

## db/db Mice

**Catalog Number:** C001274

### Strain Description

The leptin receptor (LEPR) gene, also known as the Obese Gene Receptor (OB-R) or Diabetes Gene (DB), encodes a receptor protein located on the cell surface of numerous organs and tissues throughout the body, including the hypothalamus in the brain. The hypothalamus is critical for regulating hunger, thirst, sleep, mood, body temperature, and the release of hormones with systemic effects. The leptin receptor (LEPR) in the brain binds to circulating leptin, thereby initiating downstream signaling pathways that inhibit food intake and promote energy expenditure. Beyond its role in energy homeostasis, LEPR, in conjunction with leptin, is involved in various physiopathological processes, including immune and inflammatory responses, hematopoiesis, angiogenesis, reproduction, bone formation, and wound healing <sup>[1]</sup>. Mutations in the LEPR gene have been strongly linked to obesity, hypertension, diabetes, and lipid metabolism disorders <sup>[2]</sup>.

Homozygous db/db mice, which harbor mutations in the LEPR gene, not only exhibit obesity and diabetes mellitus but also present with peripheral neuropathy and cardiomyopathy. These mice display increased metabolic efficiency and delayed wound healing following injury <sup>[3]</sup>, and they may develop hypothalamic lesions <sup>[4]</sup>. Female db/db mice specifically show reduced uterine and ovarian weights, decreased estrogen production, and infertility <sup>[5-6]</sup>. A related strain, B6-db/db (catalog number: C001291), constructed on a C57BL/6 background, similarly exhibits obesity and diabetes phenotypes. In B6-db/db mice, pancreatic islet  $\beta$ -cells undergo compensatory hyperplasia, leading to persistent hyperinsulinemia throughout their 18-20 month lifespan. These mice also demonstrate delayed wound healing, increased metabolic efficiency, and the potential presence of hypothalamic lesions.

### Application

- Research on the pathogenesis of obesity and type 2 diabetes;
- Development and screening of obesity and type 2 diabetes drugs;
- Research on endocrine defects;
- Research on metabolism research;

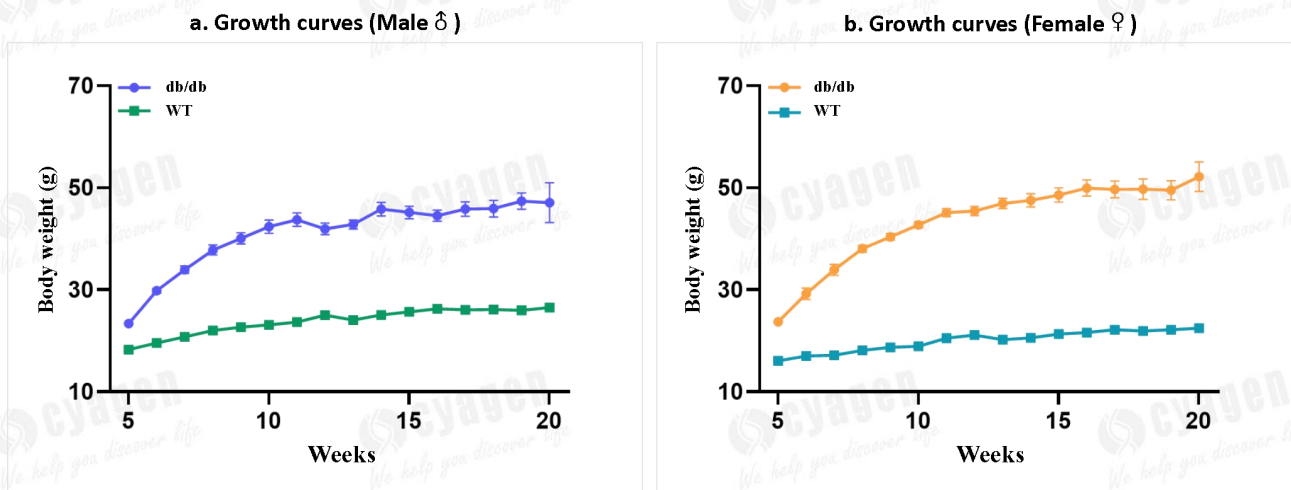
- Research on reproductive biology.

