THE PIVOTAL ROLE OF PM20D1 IN POLYCYSTIC OVARY SYNDROME-INSULIN RESISTANCE-LIPID METABOLISM DISORDER AND THE POSITIVE EFFECT OF QUERCITRIN

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Background: Polycystic ovary syndrome combined with insulin resistance (PCOS-IR) poses a serious risk to reproductive health in females. Peptidase M20 Domain containing 1 was never reported of its relationship with PCOS-IR. Quercitrin is a flavonoid that can efficiently improve both endocrine and metabolic abnormalities. However, it remains unclear if this agent can exert therapeutic effect on PCOS-IR.
Objective: The purpose of this study was to screen and confirm key molecules involved in PCOS-IR, and to investigate whether Quercitrin, a known active flavonoid and exert positive effect in the process.
Methods: The present study used a combination of metabolomic and bioinformatic methods to screen key molecules and pathways involved in PCOS-IR. A rat model of PCOS-IR and an adipocyte IR model were generated to investigate the role of quercitrin in regulating reproductive endocrine and lipid metabolism processes in PCOS-IR.
Results: Peptidase M20 domain containing 1 (PM20D1) was screened using bioinformatics to evaluate its participation in PCOS-IR. PCOS-IR regulation via the PI3K/Akt signaling pathway was also investigated. Experimental analysis showed that PM20D1 levels were reduced in insulin-resistant 3T3-L1 cells and a letrozole PCOS-IR rat model. Reproductive function was inhibited, and endocrine metabolism was abnormal. The loss of adipocyte PM20D1 aggravated IR. In addition, PM20D1 and PI3K interacted with each other in the PCOS-IR model. Furthermore, the PI3K/Akt signaling pathway was shown to participate in lipid metabolism disorders and PCOS-IR regulation. Quercitrin reversed these reproductive and metabolic disorders.
Conclusion: PM20D1 and PI3K/Akt were required for lipolysis and endocrine regulation in PCOS-IR to restore ovarian function and maintain normal endocrine metabolism. By upregulating the expression of PM20D1, quercitrin activated the PI3K/Akt signaling pathway, improved adipocyte catabolism, corrected reproductive and metabolic abnormalities, and had a therapeutic effect on PCOS-IR.

