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### Epigenetic mechanisms in Polycystic Ovary Syndrome: DNA methylation, Histone modification, and miRNA regulation

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**Abstract:** Polycystic ovary syndrome (PCOS) affects about 10% of reproductive-age women and is characterised by hormonal imbalance, irregular ovulation, and cyst-like follicles in the ovaries. Common features include high androgen levels, insulin resistance, weight gain, and abnormal lipid patterns. Symptoms can vary depending on environmental and geographic factors. Recent studies show that epigenetic changes—modifications in gene activity without altering DNA sequence—play a key role in PCOS. These include DNA methylation, chromatin remodelling, and small regulatory RNAs that control gene expression. Disruptions in these mechanisms can switch genes on or off, affecting ovarian function, egg maturation, metabolism, and immune responses. Women with PCOS often exhibit abnormal DNA methylation in ovarian tissues, particularly in genes such as CYP19A1 and INSR, which are involved in hormone regulation and insulin signalling. Changes in DNA packaging can also disturb ovarian cycles and androgen production. MicroRNAs such as miR-21, miR-93, and miR-222 further regulate follicle growth, insulin action, and hormone secretion. Environmental factors like diet, obesity, early hormone exposure, and endocrine disruptors influence these gene expression changes, contributing to varied symptoms. Emerging treatments, including metformin and other targeted therapies, aim to regulate these molecular pathways. This may allow personalised treatment approaches, improving both metabolic health and reproductive outcomes in individuals with PCOS.

**Keywords:** Polycystic Ovary Syndrome (PCOS), Epigenetics, DNA methylation, Histone modification, MicroRNA, Insulin Resistance.

## 1. INTRODUCTION

About ten per cent of women of reproductive age experience polycystic ovary syndrome. This condition combines hormonal imbalance with malfunction of energy mechanisms. Ovulation stops properly. Ovaries no longer release eggs; male hormone levels rise. An ultrasound shows clusters of small fluid-filled sacs on the ovaries. Insulin control becomes difficult, often accompanied by increased weight and abnormal lipid levels. Increased risk for type 2 diabetes and cardiovascular issues follows [1]. Decades of investigations have failed to untangle the roots: DNA, environment, and drifting hormone signals interact in ways that remain unsolved. No single cause has been found. Multiple factors always intertwine. Figures vary depending on whether doctors use Rotterdam, NIH, or Androgen Excess criteria [2]. Irregular or missed periods are a major problem. Unpredictable menstrual cycles, difficulty conceiving, excess facial or body hair and skin, acne outbreaks, and weight gain due to decreased insulin sensitivity are additional symptoms [3].

A faint clue reveals an unseen force behind PCOS. Epigenetics controls timing and progression, not by altering DNA, but by regulating gene activity in cell lineages [4]. Chromosome surroundings change, opening some genes and closing others. PCOS results from ancestry and life events. Patterns trace to these quiet regulators. Inherited material matters, but post-birth events steer the path.

## **2. OVERVIEW OF EPIGENETIC MECHANISMS**

Sometimes, cues adjust gene activity without changing DNA. As cells grow, they maintain those adjustments even as conditions shift. Molecules attach to genes, often quieting specific regions. Histones change shape, tightening or loosening their grip on DNA. Tiny RNA fragments interfere with message carriers, dialling down protein output at precise spots [8].

Activation or silencing of genes depends primarily on chromatin changes and DNA winding, which guide cell behaviour in distinct patterns. In PCOS, dysfunction often begins when errors in genetic regulation propagate effects into hormone balance, metabolism, and ovarian egg development.

### **2.1. DNA methylation**

A small label attaches to cytosine at the fifth carbon, mainly where C and G pairs are found. DNMT enzymes carry out this process [9]. This change is one of the best-known modifications in epigenetics. Proximity to gene start sites silences genes by preventing activators from binding or by recruiting repressors that compact the DNA.

Recently, abnormal DNA marker modifications have been identified in major body tissues linked to PCOS. This includes ovaries, fat deposits, and blood cells. Very subtle alterations may cause genes responsible for insulin production, hormone regulation, egg development, and more to turn on at the wrong time or stay off too long. In some instances, whole regions have lost their epigenetic marks. In others, new marks appear sharply and precisely. This complex pattern signals disturbed pathways underlying the disorder's biological processes [10].

