# 6

Fat body

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INTRODUCTION

The fat body is a dynamic organ that plays a central role in the metabolic function of the insect. It is of mesodermal origin and is located in the hemocoel, with all the cells in close contact with the insect hemolymph, facilitating exchange of metabolites. The fat body has sometimes been described as equivalent to a combination of the adipose tissue (storage function) and liver (major metabolic functions) of vertebrates, but this comparison does not do full justice to the fat body, which is also a major endocrine organ, and central to systemic immunity of insects. In addition, the fat body monitors and responds to the physiological needs of the insect during different developmental stages and under different environmental conditions, thereby coordinating insect growth with metamorphosis and reproduction.

This chapter is divided into three parts. Section 6.1 describes the structure and development of the fat body. It is followed by Section 6.2 on the storage and utilization of energy and nutrients, and, finally, Section 6.3 on the role of the fat body as an endocrine organ and nutrient sensor. The effectors of the humoral immune system derived from the fat body are considered in Chapter 5 (Section 5.3.4).
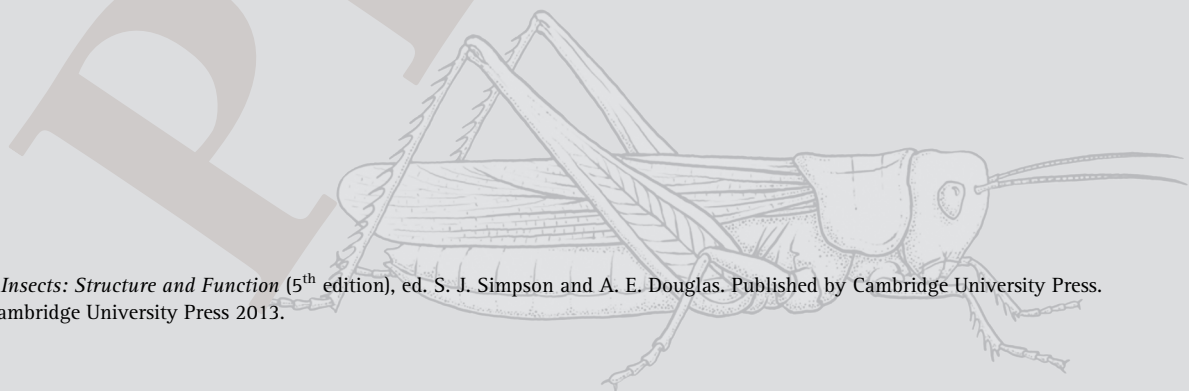
6.1 Fat body structure and development

The fat body consists of thin sheets or ribbons, usually only one or two cells thick, or of small nodules suspended in the hemocoel by connective tissue and tracheae. All of its cells are consequently in immediate contact with the hemolymph, facilitating the exchange of metabolites. There is generally a peripheral, or parietal, fat body layer immediately beneath the body wall, and often a perivisceral layer surrounding the alimentary canal can also be distinguished (Fig. 6.1). The fat body is most conspicuous in the abdomen, but components extend into the thorax and head. The structure of the fat body is generally uniform among individuals of individual species, but there is considerable variation among species, especially across different insect orders.

In hemimetabolous insects, the larval fat body persists in the adult without major changes. In holometabolous insects, the fat body undergoes a striking transformation during metamorphosis in which the tissue dissociates into individual cells. In the majority of the holometabolous insects, the adult fat cells are rebuilt from the larval fat cells, but in Hymenoptera and the higher Diptera, the adult fat cells develop *de novo* (Section 6.2.5).
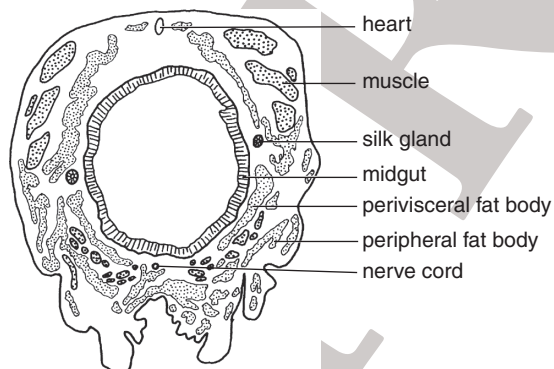

Figure 6.1 Distribution of fat body in a caterpillar in transverse section of the abdomen.

