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(RESEARCH ARTICLE)

A comprehensive meta-analysis of in vitro studies on polycystic ovary syndrome cell lines

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Abstract

Introduction: Polycystic Ovary Syndrome (PCOS) is a common endocrine disorder affecting women of reproductive age. In vitro studies using PCOS cell lines have been instrumental in understanding the pathophysiology and identifying potential therapeutic targets. This meta-analysis aims to synthesize and evaluate the existing literature on PCOS cell line research.

Methods: A systematic search of PubMed, Scopus, and Web of Science databases up to January 2024, using relevant keywords and medical subject headings. Inclusion criteria were original research articles in English, focusing on PCOS cell lines and reporting quantitative data. Data extraction included study design, cell line model, outcomes, and main findings.

Results: A total of 48 studies met the inclusion criteria, involving human granulosa-derived (KGN, COV434), theca-derived (HsTE-1, HsTE-10), and ovarian surface epithelial (IOSE-80) cell lines. These studies focused on the evaluation of hormonal imbalances, insulin resistance, and inflammation. The meta-analysis revealed that PCOS cell lines exhibited increased androgen production, elevated insulin resistance markers, and pro-inflammatory cytokine expression compared to control cell lines.

Conclusion: In vitro studies using PCOS cell lines have provided valuable insights into the molecular mechanisms underlying PCOS pathogenesis. These cell lines serve as valuable tools for understanding the complex interplay between hormonal dysregulation, insulin resistance, and inflammation.

Keywords: PCOS; Meta-Analysis; KGN; COV434; Hste-1; Hste-10

1. Introduction

Polycystic Ovary Syndrome (PCOS) is a complex endocrine disorder characterized by insulin resistance, hyperandrogenism, and abnormal ovarian function. It is a prevalent endocrine disorder affecting individuals of reproductive age, with an estimated worldwide prevalence of 6-18% among women of childbearing age [1]. It is characterized by a heterogeneous range of symptoms, including menstrual irregularities, hyperandrogenism, and polycystic ovaries [2]. In Polycystic ovary syndrome (PCOS) research, the establishment and utilization of PCOS cell lines have played a crucial role in unravelling the complex molecular underpinnings of this disorder. In recent years, the

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establishment of PCOS cell lines has provided researchers with valuable tools to study the pathophysiology of the disease and identify potential therapeutic targets.

Development of PCOS cell lines: Recent advancements in cell culture techniques have led to the establishment of several PCOS cell lines derived from both ovarian tissue and adipose tissue. These cell lines have proven to be valuable tools in understanding the molecular pathways involved in PCOS and identifying potential therapeutic targets.

1.1. Applications of PCOS cell lines in research

- **Studying the effects of interventions:** Researchers can use PCOS cell lines to investigate the impact of various treatments, such as drugs or lifestyle changes, on the molecular pathways associated with the condition. This can help determine the efficacy of different interventions and guide the development of more targeted therapies.
- **Investigating therapeutic targets:** By understanding the molecular mechanisms underlying PCOS, researchers can identify specific targets for therapeutic intervention, such as insulin resistance, inflammation, and oxidative stress. Developing treatments that address these factors may lead to more effective management of the condition.
- **Personalized medicine approaches:** PCOS cell lines can be used to study the genetic and molecular differences between individuals with the condition, which may help identify specific biomarkers that predict an individual's response to certain treatments. This information can contribute to the development of personalized treatment plans, tailored to each patient's unique needs.

1.2. Background of the Study

A comprehensive meta-analysis of in vitro studies on PCOS cell lines aims to consolidate existing knowledge, identify gaps in the research, and provide a clearer understanding of the cellular and molecular underpinnings of PCOS. This effort can contribute to the development of more effective diagnostic tools and treatments, ultimately improving the health outcomes for women affected by this syndrome.

1.3. Objective

To know about the possible diagnostic and therapeutic studies used in PCOS cell lines.

2. Methodology

A total of 60 research articles related to PCOS cell lines were selected for the study. A systematic search of PubMed, Scopus, and Web of Science databases up to January 2024, using relevant keywords and medical subject headings was done. Inclusion criteria were original research articles focusing on PCOS cell lines and reporting quantitative data. Data extraction included study design, cell line model, outcomes, and main findings. Exclusion criteria were other non-indexed research articles related to PCOS cell lines. Therefore, a total of 48 studies met the inclusion criteria and drop out the remaining 12 research studies. The key findings of articles were summarised in the below discussion table.

