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From fat fruitfly to human obesity

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Abstract

Obesity is a chronic metabolic disease that has become a global problem. Although a tremendous amount of effort has been spent to prevent and treat obesity, its etiology is still largely unknown and there are not yet sufficient strategies to control obesity. Recently, the fruit fly, *Drosophila melanogaster*, has become a useful model for studying metabolic homeostasis and obesity related disorders. The goal of this mini-review is to summarize the recent achievements of *Drosophila* models and to highlight the experimental protocols used in studying feeding behavior and energy homeostasis in the fly. The *Drosophila* models provide useful tools to understand obesity pathogenesis and to develop novel therapeutics.

Keywords

Obesity; Drosophila melanogaster; metabolic homeostasis; feeding behavior; genetic tools; fat deposition

Obesity is a chronic metabolic disease that has become a global problem. The World Health Organization (WHO) reported that there were about 1.4 billion overweight adults, 500 million obese adults, and 40 million overweight children in 2011(www.who.int). The prevalence of childhood obesity has increased up to 15% recently and the risk of obesity co-morbidities also increased at an alarming rate [1, 2]. Although the etiology of obesity is not fully clear, a lifestyle including inappropriate diet and exercise habits, genetic factors, and an ‘obesogenic’ environmental are the major contributing factors. Great effort is needed to investigate the molecular mechanisms controlling food intake and body weight and to develop novel pharmacological and non-pharmacological strategies to combat obesity. The fruit fly, *Drosophila melanogaster*, has become an excellent model for studying nutrient-sensing pathways and metabolic homeostasis in a cost-effective and expedient manner [1–

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3]. Recent studies from *Drosophila* models of diabetes and obesity illustrate that the molecular mechanisms underlying energy balance in *Drosophila* are largely conserved between humans and flies. This mini-review highlights the advantages of the experimental protocols of *D. melanogaster* in the study of feeding behavior and energy homeostasis. For other aspects of *Drosophila* work related to metabolic disorders, there are several recent excellent reviews [3–17].

1. General biology of D. melanogaster related to metabolism

The advantages of using *Drosophila* are the low cost of maintenance and rapid developmental course in the fly compared with rodents or other mammal models. The majority of disease-causing genes and fundamental physiological processes of *Drosophila* are conserved in humans. *D. melanogaster* can be used to mimic the pathogenic condition of human disorders to identify pathways and novel drug targets by taking advantage of available genetic tools. Moreover, *D. melanogaster* can be used to screen and validate small molecules for drug discovery.

The fly genome contains four chromosomes and encodes about 14,000 genes. About 75% of disease-associated genes in humans have functional orthologs in the fly [18, 19]. The fly life cycle includes four developmental stages: the embryo, the larva, the pupa, and the adult, and is very rapid compared with that of mammals. At room temperature, one pair of mating flies can produce hundreds of offspring within ~12 days.

Each developmental stage of *Drosophila* has its own specific advantages and can be used as a model system to study metabolic homeostasis. The embryo can be used to study fundamental development by assessing organogenesis, cell fate determination, pattern formation, neuronal development, and axon path finding. The larva, especially the third instar larva, and the pupa stages can be used to investigate various developmental and physiological processes, fat and sugar storage, as well as some behaviors such as foraging, feeding, and locomotor activity. The fly has various organs with functions similar to those of the mammalian gut, lung, heart, kidney, and reproductive tract. There are more than 100,000 neurons in flies that form neuronal circuits to regulate various behaviors, including feeding, circadian rhythms, sleep, learning and memory, mating courtship, grooming, aggression, and flight navigation [20].

Drosophila digestion and neuroendocrine systems are very conserved in vertebrates. Food is digested and absorbed in the crop and midgut, which is the fly counterpart of the stomach and intestine [21]. The key metabolic regulating organs in flies include fat bodies (functions as white fat tissue and liver), Malphigian tubules (functions as kidneys), oenocytes (functions as hepatocyte-like cells), and pars intercerebralis–corpora cardiac system (functions as the hypothalamus–pituitary system)[1, 21–24]. These organs integrate information on environmental changes and internal metabolic status, and coordinate physiological activities to maintain energy homeostasis [1]. Glycogen and lipids are stored in the fly fat bodies [24]. The biochemical pathways for controlling sugar and fat storage [58] are also very similar to those in human. In flies, the IPCs (insulin producing cells) in the pars intercerebralis function similarly to pancreatic β-cells. The corpus cardiaca functions

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like the pancreatic α-cells and have been shown to be involved in adipokinetic (AKH) secretion. AKH is similar to mammalian glucagon. The pars intercerebralis-corpora cardiaca system of a fly receives information on the internal metabolic status and coordinates the physiological and behavioral activities of various peripheral organs [22]. Thus, *Drosophila* models can be used to investigate various aspects of energy balance including feeding control, food perception, energy expenditure, and lipometabolism.