6.1.1 Trophocytes

The principal cells of the fat body are trophocytes (adipocytes), which store energy. In many insect orders these are the only cells present within the fat body. The trophocytes are held together by desmosomes to form sheets of tissues. The cytoplasm of adjacent trophocytes is connected through gap junctions, and the whole tissue is clothed in a basal lamina that is attached to the cells by hemidesmosomes (Fig. 6.2). The fat body of some insects additionally contain one or more of urate cells, mycetocytes and oenocytes. In a number of Lepidoptera and Diptera, the larval fat body is regionally differentiated to perform different functions. For example, in the larva of *Helicoverpa* (Lepidoptera) during the period just before pupation, protein synthesis occurs only in the peripheral fat body, while the storage of arylphorin and a very high-density lipoprotein, colored blue by non-covalently bound biliverdin, is restricted to the cells of the perivisceral fat body. In *Drosophila melanogaster* (Diptera), different pigments for the adult eye are synthesized and sequestered in different parts of the larval fat body, and in the larva of *Chironomus* (Diptera), hemoglobin synthesis appears to occur in the peripheral fat body, while storage might occur in the perivisceral fat body cells.

The form of the trophocyte varies according to developmental stage and nutritional status of the insect. In a larva soon after ecdysis, the trophocytes are generally small, with relatively little cytoplasm and little development of organelles. There are few mitochondria following the cell division preceding ecdysis (Fig. 6.3a,d), but, in a well-fed insect, there follows a preparative phase during which the trophocytes develop their capacity for synthesis. In the final larval stage of the moth *Calpodes* (Lepidoptera) the preparative period lasts about 66 hours. During this period there is extensive replication of DNA, but no nuclear division (Fig. 6.3a, b). Most of the cells become octaploid, although some cells exhibiting 16- and 32-ploidy also occur. A similar development occurs in *Rhodnius* (Hemiptera), while in *Calliphora* (Diptera), and probably in other Diptera, polyteny occurs (the
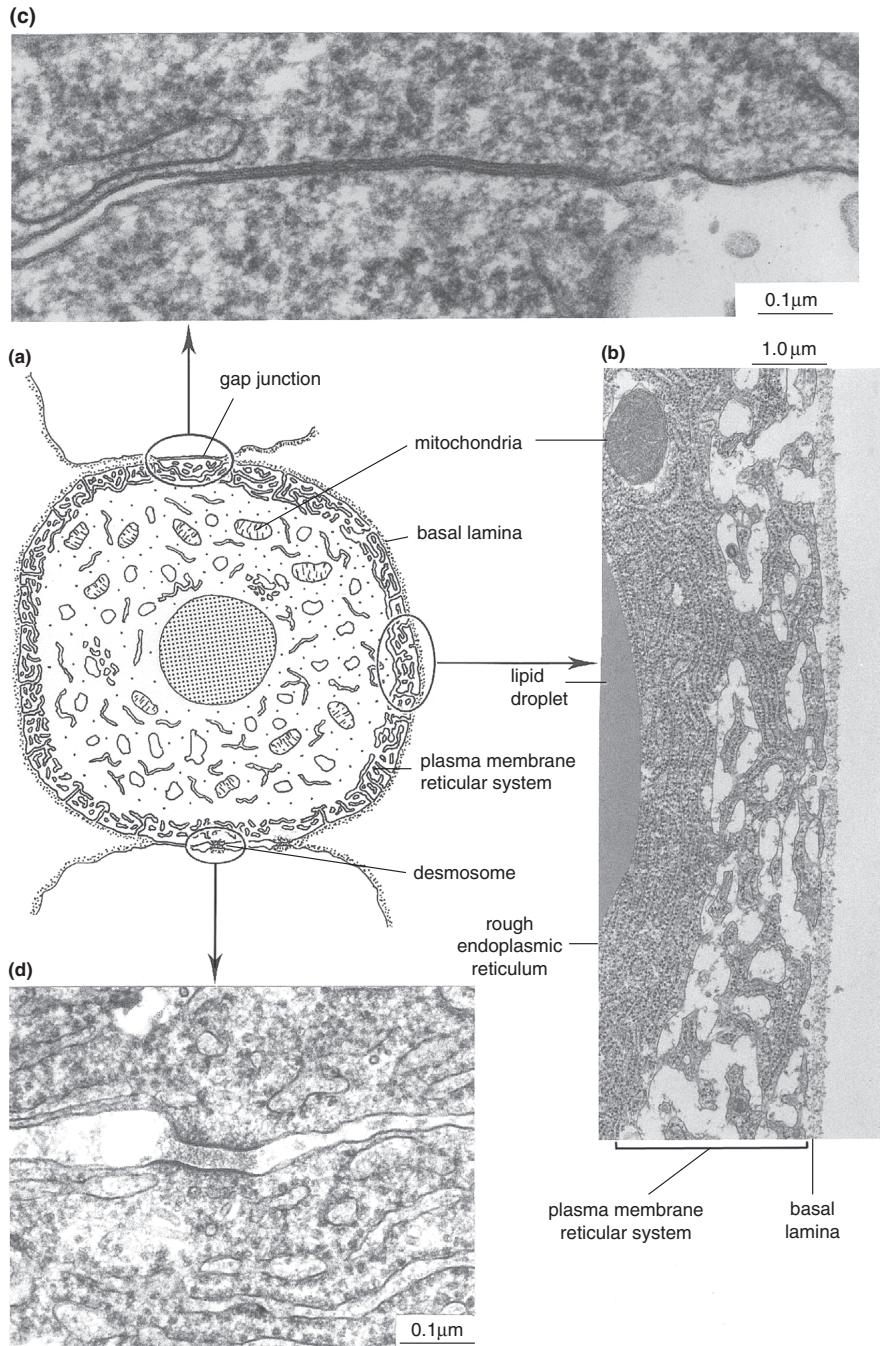
Figure 6.2 Structure of a mature trophocyte. (a) Diagram of a trophocyte. (b) Transmission electron micrograph of the plasma membrane reticular system of a trophocyte from the larva of *Calpodes*. (c) Gap junction between two trophocytes in the fat body of *Calpodes*. (d) Desmosome joining two trophocytes in the fat body of *Calpodes* (b, c and d after Dean *et al.*, 1985).
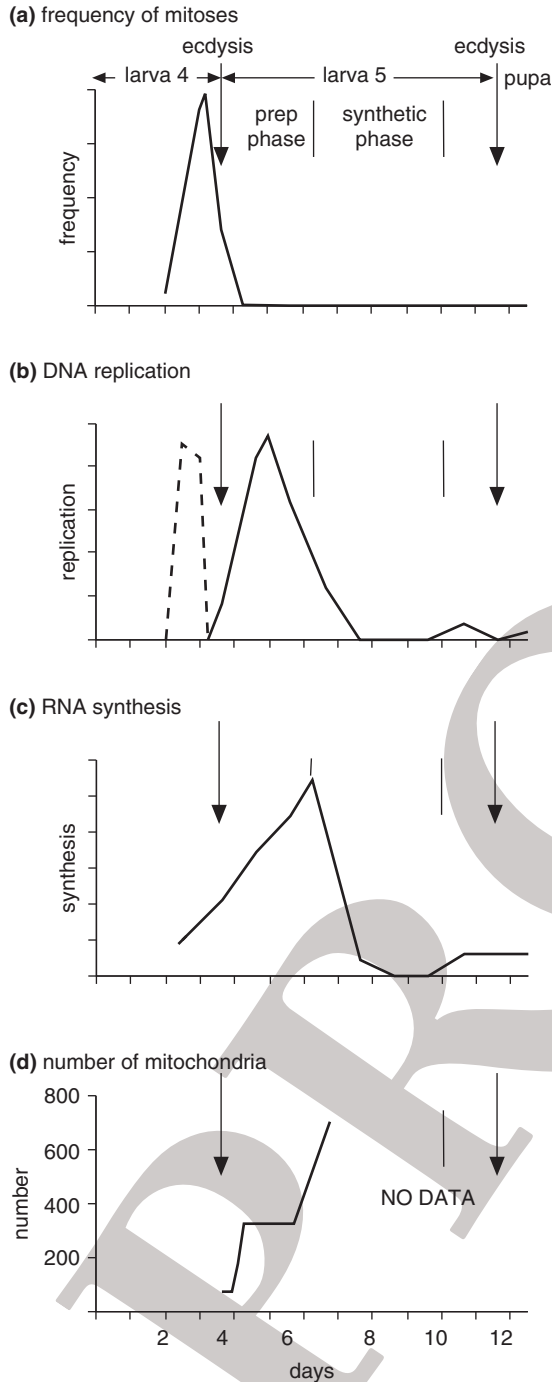
(a) frequency of mitoses