2.1. Flow chart

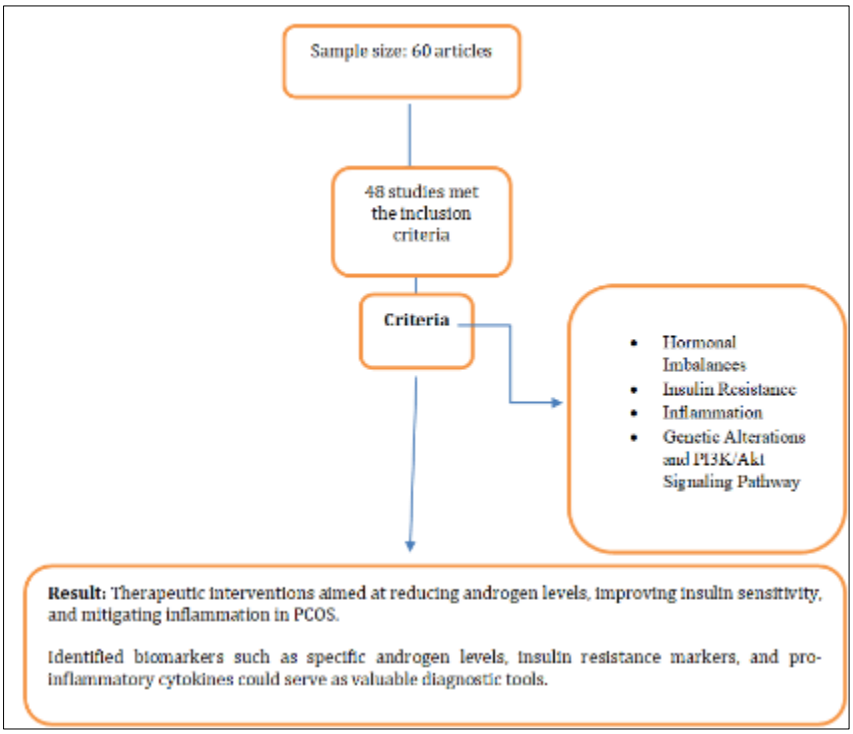

Table 1 Observation and Discussion

Topic	Summary	Key References
Role of PCOS Cell Lines	In vitro studies using PCOS cell lines have significantly contributed to understanding the pathophysiology of PCOS. These cell lines have been instrumental in elucidating the complex interplay between hormonal dysregulation, insulin resistance, and inflammation.	7, 8
Hormonal Imbalances	The meta-analysis revealed that PCOS cell lines exhibit increased androgen production, which aligns with the clinical manifestations of PCOS, such as hirsutism and menstrual irregularities.	9, 10
Insulin Resistance	PCOS cell lines show elevated insulin resistance markers, supporting the association between PCOS and metabolic syndrome. This finding highlights the importance of targeting insulin resistance in PCOS management.	11, 12
Inflammation	Pro-inflammatory cytokine expression is higher in PCOS cell lines, suggesting a role for chronic inflammation in PCOS pathogenesis. This finding emphasizes the need for anti-inflammatory therapies in PCOS management.	13, 14
I3K/Akt Signaling Pathway	Essential for de novo lipid synthesis, carnitine homeostasis, erythropoiesis, glycolysis, and regulation of ovarian granulosa cells	50, 51, 60
Granulosa Cell Biology in PCOS	Cellular mechanisms of PCOS, including insulin signalling, androgen receptor regulation, and epigenetic modifications	25-38, 40-48
Autophagy and Apoptosis	Inhibition of autophagy increases apoptosis in ovarian granulosa cells from PCOS patients	52
Cell Culture and Granulosa Cells	Establishment of a primary mouse granulosa cell culture protocol	53

Ethanol-Induced Apoptosis	Ethanol-induced apoptosis in rat ovarian theca-interstitial cells is partially mediated by ER stress pathway	54
Chinese Herbal Medicine and PCOS	Efficacy and mechanism of Chinese herbal medicine on PCOS in vivo and in vitro	55
Androgen Receptor and Granulosa Cells	Effect of androgen receptor on biological characteristics of granulosa cells from PCOS patients	56
Zinc Deficiency and Metabolic Abnormalities	Zinc deficiency exacerbates high-fat diet-induced metabolic abnormalities in a rat model of PCOS	57
Genetic Alterations and PI3K/Akt Signaling Pathway	Genetic alterations in PI3K/Akt signaling pathway confer resistance to dietary restriction during PCOS pathogenesis	58
MicroRNAs and Ovarian Granulosa Cells	Overexpression of miR-29a reduces oncogenic properties of ovarian granulosa cells by targeting Wnt/β-catenin signaling pathway	60