## Breeding Considerations

Homozygous female db/db mice are infertile and cannot reproduce naturally. Breeding must be conducted by mating heterozygous individuals, specifically by pairing heterozygous db/db mice (Catalog Number: C001505).

## Validation Data

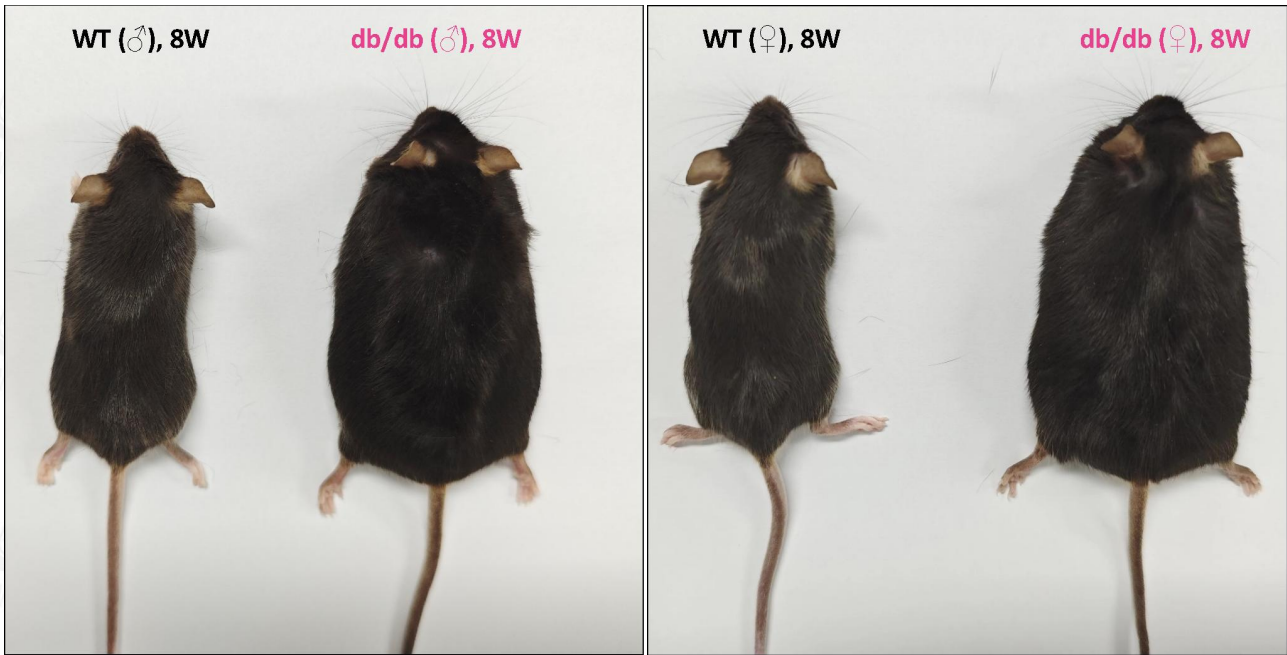
### 1. Growth Curve



**Figure 1. Growth curve comparison between male and female db/db mice and wild-type mice.**

Compared to wild-type (WT) control mice, male db/db mice showed rapid weight gain between weeks 5 and 11, with growth slowing and body weight stabilizing thereafter at approximately twice that of age-matched wild-type mice. Female db/db mice exhibited a similar trend in weight gain as the males.