(b) DNA replication

(c) RNA synthesis

(d) number of mitochondria

Figure 6.3 Changes occurring in the cells of the fat body of the caterpillar of *Calpodes* during a molt/intermolt cycle

chromosomes divide, but do not separate). At the same time RNA synthesis occurs (Fig. 6.3c), ribosomes increase in number, rough endoplasmic reticulum proliferates and the numbers of mitochondria increase by division (Fig. 6.3d). The trophocytes now have the apparatus necessary to begin synthesis. During the preparative period, the cell membrane invaginates in a series of folds which interconnect to form the plasma membrane reticular system (Fig. 6.2). In *Calpodes* the membranes in this system are separated from each other by 100–150 nm. The reticular system occupies the peripheral 1–1.5 μm of the cells and it presents an exceptionally large surface area to the hemolymph. However, this surface is negatively charged and the effect of this is to limit the access of some large charged molecules to the interior of the reticulum. It is possible that the reticulum is concerned with the docking and unloading of lipophorins. When the larva is approaching the molt to pupa, the components of the cell that have been involved in protein synthesis regress.

Immediately after eclosion, the trophocytes of adult insects commonly contain extensive lipid droplets, accumulations of glycogen and protein granules. The trophocytes in males do not show further development and they probably play no further major role in protein synthesis. In females, however, changes occur which are comparable with those occurring in larval stages. This reflects the need, in many species, for the synthesis of vitellogenins.

6.1.2 Urate cells

Urate cells, or urocytes, are present in Collembola (springtails), Thysanura (silverfish), Blattodea

(prep phase is preparatory phase) (mainly after Locke, 1970). (a) The frequency of mitoses. Mitosis is limited to the period immediately before ecdysis. (b) DNA replication. The broken line is the presumed phase of replication associated with mitosis. The solid line shows measured replication which was not associated with cell division. (c) RNA synthesis in the cytoplasm. This occurs primarily in the preparatory phase. (d) Numbers of mitochondria in one cell (from Dean *et al*, 1985).

(cockroaches) and larval Apocrita (Hymenoptera) (bees and wasps). These cells characteristically contain large crystalloid spherules of uric acid. Uric acid also accumulates as small granules in all fat body cells of larval and pupal Lepidoptera and in larval mosquitoes. For Collembola, which lack Malpighian tubules, and for Apocrita larvae, which are confined within their nest cells, the accumulation of uric acid might provide a mechanism to sequester nitrogenous waste products. This might also be true in Lepidoptera, where uric acid accumulates during the larval wandering phase and continues to accumulate during the first part of the pupal period, but then is transferred to the rectum to be excreted in the meconium. In the cockroaches, however, uric acid provides a store of nitrogen that can be recycled (Section 18.5.2).

6.1.3 Hemoglobin cells

Respiratory proteins such as hemoglobin have been thought to be unnecessary in insects because the tracheal system efficiently supplies oxygen to the respiring tissues. However, genes for hemoglobin have been detected in every insect genome sequenced to date, and intracellular hemoglobins have been identified in the fat body and tracheal system of various insects. Specialized hemoglobin cells have been described for botfly larvae (Oestridae, Diptera) and backswimmers (Notonectidae, Hemiptera) that occur in potentially hypoxic habitats (Section 17.4). Hemoglobin cells are large, measuring 20–80 μm in *Anisops* (Notonectidae) and up to 400 μm in diameter in *Gasterophilus* (Oestridae, Diptera). The hemoglobin cells are closely associated with tracheae.

6.1.4 Other cells

Mycetocytes are cells containing microorganisms that are localized in the fat body of cockroaches and some Hemiptera (Section 4.4). Oenocytes, derived from the epidermis, are also associated with the fat body in some groups, such as Hemiptera (Section 16.1.2).