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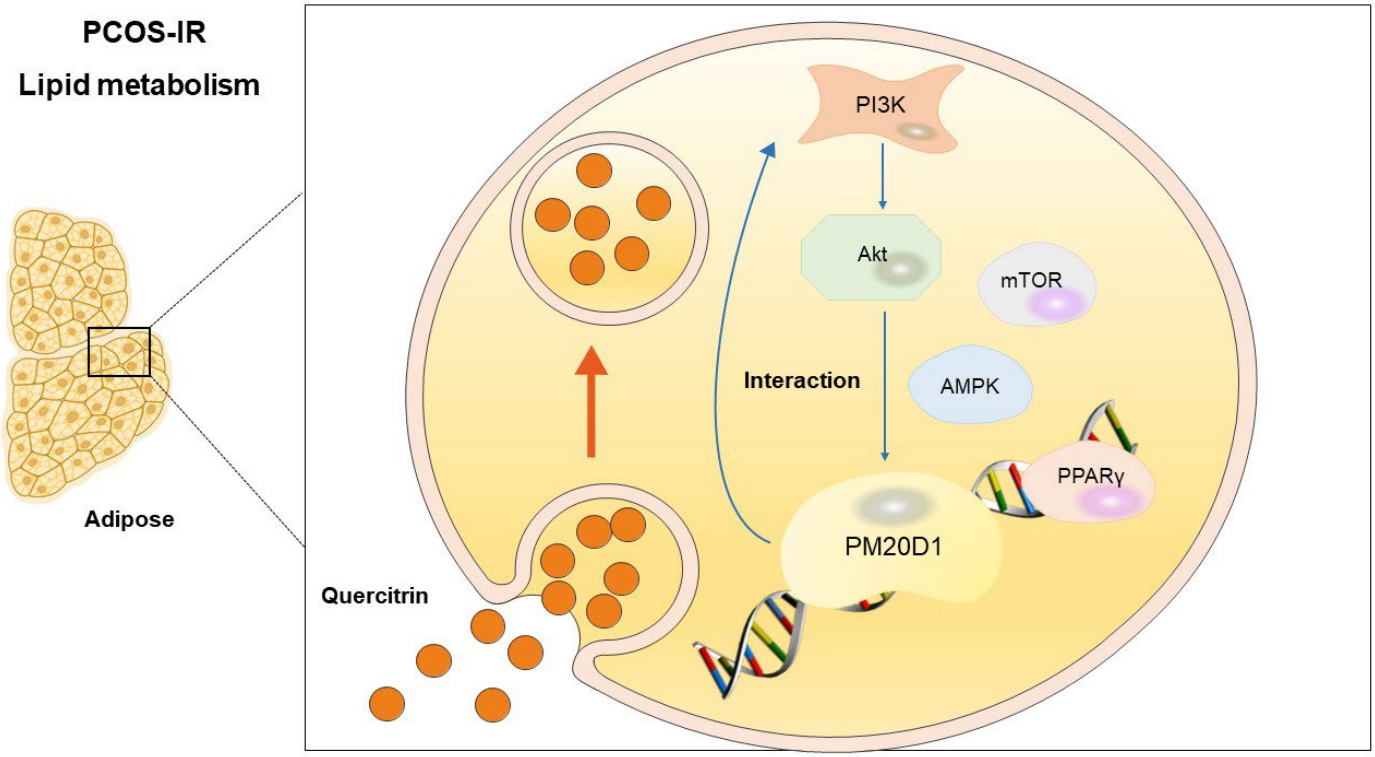
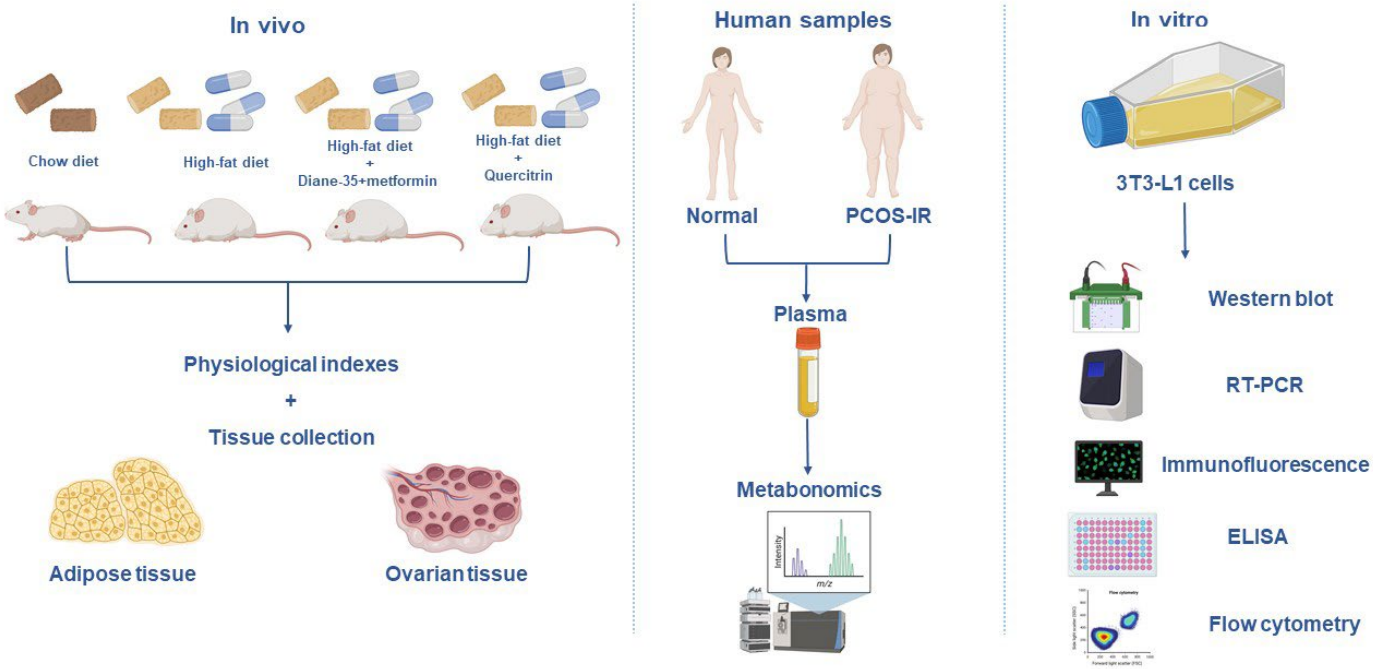

PCOS-IR
Lipid metabolism
Adipose
PI3K
Akt
mTOR
Interaction
AMPK
PPARγ
PM20D1
Quercitrin


In vivo
Chow diet
High-fat diet
High-fat diet + Diane-35+metformin
High-fat diet + Quercitrin
Physiological indexes
+
Tissue collection
Adipose tissue
Ovarian tissue
Human samples
Normal
PCOS-IR
Plasma
Metabonomics
In vitro
3T3-L1 cells
Western blot
RT-PCR
Immunofluorescence
ELISA
Flow cytometry