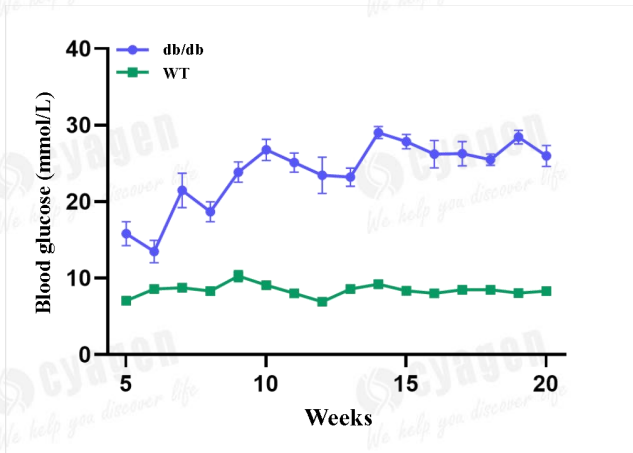
### 2. Body Size Comparison



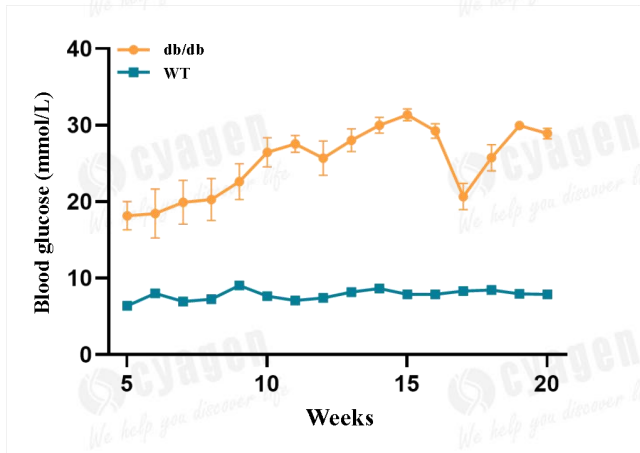
**Figure 2. Appearance comparison of male and female db/db mice with wild-type mice (WT) at 8 weeks of age.** Both male and female db/db mice exhibited significant obesity at 8 weeks of age compared to wild-type control mice (WT).

**3. Random Blood Glucose**

**a. Random blood glucose (Male ♂)**



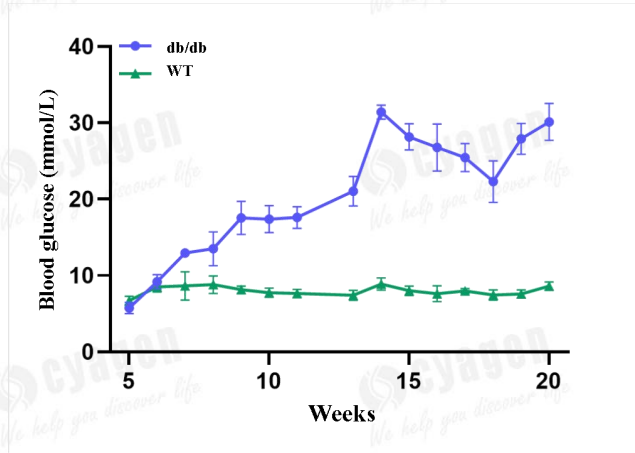
**b. Random blood glucose (Female ♀)**



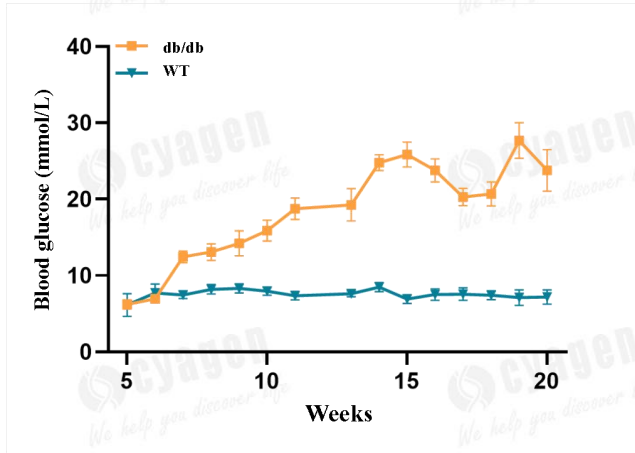
**Figure 3. Random blood glucose comparison between male and female db/db mice and wild-type mice.** Compared to wild-type (WT) control mice, random blood glucose levels in male db/db mice gradually increased between weeks 5 and 13, stabilizing after week 14 at significantly higher levels than the control group. The trend in random blood glucose levels in female db/db mice was consistent with that observed in males, except for a slight decrease at week 16.

