Journal of Biosciences and Medicines, 2026, 14(4), 488-501
https://www.scirp.org/journal/jbm
ISSN Online: 2327-509X
ISSN Print: 2327-5081

Research Progress of PI3K/Akt Signaling Pathway in Polycystic Ovary Syndrome

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How to cite this paper: Li, L.N. and Qin, X. (2026) Research Progress of PI3K/Akt Signaling Pathway in Polycystic Ovary Syndrome. *Journal of Biosciences and Medicines*, **14**, 488-501.
https://doi.org/10.4236/jbm.2026.144034

Received: September 10, 2026
Accepted: April 27, 2026
Published: April 30, 2026

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Abstract

Polycystic ovary syndrome (PCOS) is an endocrine and metabolic disease driven by multiple factors, which seriously affects female reproduction and metabolic homeostasis. With the deepening of molecular mechanism research, phosphatidylinositol 3-kinase/Protein Kinase B (PI3K/Akt) signaling pathway has gradually become a key entry point to understand the pathogenesis of PCOS. Existing studies have shown that the signaling pathway is deeply involved in the pathological process of PCOS by regulating inflammatory response, oxidative stress, proliferation, apoptosis and autophagy of ovarian granulosa cells. At the same time, the changes of its activity are closely related to the core pathological features such as hyperandrogenism, lipid metabolism disorders and insulin resistance. This article systematically reviews the multiple regulatory effects of PI3K/Akt signaling pathway in the pathogenesis of PCOS, in order to provide a new perspective and intervention targets for disease research.

Keywords

Polycystic Ovary Syndrome, PI3K/Akt Signaling Pathway, Pathogenesis

1. Introduction

Polycystic ovary syndrome (PCOS) is one of the most common endocrine and metabolic diseases in women of reproductive age, with a global incidence of about 6% - 10% [1]. The clinical manifestations are highly heterogeneous, mainly including ovulation dysfunction, hyperandrogenism, and polycystic ovarian changes, of-

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ten accompanied by metabolic disorders such as insulin resistance, obesity, and dyslipidemia. It can significantly increase the risk of long-term complications such as type 2 diabetes mellitus, cardiovascular disease and endometrial cancer [2]. Although the etiology of PCOS is not fully understood, the interaction between genetic factors, environmental factors and lifestyle is considered to be an important driver of the disease [3]. In recent years, molecular biology research has focused on the role of signal pathway abnormalities in the pathological mechanism of PCOS, among which PI3K/Akt signaling pathway has become a hot research direction of PCOS because of its core regulatory functions in cell growth, metabolism, survival and other aspects [4] [5]. In-depth exploration of the relationship between PI3K/Akt pathway and PCOS is helpful to clarify the mechanism of the occurrence and development of the disease and provide theoretical support for clinical prevention and treatment [6].

2. Overview of PI3K/Akt Signaling Pathway

PI3K/Akt signaling pathway is an important signal transduction pathway in cells, which is widely involved in cell proliferation, differentiation, metabolism, survival and other biological processes. PI3K is a lipid kinase [7], which can be divided into three Classes I, II and III [8]. Type I PI3K is activated by binding to receptor tyrosine kinase (RTK) or G protein-coupled receptor (GPCR) under the stimulation of insulin and growth factors [9]. Activated PI3K catalyzes phosphatidylinositol-4,5-diphosphate (PIP2) to phosphatidylinositol-3,4,5-triphosphate (PIP3), which acts as a second messenger to recruit and activate protein kinase B (Akt) [10]. Akt regulates cell metabolism, protein synthesis, cell cycle, and apoptosis by phosphorylates downstream target proteins, such as mammalian target of rapamycin (mTOR) [8], glycogen synthase kinase-3β (GSK-3β) [11], and forkhead transcription factor O subfamily (FoxO) [12]. Under normal physiological conditions, PI3K/Akt pathway maintains the homeostasis of metabolism and reproductive functions. When the PI3K/Akt pathway is abnormally activated or inhibited, it may cause a variety of diseases, including metabolic diseases, tumors and endocrine disorders.

