASC22* | 0.795 | 0.705 | 0.674 | 0.813 |
| rs13164856-T | *IRF1-AS1* | 0.626 | 0.687 | 0.616 | 0.704 |
| rs78025940-A | *KAZN-AS1* | NA | 0.016 | 0.087 | 0.023 |
| rs7666129-A | *LINC01060* | NA | NA | NA | NA |
| rs3813583-A | *LINC01229* | 0.536 | 0.576 | 0.715 | 0.626 |
| rs7574059-C | *LINC01826* | 0.885 | 0.653 | 0.617 | 0.624 |
| rs10505648-A | *LINC02055* | 0.723 | 0.640 | 0.914 | 0.484 |
| rs17186366-C | *LINC02529* | 0.022 | 0.042 | 0.056 | 0.111 |
| rs3813583-A | *MAFTRR* | 0.536 | 0.576 | 0.715 | 0.626 |
| rs500492-A | *SSTR5-AS1* | NA | NA | NA | NA |

As can be seen from the table, significant polymorphic loci of lncRNAs have low allele frequency values for almost all SNPs in *ARL14EP-DT* gene(exceptrs11031005-T), rs17186366-C in *KAZN-AS1* geneand rs78025940-A in *LINC02529* gene*.* Alleles of other SNPs in lncRNAs genes are quite widely distributed: The frequencies of significant polymorphic loci vary from 26 % (rs4784165-G in European population) to 98% (rs11031005-T in African population). Allele frequences of the polymorphic locus rs7666129-A in *LINC01060* gene and rs500492-A in *CCR5-AS1* gene are not available for all studied populations.

Next, we found out that 4 out of 11 lncRNAs genes are expressed exclusively in testis, according to data from Fagerberg L. et al. in NCBI Gene database (Fagerberg L. et al., 2014). These genes are: *CASC22* (Cancer Susceptibility Candidate 22); *KAZN-AS1* (KAZN antisense RNA 1); *LINC02529* (long intergenic non-protein coding RNA 2529); *LINC01826* (long intergenic non-protein coding RNA 1826). Expression of these genes in the ovary may contribute to the development of hyperandrogenemia associated with PCOS. Such aberrant expression of these lncRNAs in PCOS may lead to aberrant steroidogenesis and could potentially be used as diagnostic biomarkers.

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**Keywords:** PCOS, SNP, lncRNAs, GWAS Catalog, 1000 Genomes.

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