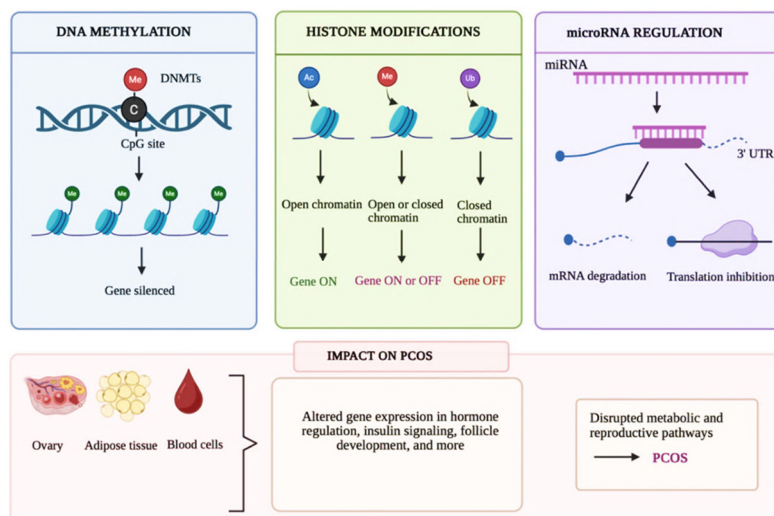
### **2.2. Histone modifications**

DNA winds tightly around proteins in the cell nucleus, acting as spools. When proteins achieve their correct form, tagging begins. DNA loosens when acetyl accumulates, shedding tight packaging. Methyl group placement determines if chromatin is packed and inaccessible or relaxed for gene activation. Highly expressed genes often encode phosphatases, altering cofactor access. Ubiquitin is a red flag. Each modification turns a gene on or off. Large changes occur without altering the DNA sequence [11].

Genes activate when chromatin loosens from histone acetylation. Other methylation changes impact DNA accessibility and gene control. Gene mutations, epigenetic shifts, and environmental factors contribute to PCOS [12]. Epigenetic changes, including DNA methylation and histone modifications, alter gene expression without altering the DNA sequence.

### **2.3. miRNA regulation**

miRNAs (MicroRNAs) are small non-coding RNA molecules about 18–24 nucleotides long. Nucleotides are the basic structural units of RNA, similar to letters in a genetic code. miRNAs regulate gene expression after transcription. They bind to complementary sequences in the 3' untranslated regions (UTRs) of target messenger RNAs. UTRs are regions of messenger RNA that do not encode protein but are important for regulation. This binding leads to mRNA degradation or translation inhibition [13]. Numerous microRNAs show altered expression in the follicular environment of women with polycystic ovary syndrome (PCOS). For example, altered levels of miRNAs have been detected in the follicular fluid of PCOS patients. These regulatory RNAs may affect ovarian function and help explain the hormonal and metabolic imbalances of the disorder [14].



**Figure 1:** Overview of epigenetic mechanisms. DNMTs (DNA methyltransferase), Me (methylation), CpG site (Cytosine-phosphate-Guanine sites), Ac (Acetylation), Ub (Ubiquitination), 3' UTR (3'-Untranslated Region) (created with BioRender.com).

Among them, miR-93 levels are elevated in the adipose tissue of PCOS women in several studies. This results in downregulation of GLUT4 synthesis and provides one possible mechanism for insulin resistance [15]. This is a clear example: epigenetic regulation plays a major role in microRNA-mediated changes in gene expression that contribute to PCOS pathogenesis. Overall, changes in DNA methylation, histone modifications, and small RNAs create an intricate gene regulatory network in metabolic and reproductive tissues. Disruptions in this system may initiate or worsen PCOS symptoms.

### 3. DNA METHYLATION IN PCOS

DNA methylation is a major epigenetic change associated with polycystic ovary syndrome. This process adds a methyl group to cytosine bases at CpG sites via enzyme activity. It typically dials down gene expression. Odd patterns in these marks often appear in ovaries, granulosa cells, fatty tissue, and blood samples from people with PCOS. Such mismatches are so common that researchers now see faulty epigenetics as central to this condition's development [16].

Some researchers examine DNA tags across the entire genetic code. This has revealed clear gaps in how these marks appear on ovarian tissue in women with polycystic ovary syndrome compared to those without it. Patterns differ; some spots are more heavily tagged; others are less so in genes tied to steroids, metabolism, and ovarian function. Altered molecular switches could disrupt egg sac development and hormone messaging. This may explain why PCOS brings uneven hormones and disturbed body chemistry [17].