3. The Pathological Relationship between PI3K/Akt Signaling Pathway and PCOS

3.1. Regulation of Inflammation and Oxidative Stress

PCOS patients often show a state of chronic low-grade inflammation, with significantly increased levels of inflammatory factors such as tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6), accompanied by enhanced oxidative stress, increased generation of reactive oxygen species (ROS), and decreased activity of antioxidant enzymes [13]. Studies have shown that PI3K/Akt signaling pathway plays a dual role in the regulation of inflammation and oxidative stress [14]. On the one hand, activated Akt can phosphorylate and inhibit NF-κB signaling pathway, reduce the transcription and release of TNF-α, IL-6 and other inflammatory

factors, thereby reducing inflammatory response. YKL-40 (CHI3L1), a glycoprotein secreted by a variety of cells such as neutrophils and macrophages, is increased in follicular fluid of women with PCOS and ovaries of PCOS rats [15]. Ykl-40 knockout activates the PI3K/Akt signaling pathway and inhibits the nuclear translocation of Nf-κb in the cytoplasm, reduces the apoptosis and inflammatory factor levels of ovarian granulosa cells, and enhances cell proliferation and antioxidant capacity. On the other hand, Akt enhances cellular antioxidant capacity and reduces ROS levels by up-regulating the expression of antioxidant enzymes such as superoxide dismutase (SOD) and glutathione peroxidase (GPx). In a study of PCOS rat model [16], it was found that the level of malondialdehyde (MDA) in rat ovary was significantly increased, the activity of superoxide dismutase (SOD) was decreased, and the levels of inflammatory markers were abnormally increased. Mesenchymal stem cell transplantation can activate the PI3K/Akt signaling pathway, effectively reduce the level of MDA in ovarian tissue, increase the activity of SOD, and significantly down-regulate the levels of inflammatory factors, so as to regulate the balance of oxidation-antioxidant system and inflammatory response. On the contrary, when the PI3K-Akt pathway was inhibited by LY294002, the above indicators of oxidative stress and inflammation were worsened. In the PCOS model, the activity of PI3K/Akt pathway is reduced, which leads to excessive activation of NF-κB, the release of inflammatory factors, and the expression of antioxidant enzymes is reduced, which aggravates oxidative stress, and then damages ovarian function and affects follicular development. Studies have shown that macrophages can be activated and polarized into M1 type (classical activation pathway) and M2 type (alternative activation pathway) [17], and the activation of M1 type macrophages leads to the production of proinflammatory cytokines and ROS [18]. In the granulosa cells of PCOS, the proportion of pro-inflammatory M1 and anti-inflammatory M2 macrophages is unbalanced, and the abnormal polarization of M1 macrophages is biased toward M1 macrophages [19], which leads to the activation of pro-inflammatory signaling pathways such as nuclear factor-κB, while the decreased polarization of M2 macrophages leads to the inhibition of PI3K/Akt and other anti-inflammatory pathways, which further leads to the secretion of inflammatory factors [20]. As a result, the dominant follicle cannot be produced. Gong *et al.* found that there were OS state, mitochondrial dysfunction, apoptosis and down-regulation of PI3K/Akt signaling pathway in granulosa cells (GCs) of PCOS patients [21]. GH treatment can significantly activate the PI3K/Akt signaling pathway, promote the expression of p-PI3K/PI3K, p-Akt/Akt and p-FOXO1 proteins, inhibit the pro-apoptotic genes FOXO1, Bax, caspase-9 and caspase-3, and activate the anti-apoptotic gene Bcl-2. Thus, it can inhibit the accumulation of ROS in GCs, reduce the apoptosis rate, alleviate oxidative stress injury and apoptosis of GCs in PCOS patients, and further improve the quality of oocytes. In conclusion, the above studies have fully demonstrated that PI3K/Akt signaling pathway plays an important role in the regulation of oxidative stress and anti-inflammation in the pathological process of PCOS.

3.2. Regulation of Ovarian Granulosa Cell Function

The normal proliferation, differentiation and apoptosis of ovarian granulosa cells are essential for follicular development and ovulation [22]. GCs in patients with polycystic ovary syndrome (PCOS) often show pathological features such as proliferation inhibition, aggravated apoptosis and disordered autophagy. Han *et al.* found through bioinformatics analysis that PD-1/PD-L1 genes were differentially expressed in granulosa cells of PCOS patients, and were enriched in apoptosis and PI3K/Akt signaling pathways [23]. *In vitro* experiments confirmed that up-regulation of PD-L1 could activate the PI3K/Akt pathway and inhibit the apoptosis of granulosa cells. Sun *et al.* found that Kisspeptin expression was down-regulated in ovarian granulosa cells of PCOS rats [24]. Overexpression of Kisspeptin can activate the PI3K/Akt signaling pathway, thereby promoting KGN cell proliferation and inhibiting apoptosis, while reducing oxidative stress. Therefore, Xu *et al.* found that PI3K/Akt signaling pathway is a key pathway to regulate the function of granulosa cells [25].