2. Genetic tools for studying energy homeostasis

Since the full genome of *D. melanogaster* was sequenced [25], it has tremendously affected the fly world and elevated its role as a model to study human biology and diseases. *Drosophila* research is considered to be at the forefront since many novel discoveries of genes, proteins, cellular pathways, and genetic concept and tools are often identified first in the fly and then validated later in mammalian models. One of the unique benefits of using the *Drosophila* system is that various genetic tools and stock collections are available [59]. Here, we highlight the utility of these genetic tools and describe their application to metabolic research.

2.1.Using Gal4/UAS system to regulate gene expression [26]

The principle of the UAS/Gal4 system is that the yeast transcriptional activator Gal4 can specifically bind to the upstream activated sequence (UAS) resulting in expression of the recombinant genes cloned downstream of the UAS sites in a tissue specific manner. Tissue-specific Gal4 driver fly lines are available in various stock centers (eg. Bloomington Center, Indiana University, USA) for many tissues [20, 27]. For metabolic studies, the most frequently used driver flies are shown in Table 1. The UAS/Gal4 system can lead to overexpression or mis-expression of any gene, and can assess any resulting metabolic phenotype [26]. Overexpression of human proteins or disease related mutants can reveal the novel functions of such proteins or gain-of-function pathogenesis pathways.

2.2.Unbiased forward genetic screens

Forward genetic screens are often performed in *Drosophila* to identify new candidate genes and to reveal new knowledge [28, 29]. Using *Drosophila* allows a small group of researchers to perform a large scale screen with clear phenotypic readouts to assess hundreds of putative mutants, which is often beyond what is feasible using vertebrate model systems. A successful example in the use of forward genetic screens in the fly is to understand insulin signaling [30]. Insulin pathway gene screens have identified novel regulators of this pathway in *Drosophila* [31, 32]. Moreover, a genetic screen can be designed to assess the phenotype only in the fly eye (or certain organs) to avoid altering the rest of the body [33].

2.3. RNAi gene knockdown screens

With the genome-wide RNAi-mediated gene silencing methodologies, robustly available *Drosophila* cell lines can be used to perform RNAi screens. Moreover, there are genome-wide transgenic UAS-RNAi flies that have been established in recent years in various fly stock centers allowing to knock down almost any genes *in vivo* [34]. For example, the Vienna Drosophila Research Center has the collection of UAS-RNAi fly lines targeting 88%

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of the fly genome. Through combination with various Gal4 drivers, virtually any gene can be knocked down in a tissue-specific manner. For example, the RNAi screens have been successfully performed in the genes that are involved in lipid droplet morphology and mitochondrial function [35, 36].

2.4.Drug screens

For drug discovery research, *D. melanogaster* can be used in either high-throughput initial screening or in the validation studies of the positive hits after traditional *in vitro* screens [20]. *Drosophila* cells, larva and adults can all be used in various drug screen designs. The advantage of the *Drosophila* system is to effectively and rapidly identify positive hits from larger compound libraries and then move the more effective hits into mammalian models. Use of flies significantly increases the positive hit rates and reduces costs at early stages of drug discovery. There are multiple successful drugs screens that have been performed to identify potential therapeutics in anti-cancer and in anti-neurodegeneration models [20]. There is no doubt that flies can also be used to screen anti-obesity and anti-diabetes related metabolic disorders as well.

3. Drosophila models for human metabolic disorders

Similar to mammalian models, there are two types of models that mimic the key features of human obesity in *Drosophila*. One is to overexpress energy fostering genes or down-regulate negative-regulation genes of energy balance [8, 12, 37]. The other is altering the diet to add high fat, high sugar, and high proteins in the fly food [8, 38–40]. Both approaches produce models that exhibit some key features of human obesity and related disorders, as summarized in Table. 2[8, 37–40].