#### 4. Fasting Blood Glucose

a. Fasting blood glucose (Male ♂)



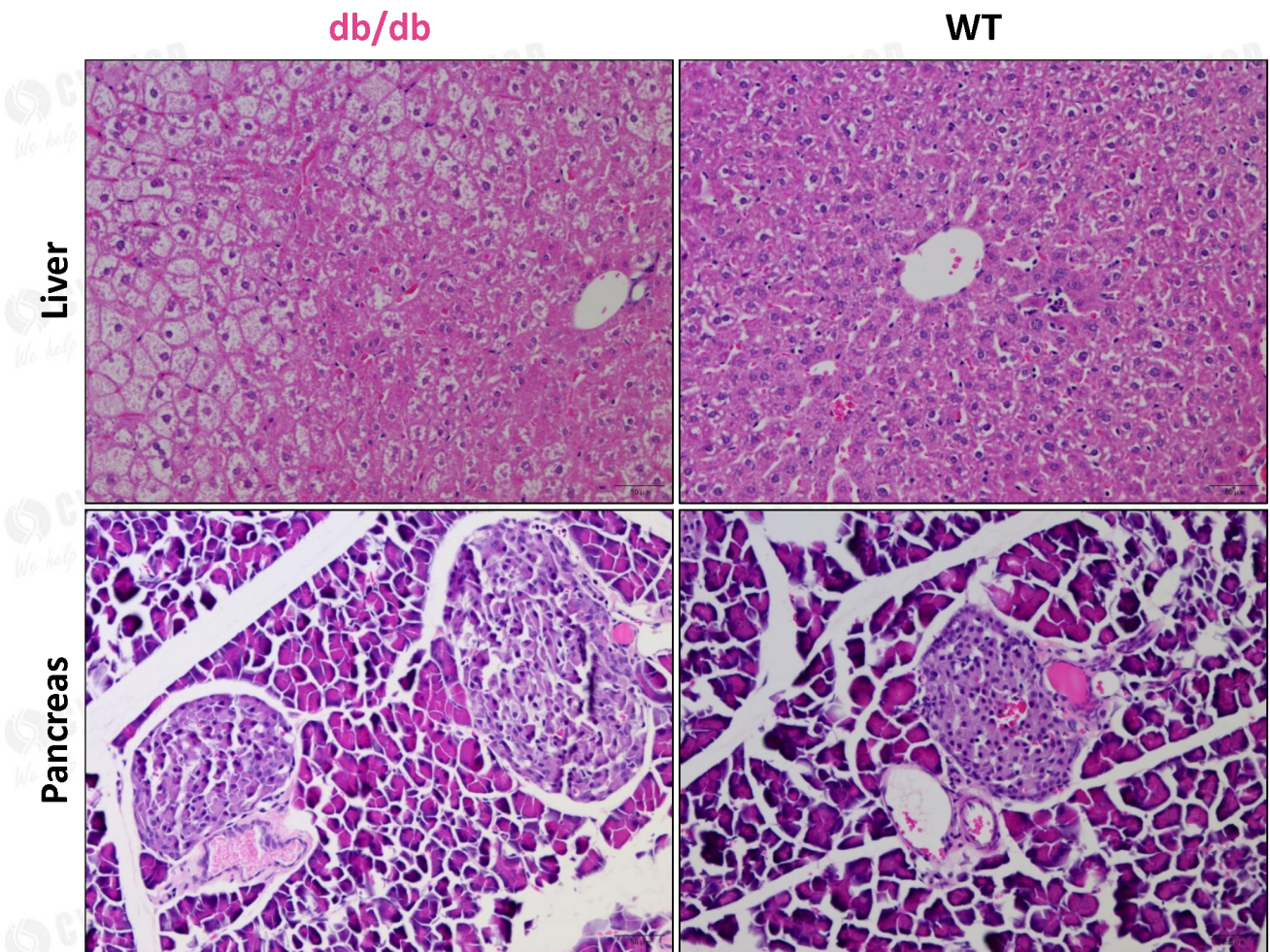
b. Fasting blood glucose (Female ♀)



**Figure 4. Fasting blood glucose comparison between male and female db/db mice and wild-type mice.**

Compared to wild-type (WT) control mice, fasting blood glucose levels in male db/db mice gradually increased between weeks 5 and 14, stabilizing after week 14 at significantly higher levels than the control group. The trend in fasting blood glucose levels in female db/db mice was consistent with that observed in males.