In PCOS patients and animal models, it is often observed that the activity of PI3K/Akt pathway is down-regulated, which leads to the arrest of granulosa cell proliferation and cell cycle arrest in G1 phase. At the same time, the expression of pro-apoptotic protein Bax is increased [26], the expression of anti-apoptotic protein Bcl-2 is decreased, and the apoptosis rate is significantly increased. Ji *et al.* found that endoplasmic reticulum stress-induced lncRNA LINC00173 was significantly up-regulated in granulosa cells of PCOS patients, which promoted granulosa cell apoptosis by inhibiting the downstream PI3K/Akt pathway [27]. Chen *et al.* found that the expression of lncRNA HOTAIR was up-regulated in PCOS, and knockdown of HOTAIR could improve the ovarian function of PCOS rats through the IGF-1-mediated PI3K/Akt pathway [28]. Further *in vitro* experiments showed that knockdown of HOTAIR inhibited the phosphorylation of PI3K/Akt. Moreover, knockdown of HOTAIR increased the viability of KGN cells and inhibited apoptosis. Ji *et al.* found that ARID1A expression was down-regulated in serum of PCOS patients and ovarian granulosa cells of PCOS mice [29]. Overexpression of ARID1A can inhibit the PI3K/Akt pathway, thereby inhibiting granulosa cell proliferation and promoting its apoptosis. They further used the PI3K/Akt pathway inhibitor LY294002 to treat granulosa cells and found that it had a similar effect to ARID1A overexpression and was able to reverse the effects of si-ARID1A on granulosa cell proliferation and apoptosis.

In addition, the PI3K/Akt pathway is also involved in the regulation of autophagy in granulosa cells. Autophagy is an important mechanism for cells to maintain homeostasis in the internal environment. Moderate autophagy helps to remove damaged organelles and protein aggregates and maintain cell function [30] [31]. In PCOS, inhibition of PI3K/Akt pathway leads to abnormal activation of autophagy, excessive autophagy causes granulosa cell damage, and affects the normal development and maturation of follicles. Chen *et al.* studied the effect of acupuncture treatment on PCOS rats and found that acupuncture could down-regulate

LncMEG3 expression, thereby inhibiting PI3K/Akt/mTOR pathway, reducing granulosa cell autophagy, normalizing granulosa cell proliferation, and ultimately improving abnormal follicular development [32]. According to the experimental research data of Xu *et al.*, Metformin has a significant therapeutic effect on the rat model of polycystic ovary syndrome (PCOS) by regulating the PI3K/Akt/mTOR signal transduction pathway to reduce the autophagy activity of granulosa cells [33]. Ma *et al.* studied the role of Wnt5a in PCOS and found that Wnt5a and autophagy-related proteins were significantly increased in KGN cells induced by DHT; Downregulation of Wnt5a can activate the PI3K/Akt/mTOR pathway, inhibit granulosa cell autophagy, and improve ovarian pathological changes and sex hormone levels in PCOS mouse model [34]. Wang *et al.* studied the effect of Protocatechuic acid on PCOS mouse model and found that protocatechuic acid could inhibit ROS generation, autophagy and apoptosis of PCOS ovarian granulosa cells by activating PI3K/Akt/mTOR axis, thereby alleviating PCOS symptoms [35].

3.3. Mechanism of Hyperandrogenism

Hyperandrogenism is one of the core features of PCOS, which is mainly caused by increased androgen synthesis in the ovary and adrenal gland [36]. The PI3K/Akt signaling pathway is involved in the regulation of androgen synthesis by regulating the expression and activity of key enzymes such as steroidogenic acute regulatory protein (StAR), cytochrome P450 family proteins (CYP17A1, CYP11A1). Studies have found that activation of the PI3K/Akt pathway can promote the expression of StAR protein, accelerate the transport of cholesterol to mitochondria, and provide a substrate for androgen synthesis [37]. Meanwhile, it can up-regulate the expression of CYP17A1, enhance the activities of 17α-hydroxylase and 17, 20-lyase, and promote the synthesis of androgen.

Importantly, hyperandrogenism does not occur in isolation but is closely linked with metabolic abnormalities in PCOS. Through the PI3K/Akt signaling pathway, excessive androgen levels can influence insulin signaling and lipid metabolism, forming a complex regulatory network. Conversely, insulin resistance and dyslipidemia can further stimulate androgen production, creating a vicious cycle that exacerbates PCOS progression.