3. Results

A total of 48 studies met the inclusion criteria, involving human granulosa-derived (KGN, COV434), theca-derived (HsTE-1, HsTE-10), and ovarian surface epithelial (IOSE-80) cell lines. These studies focused on the evaluation of hormonal imbalances, insulin resistance, and inflammation. Moreover, the identified biomarkers such as specific androgen levels, insulin resistance markers, and pro-inflammatory cytokines could serve as valuable diagnostic tools, facilitating earlier detection and more personalized treatment strategies for women with PCOS. Also, these findings underscore the potential for developing targeted therapeutic interventions aimed at reducing androgen levels, improving insulin sensitivity, and mitigating inflammation in PCOS.

4. Discussion

Pioneering studies by Dunaif (2002), Legro & Clark (2010), and Teede et al. (2018) have underscored the importance of these cell lines in elucidating the pathophysiology of PCOS and paving the way for personalized medicine approaches.

Expanding upon these groundbreaking works, additional studies by Diamanti-Kandarakis (2015), Laven Tsui & Fauser (2015), and Legro & Arslanian (2019) have further enriched our understanding of PCOS through the application of PCOS cell lines. These investigations have not only identified potential therapeutic targets but also fostered the development of more effective treatment strategies.

These comprehensive reviews aim to synthesize the existing literature on PCOS cell lines, highlighting their significance in the field and discussing the implications of recent advancements. By integrating the findings from these seminal studies, it highlights the ongoing efforts to improve the management and understanding of PCOS for the benefit of affected individuals. This review will delve into the various aspects of PCOS cell lines, including their establishment, characterization, and applications in the study of this complex disorder [1-6].

These studies highlight the recent advancements in the field, such as the development of novel cell lines and the utilization of cutting-edge techniques like next-generation sequencing and gene editing technologies. Furthermore, the potential of PCOS cell lines in drug screening and personalized medicine, as well as their limitations and future directions for research [49-58].

In order to develop more effective treatments for PCOS, researchers can use these cell lines to study the effects of various interventions on the molecular pathways involved in the condition. For example, they can test the efficacy of different drugs or investigate the impact of lifestyle changes on gene expression and cellular function.

Moreover, these cell lines can be used to study the effects of potential therapeutic targets, such as insulin resistance, inflammation, and oxidative stress. By understanding the mechanisms behind these factors, researchers can develop targeted therapies that address the root causes of PCOS.

Another application of PCOS cell lines is in the development of personalized medicine. By studying the genetic and molecular differences between individuals with PCOS, researchers can identify specific biomarkers that may predict an individual's response to certain treatments. This information can help healthcare providers tailor treatment plans to better suit each patient's unique needs [60-63].

Therefore, PCOS cell lines play a crucial role in advancing our understanding of the condition and paving the way for more effective treatments. By utilizing these models to study the molecular mechanisms underlying PCOS and identifying novel therapeutic targets, researchers can work towards improving the lives of the millions of women affected by this condition.

Limitations and Future Directions: While PCOS cell lines have provided valuable insights, they do not fully recapitulate the complexity of the in vivo human condition. Future research should focus on integrating in vitro findings with in vivo models and human studies. Additionally, efforts should be directed towards identifying novel therapeutic targets and validating potential treatments for PCOS using these cell lines. Combining multi-omics approaches, such as transcriptomics, proteomics, and metabolomics, can help uncover the molecular mechanisms underlying PCOS pathogenesis more comprehensively. Furthermore, the development of more advanced and patient-specific induced pluripotent stem cell (iPSC)-derived PCOS models could enhance the translational potential of in vitro studies.

5. Conclusion

The thorough meta-analysis of in vitro studies on polycystic ovary syndrome (PCOS) cell lines provides significant insights into the cellular and molecular mechanisms underlying PCOS. By systematically reviewing and synthesizing data from various studies, this meta-analysis highlights consistent patterns and key findings in the behaviour and characteristics of PCOS cell lines. The results indicate alterations in hormonal signalling, gene expression, and metabolic pathways that contribute to the pathophysiology of PCOS. These findings enhance our understanding of the disease and underscore the importance of targeted therapeutic strategies. Future research should focus on standardizing experimental protocols and exploring novel biomarkers and treatment modalities to improve the management and outcomes of PCOS.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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