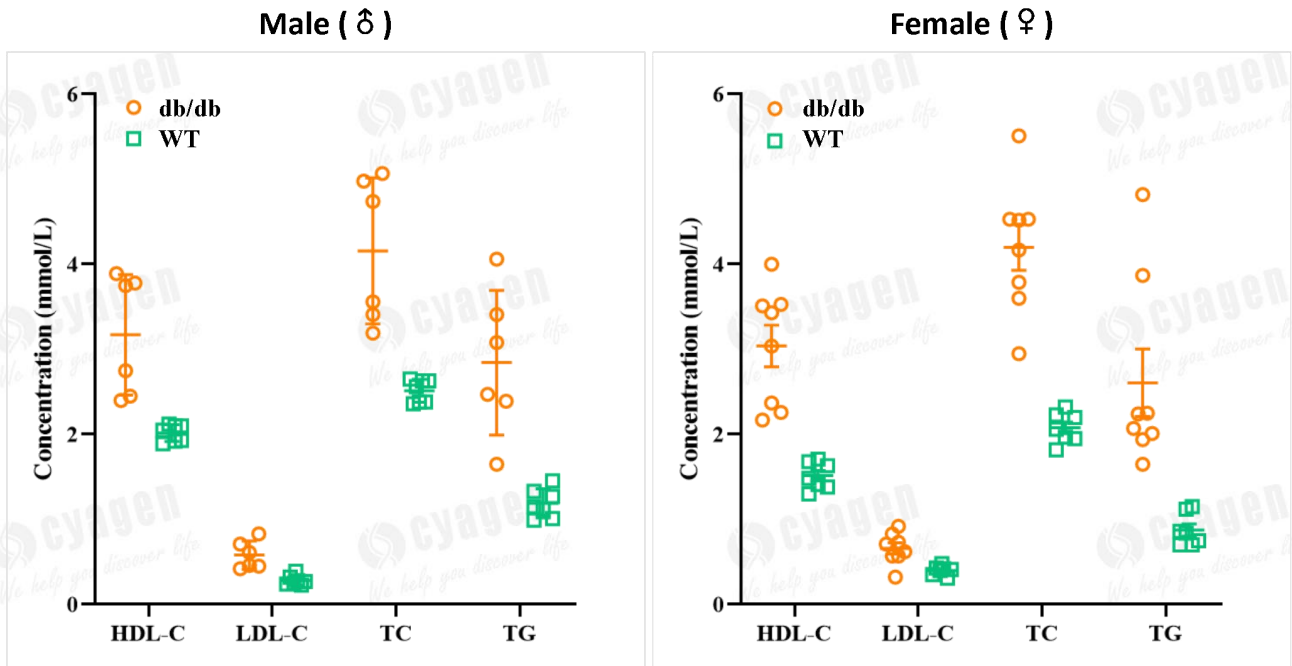
#### 5. Liver and Pancreas Pathology



**Figure 5. Comparison of liver and pancreas histology in 20-week-old db/db mice and wild-type mice.**

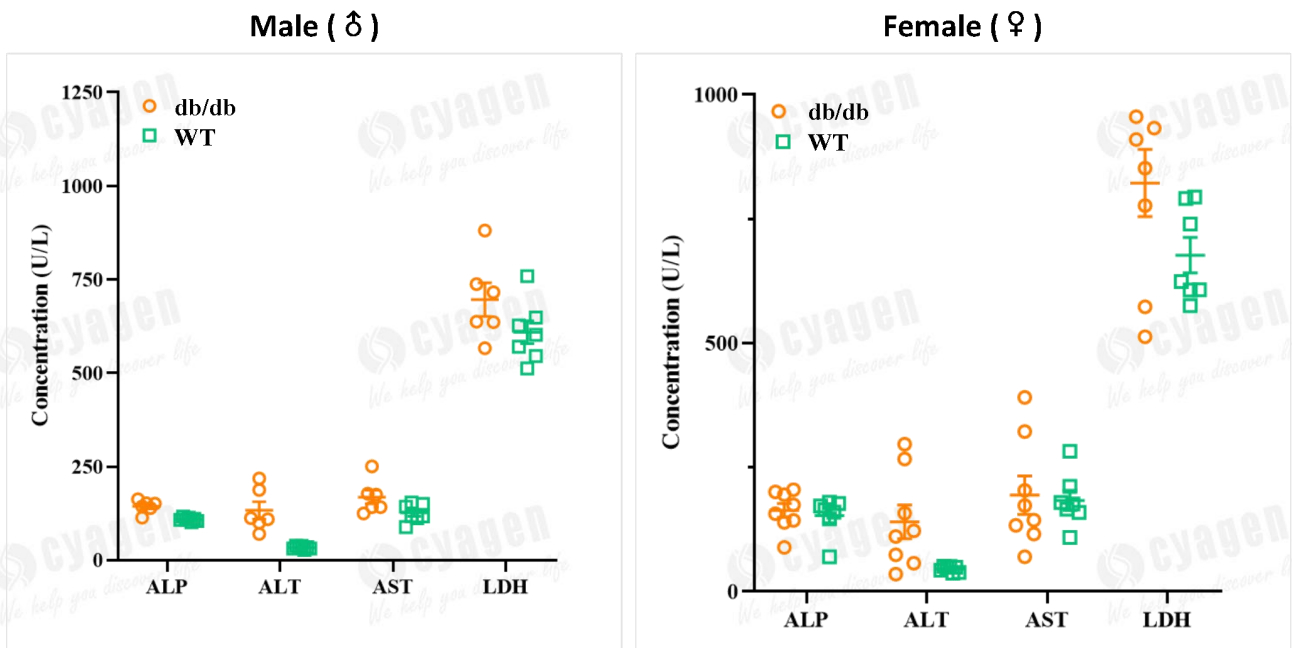
Compared to wild-type control mice, 20-week-old db/db mice showed marked hepatic steatosis, with disordered islet structure also present in the pancreas.