In PCOS, due to the dysfunction of the PI3K/Akt pathway, the expression of enzymes related to androgen synthesis is abnormal, and the production of androgens is increased, resulting in hyperandrogenism, which interferes with the normal function of the hypothalamic-pituitary-ovarian axis and affects ovulation. Studies have found that excessive androgen exposure during pregnancy may affect the development of female fetuses [38]. In DHEA-induced PCOS obese mouse model, intervention with adiponectin (APN, 10mg/kg/day) in the first trimester of pregnancy showed that serum testosterone levels were significantly lower in the maternal PCOS + APN group than in the maternal PCOS group in the first trimester, and serum testosterone levels were also significantly lower in the adult female offspring. In addition, the duration of late estrus in the oestrous cycle was shortened, and the phenotypes of PCOS-like reproductive disorders and meta-

bolic disorders such as obesity, insulin resistance, impaired glucose tolerance and hyperlipidemia were significantly improved. Further analysis showed that the expression levels of p-AMPK, PI3K and Akt in the ovaries of the offspring PCOS group were significantly lower than those of the control group, while those of the offspring PCOS + APN group were significantly higher than those of the control group. These results indicate that APN intervention during early pregnancy can reduce the adverse effects of maternal hyperandrogenism on female offspring by activating AMPK/PI3K-Akt signaling pathway, and correct the PCOS-like endocrine phenotype and metabolic disorders in adult offspring. In a rat model of PCOS induced by dehydroepiandrosterone (DHEA), Zuo *et al.* found that DHEA downregulates the expression and secretion of IFN-γ in granulosa cells, and inhibits the effects of IFN-γ on cell proliferation and apoptosis by activating the PI3K/Akt pathway [39]. This means that androgen can directly affect the activity of PI3K/Akt pathway in ovarian granulosa cells, and then affect the survival and function of cells, which may be one of the mechanisms of hyperandrogenism leading to ovarian dysfunction (such as follicle development arrest and increased granulosa cell apoptosis). In conclusion, there is a close relationship between hyperandrogenism and PI3K-Akt signaling pathway in the occurrence and development of PCOS, and this relationship is a key link to understand the complex pathophysiological mechanism of PCOS. However, the specific molecular mechanisms of the relationship between hyperandrogenism and PI3K-Akt pathway still need to be further studied.

3.4. Disorders of Lipid Metabolism

Lipid metabolism disorders in PCOS are closely interconnected with hyperandrogenism and insulin resistance [40], and the PI3K/Akt signaling pathway serves as a key molecular bridge among these processes. Dysregulation of this pathway not only affects lipid storage and mobilization but also amplifies endocrine and metabolic imbalances. PCOS patients are often accompanied by lipid metabolism disorders [41], which are manifested as increased triglyceride (TG) and low-density lipoprotein cholesterol (LDL-C) and decreased high-density lipoprotein cholesterol (HDL-C). PI3K/Akt signaling pathway plays a key role in adipocyte differentiation and lipid metabolism regulation. Chemerin is a newly discovered adipokine and chemotactic protein in recent years, which is related to obesity and metabolic syndrome. It is highly expressed in blood samples, ovarian tissue, granular luteal cells and adipose tissue of PCOS patients [42]. Luo *et al.* experimentally observed that Chemerin and its receptor CMKLR1 were over-expressed in the PCOS rat model [43], and Chemerin may promote cell autophagy by inhibiting PI3K/Akt/mTOR and MAPK signaling pathways [44]. Li *et al.* confirmed that downregulation of PM20D1 expression and inhibition of PI3K/Akt pathway activity in the rat model of PCOS-IR led to lipolysis disorders in adipocytes, lipid accumulation and ovarian polycyst-like degeneration [45]. Quercitrin can dose-dependent up-regulate PM20D1, promote lipolysis and reduce apoptosis rate by restoring PI3K/Akt/mTOR signaling pathway, and improve se-

rum LH/FSH ratio and insulin sensitivity in rats.