3.1.Genetic models of obesity

The versatility of *Drosophila* genetic tools makes it easy to generate models of human metabolic disorders. Genetic inactivation (eg. P-element insertion), mutation or RNAi often are used to generate the loss-of-function genetic models; the gain-of-function models can be generated via overexpression of human disease genes and proteins, or misexpression of fly homologs of human disease genes. For example, one genetic model that shows key features of human obesity[37], is the result of expression of human synphilin-1 protein in fly neurons that results in obesity-like phenotypes in both larva and adult flies. To generate synphilin-1 obesity transgenic *Drosophila*, the human synphilin-1 cDNA is subcloned into a fly UAS vector containing two inverted repeat elements (eg.P-elements) [37]. The resulting plasmid is co-injected with a helper construct that expresses a transposase into the germ cells of embryos. It only takes about a couple of hours to inject 100 embryos to achieve a 10–15% successful germline integration rate. The flies with synphilin-1 gene insertion (UAS-synphilin-1) are selected in the F2 generation by picking the red-eye (a marker phenotype) flies. It takes about 6 weeks from injection to selection of independent founder lines. For this process, several commercial sources can perform the service once the UAS-foreign gene constructs are available (eg. Rainbow Transgenic Flies, Inc. CA, USA). Finally, the human synphilin-1 gene can be expressed in various tissues involved in metabolic regulation by GAL4 driver fly lines [37]. The obese phenotypes can be assessed via biochemistry,

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immunostaining, and behavioral assays as listed in the next section. The human synphilin-1 expression in neurons increases food intake, body weight, and fat deposition similar to the phenotypes that are observed in the human transgenic mouse model [41].

3.2. Diet induced obesity models in flies

High calorie/high fat diet intake and improper lifestyle behaviors are the predominant causes of obesity and its comorbid conditions. Rodents fed with high-calorie diets (high fat, high glucose diet) for 2–3 weeks can develop obese-like phenotypes [42]. Similarly, regular fly food (a combination of yeast, corn starch, and molasses) with the addition of 30% coconut oil (high fat) for 5 days in adult flies causes high levels of fat deposition and results in an imbalance in insulin/glucose homeostasis [8, 39, 40]. Moreover, this high fat diet also induced fly heart dysfunction, similar to a mammalian response. Larvae fed on a high sugar diet (1M sucrose, 86.4% of calories from carbohydrates) can develop hyperglycemia, insulin resistance and accumulated fat [38]. These studies indicated that *Drosophila* can also be a useful dietary-based model for studying human metabolic disorders.

4. Assays to assess metabolic homeostasis in Drosophila

4.1. Assays using larvae

Drosophila larvae, especially in the third instar larvae stage, can be used for food intake and metabolic analysis. Below is the list of current assays that are used in metabolic homeostasis studies.

4.1.1. Triacylglycerol and glycogen measurement—Glycogen and triacylglycerol (TAG) glycogen are the major intracellular forms of stored energy in *Drosophila* [12, 43] and are found in all tissues of larvae and adults. Thus, the content of TAG and glycogen can be measured in tissue homogenates of larvae and adults. For TAG assays [37], larvae and adults are homogenized in 1% Triton-X, PBS buffer and then added to free Glycerol Reagent (Sigma) for 5 min at 37 °C. The resulting samples are measured at 540 nm with a BioTek Synergy HT microplate spectrophotometer. TAG is determined by subtracting the amount of free glycerol in the PBS-treated sample from the total glycerol present in the sample treated with TAG reagent.

For glycogen assays [37], larvae and adults are homogenized in PBS. Heat-treated homogenates are incubated with glucose reagent and/or amyloglycosidase (Sigma) at 37°C for 1 hour. Amyloglycosidase catalyzes the conversion of glycogen and trehalose into glucose. Then the samples are measured at 340 nm with a BioTek Synergy HT microplate reader. Glycogen and glucose are determined using a standard curve.

4.1.2.Larvae floating assay—This assay developed by Reis and colleagues is used to detect fat deposition in larvae [44]. The principle of this assay is that fat larvae float better in a high density solution (8–30% sucrose solution). Briefly, the 10–30 third instar larvae are placed in 10 ml vials with 8–30% sucrose (Fisher Scientific) dissolved in PBS. Then, the larvae are gently mixed and kept stable for 3–5 minutes to achieve equilibrium. The larvae that are floating at the surface (fat larvae) and staying in the bottom of vials are counted. Since this assay is a clear phenotype readout and is easy to perform, it is often used not only

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to characterize the obese-like phenotypes of larvae but also to perform genetic and therapeutic screens [37, 44].