#### 3.1. Altered methylation patterns in ovarian tissue

Granulosa cells are just a few layers deep. These cells determine how follicles develop and secrete hormones. Researchers examined these same cells in women with PCOS and found abnormal chemical modifications of genes related to steroid production and follicle development. These changes appear to inhibit estrogen production and disrupt the timing of follicle maturation. As a result, many small cysts form in the ovaries, which is typical of PCOS [18]. Irregular methylation in ovarian tissue is often linked to improper regulation of androgen synthesis and egg growth cycles. Such DNA changes can increase male hormone production—a feature of women with PCOS [19].

#### 3.2. Role of DNA methylation in metabolic dysfunction

Metabolic dysfunction, such as insulin resistance, obesity, and dyslipidemia, is closely associated with PCOS. Among epigenetic mechanisms, DNA methylation can regulate the expression of genes involved in glucose homeostasis and insulin signalling pathways. Altered DNA methylation signatures in metabolic genes in women with polycystic ovary syndrome (PCOS) might reduce insulin sensitivity, thereby contributing to the development

of metabolic syndrome [20]. On top of that, epigenetic modifications in adipose tissue can influence the release of adipokines, which mediate inflammation and lipid metabolism. Such alterations may result in insulin resistance, which in turn can increase the probability of women with PCOS being diagnosed with type 2 diabetes [21].

### **3.3. Important genes affected by DNA methylation**

#### *3.3.1. CYP19A1 (aromatase gene)*

The CYP19A1 gene encodes the aromatase enzyme. Aromatase converts androgen hormones to estrogen in ovarian granulosa cells. In PCOS, changes in DNA methylation of the CYP19A1 gene promoter have been linked to a decreased expression of the aromatase enzyme. This decrease results in reduced estrogen production and an accumulation of androgens, which, in turn, causes hyperandrogenism and prevents follicle development [22].

Variations in DNA methylation of steroidogenic genes have been linked to the development of polycystic ovary syndrome. For example, abnormal methylation of the promoter of the CYP19A1 gene, encoding the aromatase enzyme responsible for estrogen biosynthesis, has been noted in women with PCOS. Such epigenetic changes could alter aromatase expression, leading to reduced estrogen production and hormonal imbalance in ovarian follicles [23].

#### *3.3.2. INSR (insulin receptor gene)*

The insulin receptor, which facilitates glucose absorption and insulin signalling, is encoded by the INSR gene. Disordered methylation of the INSR gene has been found in PCOS women and has been linked to defective insulin signalling and insulin resistance. Epigenetic changes might be one of the causes of the metabolic disorders characteristic of PCOS patients [24].

Moreover, alterations in INSR methylation could affect ovarian function, as insulin is one of the factors that control ovarian steroidogenesis. Hence, epigenetic changes in insulin signalling cascades could explain why both metabolic and reproductive functions are affected in PCOS [25].

## **4. HISTONE MODIFICATIONS IN PCOS**

Histone modifications are a key epigenetic mechanism that alter gene expression in PCOS. Histones are the proteins around which DNA coils to make nucleosomes, the basic units of chromatin. Chemical modifications to histone proteins alter chromatin flexibility and affect gene transcription. One of the major histone modifications is acetylation and methylation of lysine residues in histone tails. Through these modifications, chromatin accessibility is regulated, and the transcriptional state of genes, whether activated or repressed, is determined [26].

### **4.1. Histone acetylation**

Histone acetylation is facilitated by histone acetyltransferases (HATs), which transfer acetyl groups to lysine residues on histone proteins. The net effect of this modification is to cancel the positive charge of histones, which diminishes their binding to negatively charged DNA. Consequently, chromatin structure loosens, setting the stage for gene transcription [27].

In PCOS, histone acetylation changes have been observed in genes related to ovarian steroidogenesis and follicular development. A drop in histone acetylation at the regulatory regions of these genes may lead to reduced production of proteins essential to healthy ovarian function [28].

Histone deacetylases (HDACs) remove acetyl groups from histones and promote chromatin condensation. Dysregulation of HDAC activity has been implicated in abnormal follicular development and androgen production in PCOS [29].