6.1.5 Development and maturation of the fat body

The origin of the insect fat body has primarily been studied in *Drosophila melanogaster*, where technical advances in cell biology tools (e.g., green fluorescent protein tags), the availability of the complete genome sequence and extensive genetic tools have allowed cell lineage tracing studies. These studies reveal the mesodermal origin of the fat cells and the formation of the fat body by the coalescence of individual embryonic fat-cell clusters.

The fat body of the *D. melanogaster* larva is derived from cell clusters that arise from the embryonic mesoderm. The organization of the cell clusters depends upon patterning genes, including the pair-rule genes that subdivide the mesoderm and establish segment identity. These, in turn, serve to establish the expression of a transcription factor, Serpent (a member of the family of GATA transcription factors characterized by their ability to bind to the DNA sequence GATA), which specifies the fat-cell fate. The progenitor fat cells proliferate and coalesce to form the three morphological domains of the fat body: the dorsal fat-cell projections, which extend in the anterior direction from the posterior–dorsal region of the lateral fat body; the lateral fat body, which spans the lateral region of the embryo; and the ventral commissure, which extends from the anterior fat body and spans the ventral midline. The embryonic fat body persists into the larva and the domain structure identified in the embryo is maintained in the larva. This organization is likely to characterize all Diptera, although a detailed comparative study has not been carried out.

Metamorphosis in holometabolic insects is characterized by a complete change in body plan controlled in part by pulses of the steroid hormone 20-hydroxyecdysone (20E) (Section 15.3) that induce programmed cell death of most larval tissues, except for the fat body. For example, during metamorphosis of the skipper butterfly, *Calpodes ethlius*

(Lepidoptera), the individual fat cells reorganize into nodular clumps surrounding the tracheoles, and then undergo classical autophagy, where the intra-cellular remodeling takes place. The mitochondria, microbodies and rough endoplasmic reticulum become sequestered in organelle-specific autophagic vacuoles and are destroyed by hydrolytic enzymes, but the cell retains its integrity. After intra-cellular remodeling, a new round of organelle biogenesis takes place to generate the adult fat.

The larval fat body of *D. melanogaster* and probably other Diptera is also refractive to 20E-triggered programmed cell death. In the pupal *D. melanogaster*, the larval fat body persist but the tissue dissociates into individual cells. The resultant cells become dispersed throughout the pupa and are carried forward into the adult. At 3–4 days post-eclosion, the larval fat cells are replaced by adult fat cells that arise *de novo* from cells of the dorsal thoracic and eye-antennal imaginal discs and larval histoblasts. The mechanism linking ecdysteroid signaling and fat body remodeling is not fully understood, but appears to be an intrinsic property of the fat body tissue and not determined by signaling or interactions with other organs.

6.2 Storage and utilization of energy and nutrients

The fat body functions in many aspects of energy storage and synthesis of proteins, lipids and carbohydrates. Lipids are stored as triglycerides, and carbohydrates are stored as glycogen, i.e., polymers of glucose. The mobilization of these macronutrients is controlled by the adipokinetic hormone (AKH) family of peptides and the family of insulin-like peptides (ILPs). AKH is produced by the corpus cardiaca, whereas ILPs are produced in the median neurosecretory cells of the brain, the corpus allatum, the corpus cardiaca and peripheral tissues including the fat body. The ratio of triglyceride to glycogen in the fat body varies among insect species, and with

lifecycle stage and environmental stress, with triglycerides being the primary component.

In holometabolous insects, animals do not feed during metamorphosis, and in some cases the adult itself may not feed, e.g., the silkworm moth, *Bombyx mori* (Lepidoptera). Therefore, adequate nutrients must be stored in the fat body during the larval stage to support development of the adult tissues and to support the adult until feeding. This life history trait places the larval fat body in a unique position where energy storage and utilization is monitored for both immediate use and later use by the pupa and adult. Thus, the cells of the larval fat body serve as a physical link to carry larval nutrients into the adult. These larval fat cells provide nutrient reserves important for ovary maturation in the adult and can be mobilized in the event of adult starvation stress.

