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| --- | --- | --- | --- | --- | --- | --- |
| **S. Table 4 Metabolic pathways and significantly different metabolites are associated with lipid metabolism and enriched in the overexpressed or the knockdown groups.** | | | | | | |
| Pathway | N vs. S comparison | G vs. S comparison | C vs. T comparison | C vs. F comparison | Reproductive functions reported | Reference |
| FoxO signaling pathway | - | Adenosine 5’-Monophosphate | Adenosine 5’-Diphosphate; D-Glucose | Adenosine 5’-Monophosphate; D-Glucose; Adenosine 5’-Diphosphate | FOXO1 may play a key role in granulosa cells to modulate lipid and sterol biosynthesis, thereby preventing elevated steroidogenesis during early stages of follicle development | 1 |
| Carbon metabolism | Glycine; L-Cysteine; L-Alanine | - | Succinic Acid | Glycine | The evidence indicating that carbon from α-linolenate and linoleate is readily recycled into newly synthesized lipids. This pathway consumes the majority of these fatty acids that is not β-oxidized as a fuel. | 2 |
| Glycerolipid metabolism | UDP-glucose | - | Glycerol 3-phosphate | Glycerol 3-phosphate | The regulation of lipolysis and importance of intracellular glycerolipid/fatty acid cycling within trophoblasts warrants attention. | 3 |
| Glycerophospholipid metabolism | Phosphocholine; Lysopc 14:0; Choline; Lysopc 18:2; Lysopc 18:1 | - | Lysopc 18:1; Phosphocholine; Lysopc 14:0; Glycerol 3-phosphate | Glycerol 3-phosphate; Diethanolamine | The findings indicate a high complexity of glycerophospholipid metabolism and a distinct acyl specificity in intact cells that are not apparent from studies *in vitro* | 4 |
| Starch and sucrose metabolism | UDP-glucose | - | D-Glucose | D-Glucose | Sucrose metabolism plays pivotal roles in development, stress response, and yield formation, mainly by generating a range of sugars as metabolites to fuel growth and synthesize essential compounds (including protein, cellulose, and starch) and as signals to regulate expression of microRNAs, transcription factors, and other genes and for crosstalk with hormonal, oxidative, and defense signaling | 5 |
| Primary bile acid biosynthesis | Glycine; Cholesterol; 2-Aminoethanesulfonic Acid | 2-Aminoethanesulfonic Acid; Cholesterol | - | Glycine | For the first time evidence that all aspects of the bile acid synthesis pathway are present in the human ovarian follicle，the functional evidence that bile acids are produced by the human follicular granulosa cells in response to cholesterol presence in the culture media. | 6 |
| Aminoacyl-tRNA biosynthesis | L-Threonine; Glycine; L-Alanine; L-Cysteine; L-Isoleucine | L-Threonine | - | Glycine; L-Asparagine Anhydrous | The different groups of lipids composed the high molecular complex aminoacyl-tRNA synthetases, some of them play structural role and other (prostaglandins, some phospholipids) are the regulatory components of the complex. | 7 |
| Biosynthesis of unsaturated fatty acids | EPA [5Z,8Z,11Z,14Z,17Z-eicosapentaenoic acid]; Linoleic Acid (C18:2N6C); Hexadecanoic Acid (C16:0) | Oleate | - | EPA [5Z,8Z,11Z,14Z,17Z-eicosapentaenoic acid]; Linoleic Acid (C18:2N6C) | Unsaturated fatty acids are found in membranes as esterified phosphor-glycerides (also known as phospholipids). | 8 |
| Fatty acid biosynthesis | Hexadecanoic Acid (C16:0); Palmitoleic Acid (C16:1) | Oleate | - | Palmitoleic Acid (C16:1) | Fatty acid biosynthesis and membrane lipid formation represent major metabolic energy commitments for growing bacterial cells | 9 |
| Ferroptosis | L-Cysteine; Glutathione Reducedform | L-Cystine; Vitamin E | - | Vitamin E | support that changing membrane properties during lipid peroxidation occur during ferroptosis and could lead to cell death | 10 |