### **4.2. Histone methylation**

Histone methylation is the process of modifying histone proteins by adding methyl groups to certain lysine or arginine residues. This kind of change can either promote or inhibit gene transcription based on where and how much methylation occurs. Changes in histone methylation patterns have been identified in genes controlling ovarian follicle maturation, steroid hormone biosynthesis, and metabolic signalling pathways in PCOS [30]. For example, methylation of inhibitory histone marks might downregulate genes required for normal follicular development, leading to follicle arrest. Moreover, histone methyltransferases and demethylases have been implicated in regulating androgen biosynthesis and ovarian cell growth. The misregulation of these enzymes might lead to overproduction of androgen and ovarian dysfunction in PCOS [31].

### 4.3. Role in ovarian steroidogenesis and follicular development

Epigenetic changes, such as DNA methylation and histone modifications, regulate when genes involved in ovarian steroidogenesis are expressed. These gene regulatory mechanisms determine how many copies of the key enzymes involved in androgen and estrogen production are produced. Epigenetic changes in the control of steroidogenic gene expression can lead to excess androgen synthesis and reduced estrogen production, which is the hallmark of follicular failure and the hormonal imbalances in polycystic ovary syndrome [32].

On top of that, if histone-dependent chromatin remodelling goes awry, this could compromise granulosa cell function and disrupt the sequence of events leading to follicle growth and ovulation. In fact, such abnormalities could cause defective folliculogenesis and the build-up of immature ovarian follicles, which is a typical characteristic of PCOS [33].

### 4.4. MicroRNAs IN PCOS

MicroRNAs (miRNAs) are tiny, non-coding RNAs that control gene expression through binding to matching sequences in the target messenger RNAs. Such molecules are vital for mediating cellular activities such as growth, programmed cell death, maturation, and metabolism. Recent research has found that many miRNAs are downregulated in ovarian tissue, granulosa cells, and the blood of women with PCOS. These miRNAs control the genes that govern steroid hormone production, insulin signalling, and follicular growth [34].

**Table 1:** Key microRNAs involved in PCOS and their biological effects

| microRNA | Expression in PCOS                       | Main Target/Action                                  | Effect on PCOS   | Reference                  |
|----------|--|---|--|----------------------------|
| miR-21   | Altered in granulosa cells               | Regulates apoptosis & cell survival pathways        | Disordered follicular development, ovarian dysfunction; also affects inflammation & metabolism             | [35], [36]                 |
| miR-93   | Increased (especially in adipose tissue) | Inhibits GLUT4; targets CDKN1A                      | Insulin resistance, reduced glucose uptake; promotes granulosa cell growth, affects follicular development | [1], [3], [15], [37], [38] |
| miR-222  | Increased (ovary & blood)                | Regulates genes in cell growth & insulin signalling | Alters granulosa cell proliferation, steroidogenesis; contributes to metabolic abnormalities               | [39], [40]                 |

## 5. REGULATION OF GRANULOSA CELL FUNCTION AND ANDROGEN PRODUCTION

MicroRNAs (miRNAs) exert significant influence on various granulosa cell functions, including cell growth, programmed cell death, and steroid hormone synthesis. When miRNAs are deregulated, they can interfere with these very processes, leading to follicular arrest and aberrant ovarian morphology. On the other hand, some microRNAs directly modulate enzymes involved in androgen biosynthesis. Changes in the expression of these miRNAs can lead to androgen overproduction, a major characteristic of PCOS [41].

Taken together, the above observations emphasise the fundamental role played by microRNA-directed epigenetic regulation in PCOS development. An in-depth study of these regulatory pathways could pave the way for uncovering disease mechanisms and discovering novel therapeutic targets.

## 6. EPIGENETIC REGULATION OF METABOLIC PATHWAYS IN PCOS

Metabolic disturbance is a main characteristic of polycystic ovary syndrome (PCOS) and comprises insulin resistance, hyperinsulinemia, dyslipidemia, and chronic low-grade inflammation. Recent studies indicate that epigenetic factors play a significant role in regulating the metabolic processes underlying PCOS aetiology. For instance, DNA methylation, histone modifications, and microRNA levels may affect the transcription of genes that regulate glucose metabolism, lipid balance, and inflammatory states [42].

The PI3K/AKT route (phosphatidylinositol-3-kinase/protein kinase B), in fact, stands as one of the key signalling networks that regulate metabolism in PCOS. It is involved in the transmission of insulin signals and oversees several physiological processes, including glucose uptake, glycogen synthesis, and cellular preservation. Changes in the epigenetic landscape of genes in the PI3K/AKT signalling pathway have been identified as a source of insulin resistance in PCOS cases [43].