6.2.1 Lipids

The fat body is the principal storage site of lipids in insects. Most of the lipid is present as triacylglycerol (triglyceride), which commonly constitutes more than half of the dry weight of the fat body. The amount stored varies with the stage of development and state of feeding of the insect. Lipid stores normally increase during periods of active feeding and decline when feeding stops (Fig. 6.4) or when large quantities of lipid are used during oogenesis or prolonged flight.

The lipids are stored in lipid droplets within the trophocytes. Many triglycerides are synthesized from diacylglycerides derived from fatty acids or proteins. Fatty acids can be rapidly taken up by the fat body and converted to triglycerides. Dietary carbohydrates can also be converted to triglycerides in the fat body. Lipids are important because they are a more efficient form of energy storage than carbohydrates, for two reasons. First, lipids contain approximately twice the amount of energy per gram than carbohydrates, and second, glycogen contains substantial water of hydration, while lipid droplets contain little or no
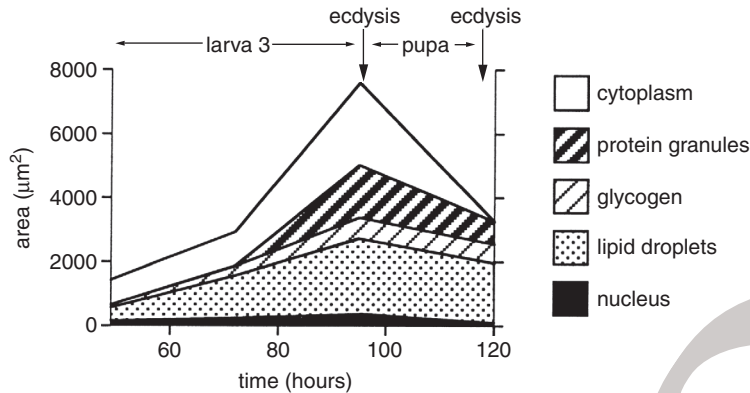
Figure 6.4 Changes in the amounts of the major components of a trophocyte during the final larval and pupal stages of *Drosophila*. The major increases occur during the period of feeding. Amounts are expressed as the areas occupied by the components in cross-sections of the tissue. Data from Butterworth *et al.* (1965).

water. Although water of hydration may be released when glycogen is metabolized under dry conditions, its additional weight is disadvantageous for activities such as flight.

Factors stimulating lipid synthesis in insects have not been defined, but the target of rapamycin (TOR) signaling pathway has been implicated in the regulation of nutrient uptake, storage and metabolism. There is considerable evidence that juvenile hormone inhibits lipid synthesis, but its mechanism of action is not known.

6.2.2 Proteins and amino acids

The fat body is the principal site of synthesis of hemolymph proteins, described in Section 5.3.4. In the larva of *Calpodes*, the fat body synthesizes 14 out of 26 hemolymph polypeptides, amounting to about 90% of the total hemolymph protein. In adult females the fat body produces vitellogenin, the protein that will form most of the yolk protein in the eggs.

Diapause proteins are also produced by the fat body. For example, adult Colorado potato beetles, *Leptinotarsa* (Coleoptera), enter diapause under short-day conditions. The adult beetles synthesize vitellogenins and diapause proteins under all conditions. If newly eclosed beetles experience long days, vitellogenins are synthesized at a high rate, and

production of diapause proteins is low. In short days (less than ten hours of light), however, relatively little vitellogenin, but more of the diapause proteins are produced.

As the insect prepares to pupate, protein synthesis in the fat body stops. Proteins, originally synthesized in and secreted by the fat body are now removed from the hemolymph and stored as granules in the fat body (Fig. 6.5). Some protein uptake does occur during the phase of protein synthesis, but the uptake is non-selective and proteins are hydrolyzed within the cells. Protein breakdown ceases at the end of the period of synthesis, and the uptake of proteins is selective; different proteins are taken up to different extents. In both *Helicoverpa* (Lepidoptera) and *Sarcophaga* (Diptera), this selective uptake of specific proteins is dependent on the appearance of specific receptor proteins in the plasma membranes of the fat body. A precursor of the receptor protein is already present in the larval fat body of *Sarcophaga*, and its conversion to the receptor for the uptake of storage protein is activated by molting hormone in the hemolymph before pupation. In *Helicoverpa*, the receptor protein for the blue-colored protein is formed *de novo* at the time of pupation. This receptor is only present in the membranes of cells in the perivisceral fat body, not in the peripheral fat body.