4.1.3.Fat body staining assays—The fat body is distributed throughout the organs in larvae and in adult flies [1]. Fat body cells contain lipid droplets storing triglyceride. Similar to mammalian system, there is a controlled balance between lipolysis and lipogenesis in flies. A triacylglycerol lipase, *brummer* (*bmm*), in *Drosophila* catalyzes triglyceride to fatty acid under starvation, which is similar to human lipase [45, 46]. Another conserved gene, *Adipose* (*Adp*), reduces fat storage and decreases fat body size via inhibiting PPARγ activity [47].The fat body cells in the dissected larvae can be assessed by fluorescence labeling [37, 48]. Fat deposition and lipolysis status can be reflected in the size and number of lipid droplets and fat body cells.

A. **Phalloidin/DAPI staining assays:** Fat body cells of larvae can be stained with Phalloidin (red) and DAPI (nuclei staining, blue) [37, 48]. Briefly, fat bodies of the third-instar larvae are dissected on a slide,fixed with 4 % formaldehyde, and blocked with 5% normal goat serum. Alexa Fluor 568 phalloidin (Invitrogen) is added on the fat body slide for 5–10 min. Then the slides are mounted in Vectashield with DAPI. The fat body cells can be imaged under a fluorescent microscope. Fat body cell size can be quantified with NIH ImageJ software.

B. **Lipid droplet staining by nile reds** [37, 48]. Fat bodies of third-instar larvae are dissected and fixed with 4% formaldehyde. Nile red (0.00002% in 75% glycerol) is added in fat body slides for 5 min. Slides are imaged under a fluorescent microscope with an excitation wavelength of 450–500 nm and an emission of 515–560 nm. The Nile red labeled lipid droplets can be quantified by the number and size with NIH ImageJ software.

4.1.4. Larvae Feeding assays [60, 61]—*Drosophila* larvae provide a great model to study food response behavior including foraging, food intake, compensatory feeding, and stress-resistant food procurement. It is relatively easier to synchronize populations of larvae that display largely uniform feeding activity than to use adults.

To study the specific role of signaling molecules or neurons in the regulation of feeding behavior, there are two types of larvae feeding assays: liquid food and solid food [60,61]. The liquid food assay can quantify the initial feeding rate of individual fed or fasting larvae, offering a simple way to measure the motivational state of feeding in larvae. However the shortcoming to this approach is that larvae tend to burrow into the soft medium, making it difficult to measure feeding behavior for a relatively long period of time (e.g., >60 sec). The solid food assay is suitable and an easy way to measure feeding activity for a long time to eliminate the larval burrowing problem [61]. The soft or solid larvae food is made from a mixture of glucose, agar, and water in the Petri dish. For solid food, the concentration of glucose and agar are higher and the resulting paste is air-dried overnight. Generally 15–25 larvae are placed onto the paste in one Petri dish and allowed to settle for a few minutes, and then the Petri dishes are placed under the microscope to observe the number of mouth-hook contractions for 10 or 30 sec.

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The feeding assays are often used to compare intakes of fed and hungry larvae (hungry larvae are more likely to display aggressive behavior). They are also used to compare the feeding response to soft and hard sugar media as a measure of the motivation to eat [60,61]. To consume the same amount of food, larvae need to work harder with hard media to pulverize the agar block with their mouth hooks. Moreover, to further enrich the assays to measure food intake under different energy states with quantified food ingestion, feeding assays can be carried by adding colored dyes or radioactive isotopes in the food [60, 61]. The combination of two or more complementary food behavior assays can provide more information about the role of interesting genes or neurons in feeding behavior.

4.1.5. Larval crawling assay [49]—This assay is used to determine the early stage changes in the crawling abilities of larvae or to test the effects of human disease genes or drugs on their locomotion activity. One method is that larvae with genetic mutations or treated with drugs are placed in the Petri dish with measuring squares marked on the bottom. The distance that each larvae moves across the Petri dish in 30 to 60 sec is measured. Another method is to place larvae in the Petri dish with liquid solution and monitor the numbers of larvae body changing directions under the dissection microscope. This basic crawling assay can also be used in combination with stress, temperature changes, or bright light to assess additional behavioral response levels.

4.1.6. Immunostaining—All tissues in larvae and adult flies can be used to perform immunostaining to assess the protein expression patterns and protein posttranslational modifications after genetic alteration, energy status changes, or drug treatment. For example, to observe the development of energy balance regulating neurons (eg. dopamine or serotonin), dissected larvae or whole adult fly brains can be labeled with anti-TH or anti-serotonin antibodies then probed with fluorescent-linked secondary detection antibodies (alexFlour 568, Invetrogen). The neuron number and network can then be visualized under fluorescent or confocal microscopy [39].