Insulin receptor function and the transmission of signals far down the line can be hampered by aberrant DNA methylation of genes encoding players in the insulin signalling pathway. Consequently, the transport of glucose into skeletal muscle and fat cells is limited, which, in turn, leads to increased blood glucose levels (hyperglycemia) and the body's attempt to counterbalance by producing more insulin (hyperinsulinemia) [44]. Besides, hyperinsulinemia leads to greater stimulation of Graafian follicle cells in the ovaries to secrete steroid hormones excessively, which makes the situation worse when the metabolic component is joined with the reproductive one in PCOS.

MicroRNAs also play a significant role in regulating metabolic pathways in PCOS. Some miRNAs can even directly target genes involved in insulin signalling and glucose metabolism. For example, studies of dysregulated miRNAs indicate that they may lower the levels of proteins involved in insulin receptor signalling and glucose transporter expression, thereby leading to metabolic disorders [45]. Persistent inflammation is yet another major factor underlying metabolic dysfunction in PCOS. Changes at the epigenetic level of inflammatory genes may lead to enhanced production of pro-inflammatory cytokines such as tumour necrosis factor- and interleukin-6. These cytokines disrupt insulin signalling, leading to various metabolic problems [46].

Thus, the study of epigenetic control of metabolic pathways provides a plausible biological basis for the association between reproductive and metabolic issues in PCOS. A deeper insight into these molecular mechanisms could reveal potential points of intervention for therapies focused on metabolic improvements in women with PCOS.

## **7. ENVIRONMENTAL INFLUENCES ON EPIGENETICS IN PCOS**

Environmental factors play a crucial role in shaping the epigenetic landscape and may contribute significantly to PCOS development. Unlike genetic mutations, epigenetic modifications are dynamic and can be influenced by external stimuli such as diet, lifestyle, hormonal exposure, and environmental chemicals [47].

### **7.1. Diet and obesity**

Dietary patterns, along with obesity, are significant environmental factors that influence large-scale epigenetic modifications. Consuming more calories than needed and/or following a high-fat diet leads to DNA methylation changes in genes regulating metabolism, such as insulin signalling and lipid metabolism. These genetic alterations can cause insulin resistance and chronic inflammation, which, in turn, can be considered risk factors for PCOS development [48].

Along with changes in adipokine secretion and the production of inflammatory cytokines caused by obesity, an epigenetic regulatory mechanism is also modified. Such changes affect ovarian steroidogenesis and follicle development, leading to reproductive problems [49].

### **7.2. Prenatal androgen exposure**

One of the major factors that has been linked to the developmental origins of PCOS is prenatal exposure to high androgen levels. Several animal experiments demonstrate that androgen exposure during fetal development epigenetically reprograms changes that persist into adulthood and disrupt both reproductive and metabolic function [50].

Epigenetic modifications that take place may target genes involved in ovarian follicle development, insulin signalling, and androgen biosynthesis. Therefore, prenatal androgen exposure could be a risk factor for the development of PCOS in an individual.

### **7.3. Endocrine disrupting chemicals**

Exposure to endocrine-disrupting chemicals such as bisphenol A (BPA), phthalates, and pesticides has been linked to epigenetic changes associated with PCOS. These chemicals might disrupt hormone signalling pathways and alter DNA methylation or histone modifications in reproductive tissues [51].