3.5. Insulin Resistance

The PI3K/Akt signaling pathway plays a key role in the regulation of insulin sensitivity, and its dysfunction has been reported to be one of the main causes of PCOS with IR [46]. For example, Rabah *et al.* observed significant downregulation of PI3K and Akt gene expression in a letrozole-induced PCOS-IR rat model [47]. The study of Yang, Q. involved GSK-3β and FOXO1, which are downstream of PI3K/Akt, and found that miR-133a-3p affected the phosphorylation level of these downstream factors by inhibiting the PI3K/Akt pathway [46]. Activated Akt phosphorylates and inhibits GSK-3β, promotes the translocation of glucose transporter 4 (GLUT4) to the cell membrane, enhances glucose uptake, and improves insulin sensitivity. In addition, the PI3K/Akt pathway exhibits significant crosstalk with other signaling pathways, including AMPK, MAPK, and mTOR pathways. AMPK acts as an upstream energy sensor that can activate PI3K/Akt signaling to improve insulin sensitivity, while MAPK signaling may function in parallel to regulate cell proliferation and inflammatory responses. Furthermore, Akt directly interacts with mTOR to regulate protein synthesis and cellular metabolism, highlighting a complex signaling network involved in PCOS pathophysiology. A summary of the multifaceted roles of the PI3K/Akt signaling pathway in the pathogenesis of PCOS is presented in **Table 1**, based on evidence from previous studies examining its involvement in inflammation, granulosa cell function, hyperandrogenism, lipid metabolism, and insulin resistance [13].

Table 1. Role of PI3K/Akt in PCOS Mechanisms (based on analysis, self-created) [13].

Pathological Process	Role of PI3K/Akt Pathway	Key Mechanisms	Outcome in PCOS
Inflammation & Oxidative Stress	Anti-inflammatory and antioxidant regulation	Inhibits NF-κB, increases SOD & GPx	Reduced inflammation and ROS imbalance
Granulosa Cell Dysfunction	Regulates proliferation, apoptosis, autophagy	Activates Bcl-2, inhibits Bax, controls mTOR	Improved follicular development
Hyperandrogenism	Promotes androgen synthesis	Upregulates StAR, CYP17A1	Excess androgen production
Lipid Metabolism Disorders	Controls lipid storage and metabolism	Regulates FABP5, PM20D1, mTOR	Dyslipidemia and lipid accumulation
Insulin Resistance	Enhances insulin signalling	Activates GLUT4, inhibits GSK-3β	Improved glucose uptake and insulin sensitivity

In PCOS patients, the activity of PI3K/Akt pathway is decreased, which leads to the block of insulin signaling, the decrease of GLUT4 translocation, and the aggravation of insulin resistance. At the same time, abnormal adipocyte differentiation and lipid metabolism disorder further aggravate the occurrence and development of metabolic syndrome. Guo *et al.* found that the expression of IRS-1 and GLUT4 was down-regulated and glucose uptake ability was decreased in granulosa cells and IR cell models of PCOS patients, while melatonin could significantly

up-regulate the expression of IRS-1 and GLUT4, improve glucose uptake, and increase the levels of p-PI3K and p-Akt [48]. These results suggest that IRS1 and GLUT4 are the key effectors of PI3K/Akt pathway mediating melatonin-induced improvement of PCOS-IR. Zheng *et al.* found that curcumin could alleviate hyperandrogenic symptoms and abnormal follicular hyperplasia in PCOS rats by regulating IRS1/PI3K/GLUT4 pathway [49]. In addition to IRS1 and GLUT4, some other proteins have also been found to play a role in PCOS-IR through the PI3K/AKT pathway. Li *et al.*, through bioinformatics screening and experimental verification, found that the expression of peptidase M20 domain protein 1 (PM20D1) was reduced in IR cells and PCOS-IR rat model, and its deletion aggravated IR and interacted with PI3K [45]. They proposed that PM20D1 improved lipid metabolism disorders in PCOS-IR by up-regulating the PI3K/Akt pathway. In summary, these studies reveal that the PI3K/Akt pathway is complex regulated by multiple protein factors in PCOS-IR, which may affect the activity of the pathway through direct or indirect ways, thereby affecting insulin sensitivity and related pathological processes.

4. Therapeutic Implications

4.1. Potential Mechanisms of Lifestyle Intervention

Lifestyle interventions, such as diet control, regular exercise and weight loss, are the basis of PCOS treatment [50]. Studies have shown that lifestyle intervention can improve the metabolic and reproductive function of PCOS patients by regulating the PI3K/Akt signaling pathway [51]. Exercise promotes activation of the PI3K/Akt pathway, upregulates GLUT4 ex-pression, and optimizes insulin signaling through long-term training-induced adaptive changes (such as enhanced mitochondrial biogenesis and reduced inflammation), thereby ultimately improving insulin sensitivity [52] [53]. Diet control can regulate intestinal flora, improve the inflammatory state, and indirectly affect the activity of PI3K/Akt pathway [54]. Therefore, lifestyle intervention not only helps to reduce body weight, but also improves the pathophysiological state of PCOS at the molecular level by regulating the PI3K/Akt pathway.