4.2.Assays using adult flies

4.2.1.Body weight and life span measurement—For adult flies, body weight can be measured using a microbalance. Generally, 1 adult fly weights around 100 μg. Fly survival also can be measured to reflect the dysfunction of metabolic balance. Normal adult flies survive about 2–2.5 months. Energy status or metabolic disorders can alter fly life span based on the severity of impairment. For example, fat flies are more resistant to starvation and survive longer [37].

4.2.2.Adult fly feeding assay—Capillary feeder (CAFE) assay is a method to measure ingestion by individual or grouped fruit flies for minutes or for days in a precise, real-time manner [50]. This method can also be used to determine meal volume and meal frequency. The fly can ingest about 1.7 fold of their body mass over 24 h. In addition, the CAFE can also be used for the oral delivery of drugs [50]. In the CAFÉ assay (34), a *Drosophila* wide vial that contains 15 ml 1% agar at the bottom is used to provide a humid condition, and then covered with a foam plug. A truncated 200 μl pipette tip is inserted through the foam plug, which holds a 5 μl glass capillary tube. The feeding solution (eg.5% sugar) or drugs

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can be held in this capillary. The intake volume and frequency can be assessed with time by measuring the amount of consuming solution in the capillary. An identical vial set without flies is used to determine evaporative losses. Typically there is less than 10% of ingested volumes for evaporative losses that has to be subtracted from experimental readings [50]

4.2.3. Climbing assay and actometer test—Similar to mammalian models, fly locomotor activity is an important parameter of energy expenditure and can be measured in two ways: climbing assay and actometer test. A climbing assay is also named negative geotaxis assay and is often used to determine locomotor activity, however it is time consuming [51]. The tested flies are anesthetized by CO_2 exposure, and put in a plastic column (diameter, 1.5 cm; length, 25 cm). After a 30-min recovery from anesthesia, flies are gently tapped to the bottom of the cylinder. The flies that can climb to or above the median line of the column within 10 seconds are counted. This method can also be used to observe the effects of mutant genes and drugs on movement activity.

The actometer test is similar to the open field activity assay in rodents. A single fly is placed in a small tube that is connected to the controlling computer. The one end of each small tube contains food. The principle of this test is that every time the fly crosses an infrared beam (locomotion actograms), the computer records the number of beam-breaks [51]. The actometer assay more precisely monitors the pattern and total activity of flies, although it is costly to purchase the Actometer sets.

4.2.4. CO2 Emission Assay [39]—is another assay to measure energy expenditure. Flies are anaesthetized with N2 for quick recovery and placed in a L1-COR CO2 analyzing chamber (Sable Systems, Inc.). After 30 minutes recovery from anesthesia, the CO2 concentration can be measured and normalized by fly body weight.

Other assays such as western blots to determine protein levels and phosphoryaltion status, immunostaining to assess the protein expression patterns, biochemistry assays to measure the TAG, glucose and glycogen levels can also be done in adult flies as described in the larvae assays.

4.2.5. Drug delivery methods [20]—Drugs can be delivered to larvae via injection into larvae body, or drugs can be added into liquid or solid media. 2% yeast is often added into the food media to motivate feeding behavior and insure the ingestion of a drug. For adult flies, drugs can also be delivered together with food as a mixture or given via injection into fly abdomen. Some special type of drugs can also be given via an aerosol or gas. Some drugs can be delivered as a direct exposure to the nerve cord. Generally the delivery of drugs via the feeding route has the highest throughput and is most often used for drug screens.

5. Drosophila genes involved in energy balance

With recent advances in whole genome sequencing, many metabolic related and obesity-linked genes have been discovered in humans [2, 12, 52–54]. Most of these genes have orthologues in *Drosophila* as summarized in Table 3. Some of these genes (AMPK, Sir2, hedgehog, etc) are heavily investigated in the obesity field. The study of the functions of

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these genes in *Drosophila* are likely to provide pioneering knowledge of their roles in the regulation of energy balance and provide novel targets for therapeutic developments. For example, studying the genes that are involved in insulin and lipid signaling pathways [8, 10] revealed the certain mechanisms related to growth control and energy homeostasis [8, 10, 55–57].

Conclusions

Drosophila has become an excellent model system to tease apart essential metabolic regulators and pathways. Drosophila models not only contribute to pathogenesis research to identify more novel players underlying energy homeostasis but also provide a useful *in vivo* model to develop rationale therapeutics. Although the *Drosophila* system provides a rapid *in vivo* model, it is still important to combine mammalian models and human studies to fully understand obesity and its co-morbidities and to eventually combat them.