**6. Lipid Metabolism Parameters**



**Figure 6. Comparison of lipid metabolism parameters between db/db mice and wild-type mice.** Compared to wild-type control mice, male and female db/db mice showed significantly elevated lipid metabolism parameters, indicating a pronounced hyperlipidemia phenotype. (HDL-C: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol; TC: Total cholesterol; TG: Triglycerides.)

**7. Liver Function Indicators**



**Figure 7. Comparison of liver function indicators between db/db mice and wild-type mice.** Compared to wild-type control mice, male and female db/db mice showed varying degrees of elevation in liver function indicators, suggesting abnormal liver metabolism in this strain. (ALP: Alkaline phosphatase; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; LDH: Lactate dehydrogenase.)

### Conclusion

The db/db mouse model exhibits classic type II diabetes phenotypes, including obesity, hyperglycemia, and hyperlipidemia, as evidenced by assessments of body weight, blood glucose, lipid biochemistry, and liver function indicators. Additionally, db/db mice demonstrate hepatic steatosis, liver function abnormalities, and disordered pancreatic structure. Collectively, the db/db mouse is a spontaneously occurring model of severe obesity, hyperglycemia, hyperlipidemia, liver function abnormalities, hepatic steatosis, and pancreatic structural disorder. It is highly suitable for research into type II diabetes, obesity, and other metabolic disorders, as well as for pharmacological efficacy evaluations related to these conditions

### References

- [1] Chen H, Charlat O, Tartaglia LA, Woolf EA, Weng X, Ellis SJ, Lakey ND, Culpepper J, Moore KJ, Breitbart RE, Duyk GM, Tepper RI, Morgenstern JP. Evidence that the diabetes gene encodes the leptin receptor: identification of a mutation in the leptin receptor gene in db/db mice. *Cell*. 1996 Feb 9;84(3):491-5.
- [2] Yoon JW, Leiter EH, Coleman DL, Kim MK, Pak CY, McArthur RG, Roncari DA. Genetic control of organ-reactive autoantibody production in mice by obesity (ob) diabetes (db) genes. *Diabetes*. 1988 Sep;37(9):1287-93.
- [3] Kämpfer H, Paulukat J, Mühl H, Wetzler C, Pfeilschifter J, Frank S. Lack of interferon-gamma production despite the presence of interleukin-18 during cutaneous wound healing. *Mol Med*. 2000 Dec;6(12):1016-27.
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- [5] Garris DR. Estrogenic stimulation of ovarian follicular maturation in diabetes (db/db) mutant mice: restoration of euglycemia prevents hyperlipidemic cytoatrophy. *Cell Tissue Res*. 2004 Nov;318(2):365-73.
- [6] Garris DR, Garris BL. Genomic modulation of diabetes (db/db) and obese (ob/ob) mutation-induced hypercytolipidemia: cytochemical basis of female reproductive tract involution. *Cell Tissue Res*. 2004 May;316(2):233-41.

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