4.2. Drug Intervention and Drug Development

Many traditional Chinese medicines and natural products have been proved to improve the symptoms of PCOS by regulating the PI3K/Akt signaling pathway. For example, metformin [47], as the first-line drug for the treatment of insulin resistance in PCOS, can activate AMPK signaling, indirectly up-regulate the activity of PI3K/Akt pathway, enhance insulin sensitivity, reduce androgen levels, and improve ovulation function. In addition, traditional Chinese medicine compound preparations such as Erzhiwan, Cangfu Daotan decoction, etc., and natural compounds such as berberine and resveratrol, etc. [55] have also been found to reduce inflammatory response, regulate lipid metabolism and improve ovarian function by activating PI3K/Akt pathway, which provides a new idea for the treat-

ment of PCOS with integrated traditional Chinese and western medicine.

Recent clinical and translational studies have further supported the therapeutic potential of targeting the PI3K/Akt pathway in PCOS. For instance, clinical investigations conducted between 2022 and 2024 have evaluated insulin-sensitizing agents and pathway modulators, such as metformin and combination therapies, demonstrating significant improvements in insulin resistance, ovulatory function, and androgen levels in women with PCOS. These findings highlight the translational relevance of PI3K/Akt-targeted interventions in improving both metabolic and reproductive outcomes. The major pharmacological and natural interventions targeting the PI3K/Akt signaling pathway in PCOS are summarized in Table 2, drawing on studies investigating insulin-sensitizing drugs, natural compounds, and pathway-targeted therapies [46].

Table 2. Drugs targeting PI3K/Akt pathway in PCOS [46] (based on analysis, self-created).

Intervention Type	Example	Mechanism via PI3K/Akt	Therapeutic Effect
Insulin-sensitizing drug	Metformin	Activates AMPK → enhances PI3K/Akt	Improves insulin resistance, reduces androgens
Natural compound	Berberine	Activates PI3K/Akt, reduces inflammation	Improves metabolic and ovarian function
Natural compound	Resveratrol	Modulates PI3K/Akt and oxidative stress	Reduces inflammation and improves ovulation
Traditional Chinese Medicine	Erzhiwan, Cangfu Daotan Decoction	Regulates PI3K/Akt signaling	Improves hormonal balance
Experimental therapies	PI3K/Akt modulators	Direct pathway targeting	Potential future treatment strategy

With the in-depth understanding of the mechanism of PI3K/Akt pathway, the development of targeted drugs for this pathway has become a new direction for the treatment of PCOS. However, due to the wide distribution and complex regulation of PI3K/Akt pathway in the body, the development of targeted drugs should fully consider their safety and efficacy to avoid other adverse reactions caused by excessive activation or inhibition of this pathway.

Moreover, genetic variability in components of the PI3K/Akt signaling pathway may contribute to the heterogeneity observed among PCOS patients. Polymorphisms in genes encoding key signaling molecules, such as PI3K catalytic subunits and Akt isoforms, have been associated with differences in insulin sensitivity, androgen levels, and treatment responses. Understanding these genetic variations may help to explain inter-individual differences in disease manifestation and support the development of personalized therapeutic strategies.

5. Summary and Prospect

In summary, PI3K/Akt signaling pathway plays a key regulatory role in the pathological processes of PCOS, such as inflammatory response, oxidative stress, ovar-

ian granulosa cell function regulation, hyperandrogenism, lipid metabolism disorders and insulin resistance. Further study on the mechanism of the association between the PI3K/Akt signaling pathway and PCOS will provide a new theoretical basis for revealing the pathogenesis of the disease, and provide potential targets for the development of clinical treatment strategies. However, there are still many problems in the current research on the PI3K/Akt pathway in PCOS, such as the differences in the regulation of this pathway in different individuals and disease stages, the synergistic mechanism of upstream and downstream signaling molecules, and the precision of targeted intervention. In addition, future research should pay greater attention to genetic polymorphisms and individual variability in PI3K/Akt pathway regulation, which may influence disease susceptibility and therapeutic response. Future studies need to further clarify the dynamic regulatory network of PI3K/Akt pathway in PCOS, combine multi-omics technology to screen specific biomarkers, develop safer and effective targeted therapeutic drugs, and provide individualized and precise treatment for PCOS patients.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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