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Highlights

- We reviewed recent Drosophila models of human obesity
- We highlight the fruitfly methods in the studying of energy homeostasis
- The use of Drosophila screens can identify novel obese-related genes and therapeutics
- *Drosophila* provide an excellent model to study feeding behavior and energy balance

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Table 1

The most frequently used UAS-Gal4 driver fly lines in obesity research [37]

Gal 4 Lines	Expressing Positions
c673a-Gal4	IPCs, mushroom body, and the ventral ganglion
Fruitless-Gal4 (Fru-Gal4)	IPCs, mushroom body, the subesophageal ganglion, and the ventral ganglion (broader distribution throughout the brain compared with c673a-Gal4)
Ddc-Gal4	Predominately dopaminergic neuron
TH-Gal4	Dopaminergic neuron
TPH-Gal4	Serotonergic neuron
Elav-Gal4	Pan-neuron
ppl-Gal4	Fat body
Dilp2 –Gal4	Insulin producing cells
Actin5c-Gal4	Ubiquitous expression

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Table 2

Key features of two types of obesity Drosophila models [8, 37–40]

Approaches and obese features	Genetic models	Diet induced models
Approaches	overexpress energy fostering genes; down-regulate negative-regulation genes of energy balance (example: refs. 37)	high fat, high sugar, and high proteins in diets (example: refs: 38–40)
Fat deposition	Increase TAG Increase fat body size and lipid droplets	Increase TAG Increase fat body and lipid droplets
Glucose	NTD	increase
Body weight	Increase in adult fly NTD (larva)	Increase in larva NTD (adult fly)
Insulin resistance	NTD	Yes
Activity(geotaxic)	No change	decrease
Food intake	increase	NTD
Heart Dsyfunction	NTD	Yes

* NTD, not determined

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Table 3

Metabolic and Obese-associated genes in Drosophila [2, 12, 52–54]

Human	D. melanogaster	Biological functions
enzymes		
AMPK	dAMPK	ATP sensor
TOR	mTOR	Signaling pathway
Acyl-CoA dehydrogenases	enigma	Metabolic pathway
PRKD1	PKD	Regulates insulin secretion
Lipid ω-hydrolases	Cyp4g1	Lipid metabolism
VLCFA acyl-CoA synthesis	Bubblegum	Metabolic pathway
HMGCR	Hmgcr	Regulates cholesterol production
GNPDA2	Oscillin	
NUDT3	Aps	
FANCL	Fancl	
QPCTL	CG5976	
Ligands, receptors and transporter		
Insulin/IGFs	Dilp2,3,5	Insulin pathway
IRS1-4	chico	Insulin pathway
AKH^A	glucagon	Glucagon/glucose regulation
UCP5/BMCP1	dUCP5	Lipid/glucose regulation
SH2B1	Lnk	Signals in insulin pathway
GPRC5B	boss	Possible glucose sensor
LRP1B	Lrp1	
NRXN3	Nrx-1	
NEGR1	CG11320	
Protein process		
SEC16B	Sec16	Regulates Ca^2 + stores
MTCH2	Mtch	Regulates Ca^2 + stores
MTIF3	CG13163	
RPL27A	RpL27A	
Transcription factors		
FOXO1,3a,4	dFOXO	Lipid and sugar metabolism
4E-BP	4E-BP	Metabolic pathway
SREBP-1a/SREBP-2	dSREBP	FAs regulation
TUB	King-tubby	Affects late-onset obesity
ZNF608	sbb	Regulates histone methylation for gene expression
TFAP2B	AP-2	Potential protein interactions in adipocytes
NPDC-1	dATF2	Gene regulation
ETV5	ETS96B	

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Human	D. melanogaster	Biological functions
Fat tissue related genes		
ATGL	brummer	Lipid regulation
adp	dAdp	Regulation fat storage
HGNC/KIAA1692	melted	Lipid regulation
Mnk1/2	Lk6	Lipid regulation
NPC1	NPC1a	Lipid regulation
NPC1L1	NPC1b	Lipid regulation
Perilipin/ADRP	Lsd2	Lipid regulation
SCD1	Desat1	Lipid regulation
NTE	Swiss cheese	Lipid regulation
FERM domain proteins	expanded	Lipid regulation
Unknown functions		
KCTD15	CG10440	Potential protein interactions in adipocytes
TMEM18	CG30051	
PTBP2	heph	
Other unidentified genes		