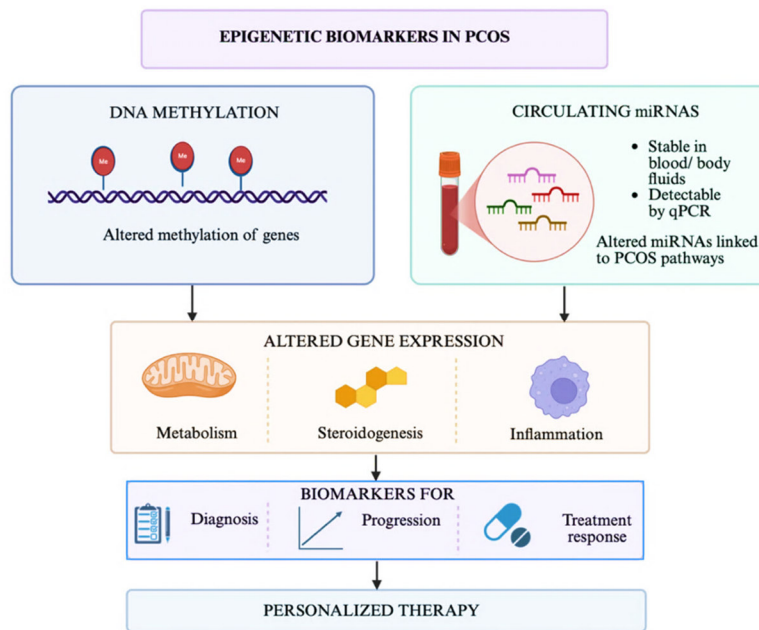
These kinds of epigenetic changes can interfere with the process of ovarian folliculogenesis and production of steroid hormones, which in turn may lead to PCOS. The latest studies indicate that the environment may interact with an individual's genetic makeup to determine disease risk.

## 8. EPIGENETIC BIOMARKERS IN PCOS

Genome-wide epigenetic studies have identified numerous genes with altered methylation in ovarian and granulosa cells of women with polycystic ovary syndrome, suggesting that DNA methylation patterns may serve as potential biomarkers for diagnosing the disease and its progression [17]. It has been documented that changes in the methylation of genes regulating metabolism, steroidogenesis, and inflammatory pathways contribute to the complicated pathophysiology of PCOS [52]. These epigenetic modifications alter gene expression without altering the DNA sequence and can simultaneously reflect both inherent susceptibility and environmental factors linked to PCOS [53].

Circulating microRNAs have also been recognised as potential non-invasive biomarkers for PCOS. Since miRNAs are stable in blood and other bodily fluids, they can be detected using molecular techniques such as quantitative PCR. Certain miRNAs linked to ovarian function and insulin signalling have been found to show differential expression in PCOS patients [54].

Additionally, epigenetic biomarkers could shed light on disease burden and the effectiveness of treatment. Thus, tracking epigenetic modifications could improve clinical decision-making and lead to the development of personalised treatment plans for PCOS.



**Figure 2:** Epigenetic biomarkers in PCOS. qPCR(quantitative PCR) (created with BioRender.com)

## 9. EPIGENETIC THERAPEUTIC TARGETS

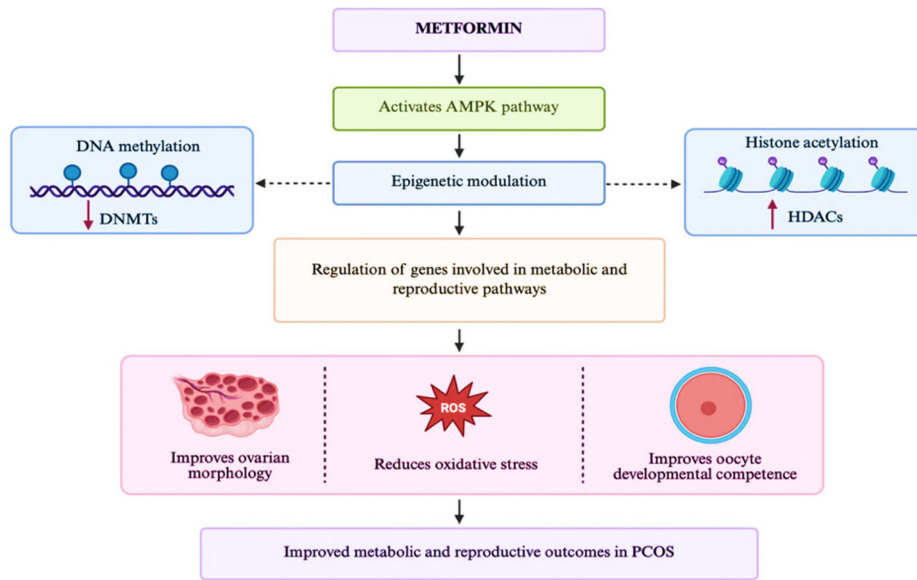
### 9.1. Pharmacological modulation of epigenetic pathways

Since many epigenetic changes are reversible and can regulate gene expression in reproductive and metabolic pathways, epigenetic changes have been gaining attention as potential targets for therapy of PCOS. Changes in DNA methylation, histone modifications, and miRNA expression were found in the ovaries and granulosa cells of PCOS women. This finding implies that treatment of these pathways may improve ovarian function and metabolism [55].