| Glutathione metabolism | L-Ornithine; Spermidine; Glycine; L-Cysteine; Glutathione Reducedform | L-Ornithine; Spermidine | - | Glycine; Spermidine | When the hepatic glutathione depletion reaches a threshold level, lipid peroxidation develops and severe cellular damage is produced. | 11 |
| Arginine and proline metabolism | 4-Guanidinobutyric Acid; L-Ornithine; Spermidine | L-Ornithine; Spermidine | - | Spermidine | Arginine favoring lipogenesis in muscle but lipolysis in adipose tissue. proline catabolism regulates lipid metabolism. | 12, 13 |
| Ubiquinone and other terpenoid-quinone biosynthesis | - | Vitamin E | - | Vitamin E | Vitamin E, an antioxidant in the lipid compartment of cells (i.e., membranes) | 14 |
| Biotin metabolism | Biotin | - | - | Biotin | Pharmacologic doses of biotin had no effect on tissue cholesterol content or serum lipoprotein profile | 15 |
| mTOR signaling pathway | - | Adenosine 5’-Monophosphate | - | Adenosine 5’-Monophosphate | mTOR signaling to promote anabolic metabolism, such as protein synthesis and lipid synthesis, and to inhibit catabolic pathways, such as lysosome biogenesis and autophagy | 16 |
| Vascular smooth muscle contraction | - | Norepinephrine | - | Cyclic Amp | predict that therapy to lower the levels of cholesterol in the serum of patients would reduce the occurrence of cardiovascular events associated with abnormal vascular contractions | 17 |
| Thiamine metabolism | Glycine; L-Cysteine; Nicotinic Acid Adenine Dinucleotide | - | - | Glycine; Thiamine Monophosphate | Thiamine inhibits lipid peroxidation in rat liver microsome and free radical oxidation of oleic acidin vitro | 18 |
| Caffeine metabolism | - | Xanthosine | Xanthosine | - | Caffeine ingestion stimulates both lipolysis and energy expenditure | 19 |
| Tyrosine metabolism \* | L-Thyroxine | Norepinephrine | - | - | Thyroid hormones play a role in the modulation of the FSH/LH-mediated control of granulosa cell function | 20 |
| Arginine biosynthesis/ D-Arginine and D-ornithine metabolism \* | L-Ornithine | L-Ornithine | - | - | l-Ornithine intake caused anorexia and reductions of body weight and abdominal fat. | 21 |
| alpha-Linolenic acid metabolism \* | Stearidonic Acid | Stearidonic Acid | - | - | The principal biological role of alpha-linolenic acid (alphaLNA; 18:3n-3) appears to be as a precursor for the synthesis of longer chain n-3 polyunsaturated fatty acids (PUFA) | 22 |
| Taurine and hypotaurine metabolism \* | 2-Aminoethanesulfinic Acid; L-Alanine; L-Cysteine; Guanidinoethyl Sulfonate; 2-Aminoethanesulfonic Acid | Guanidinoethyl Sulfonate; 2-Aminoethanesulfonic Acid | - | - | hypotaurine might inhibit lipid peroxidation in vivo by scavenging the initiator hydroxyl radical. | 23 |
| Glycolysis/Gluconeogenesis # | - | - | D-Glucose | D-Glucose | In adipocytes, glucose is stored primarily as lipid | 24 |
| Insulin signaling pathway # | - | - | D-Glucose | Cyclic Amp; D-Glucose | The insulin signaling pathway is a highly conserved regulator of metabolism, regulating multiple physiological functions including lipid metabolism | 25 |
| Lysosome # | - | - | Adenosine 5’-Diphosphate | Adenosine 5’-Diphosphate | cholesterol abnormalities determine lysosomal dysfunction and endocytic traffic jam in LSDs by impairing the membrane fusion machinery. | 26 |

“-” represent no enriched metabolic on this pathway

“\*” represent pathway is overexpress SCD [special](javascript:;) enriched

“#” represent pathway is knockdown SCD [special](javascript:;) enriched

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