### 9.2. Metformin and epigenetic regulation

Metformin, a well-known insulin-sensitising medication, is frequently used for treating PCOS. Besides its metabolic effects, new research indicates that metformin might also work epigenetically by altering DNA methylation and miRNA expression [45]. The drug is known to stimulate the AMPK pathway, which governs cellular energy metabolism and gene expression. In this way, metformin could alter epigenetic marks associated with metabolic and reproductive pathways in PCOS [56]. Moreover, metformin has been reported to affect epigenetic factors, such as DNA methyltransferases (DNMTs) and histone deacetylases (HDACs), which, in turn,

help rectify ovarian morphology, reduce oxidative stress, and improve oocyte developmental competence in PCOS experimental models [57].



**Figure 3:** Metformin and epigenetic regulation. AMPK (AMP-activated protein kinase), DNMTs (DNA methyltransferases), HDACs (Histone deacetylases), ROS (Reactive oxygen species) (created with BioRender.com)

### 9.3. Targeting chromatin-modifying enzymes

Besides conventional drugs, targeting chromatin-modifying enzymes has also been proposed as a therapeutic approach. Enzymes such as DNA methyltransferases (DNMTs) and histone deacetylases (HDACs) regulate DNA methylation and histone acetylation, respectively. These processes control the chromatin structure and gene transcription. Experimental work shows that altering the activity of these epigenetic enzymes can reverse abnormal gene silencing and restore normal expression of genes involved in steroidogenesis, follicular development, and insulin signalling in PCOS [3, 58].

### 9.4. MicroRNA-based therapeutic strategies

Moreover, microRNA-targeted therapy is a promising approach for treating PCOS. The imbalanced expression of microRNAs has been shown to affect various biological processes, including insulin signalling, ovarian steroidogenesis, and follicular development. Restoring microRNA expression with synthetic mimics or inhibitors could be a new approach to correcting gene regulation, thereby improving metabolic and reproductive outcomes in PCOS [59].

## 10. FUTURE PERSPECTIVES

Genomic technologies have significantly advanced our understanding of the molecular changes that cause PCOS. Most likely, future studies will be centred on multi-omics that integrate genomics, epigenomics, transcriptomics, and metabolomics to provide an overall insight into the disease mechanism. These comprehensive approaches could be instrumental in discovering new molecular pathways associated with PCOS and identifying therapeutic targets. Furthermore, epigenetics could play a significant role in tailoring treatments to an individual patient's molecular profile, a main goal of precision medicine [60].

Therapeutic interventions based on epigenetics are at the forefront of research. Epigenetic changes being reversible, targeting epigenetic regulators such as DNA methyltransferases, histone-modifying enzymes, and microRNAs offers a novel therapeutic window. In addition, further clinical trials are needed to confirm the safety and effectiveness of these targeted therapeutic agents and to explore their potential to improve reproductive and metabolic outcomes in PCOS patients [61].

Besides, things that relate to our environment and way of life, like what we eat, whether we're overweight, how much we move, or even the chemicals that mess with our hormones, can also change how genes work without altering the DNA itself and maybe cause PCOS. Understanding how these environmental factors interact with

genetic and epigenetic changes will help identify ways to prevent PCOS and improve reproductive health. In line with this, it is recommended that further studies investigate how environmental factors and epigenetic changes influence PCOS development [45].

The bottom line is that researching the epigenetic factors will give us a better knowledge of PCOS, and who knows, it could even provide new ways to diagnose and treat those who are suffering from this disorder.

## 11. CONCLUSION

PCOS is a multifactorial disorder influenced by genetic, metabolic, and environmental factors. Increasing evidence indicates that epigenetic mechanisms, including DNA methylation, histone modifications, and microRNA regulation, play an important role in the pathogenesis of PCOS by altering gene expression involved in ovarian steroidogenesis, follicular development, and insulin signalling. Abnormal epigenetic patterns may contribute to hormonal imbalance, impaired folliculogenesis, and metabolic disturbances observed in affected women.

Recent studies suggest that epigenetic markers may serve as potential biomarkers for disease diagnosis and progression, while therapeutic agents such as metformin and other epigenetic modulators may help restore normal gene regulation. Further research is required to better understand the epigenetic landscape of PCOS and to develop targeted therapeutic strategies for improved clinical management.

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