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The factors regulating protein synthesis and storage are not known with certainty, although both juvenile hormone and ecdysteroids are involved. For example, the synthesis of arylphorin in the larval silkworm *Bombyx* is suppressed by juvenile hormone. Synthesis is initiated when juvenile hormone is no longer detectable in the hemolymph of the final larval stadium hemolymph. In adult insects of most orders, synthesis of vitellogenin is stimulated by juvenile hormone, although in Diptera this function is performed by ecdysteroids (see Fig. 13.10).

Figure 6.5 Amounts of blue-colored very-high-density lipoprotein present in the fat body and hemolymph in various stages of development of *Helicoverpa* (after Haunerland *et al.* 1990).

The fat body plays an important role in amino acid metabolism, principally because it is a major site of transamination between amino acids (Section 4.1.2). It also contributes to the regulation of the amino acid tyrosine content of the hemolymph. Tyrosine functions in cuticle sclerotization and accumulates in the hemolymph just before a molt (Section 16.6.2). In the inter-molt period of some insects, tyrosine is taken up from the hemolymph and stored in large vacuoles in the trophocytes. This has been most comprehensively studied in the fourth larval stadium of *Calpodes*, where the uptake of tyrosine begins about one day after ecdysis. Shortly before the next ecdysis, tyrosine is released into the hemolymph (Fig. 6.6). Additionally or alternatively, some insects store conjugated tyrosine (e.g., as glucoside) in the hemolymph (see Fig. 16.17).
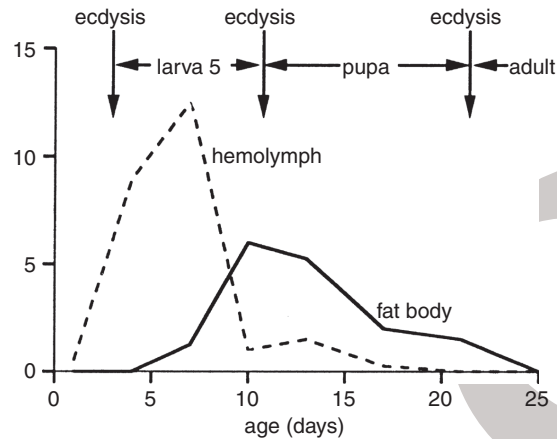
6.2.3 Carbohydrates

Carbohydrate is stored in the fat body as glycogen and circulates in the hemolymph in the form of trehalose. The amount of stored glycogen in the fat body is determined in part by the levels of trehalose in the hemolymph. Both glycogen and trehalose are synthesized in the fat body from UDP-glucose, which is derived from dietary carbohydrates or amino acids. As the level of trehalose rises, its synthesis in the fat body is inhibited and UDP-glucose is diverted to glycogen synthesis. Glycogen also serves as a source of cryoprotectants in over-wintering insects.
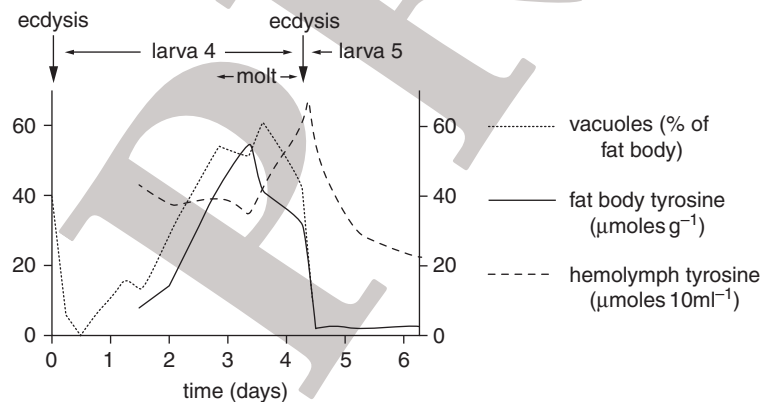
Figure 6.6 Changes in the tyrosine content of the fat body and hemolymph of *Calpodes* larva. Tyrosine in the fat body is sequestered in vacuoles and the proportion of the fat body occupied by vacuoles is paralleled by changes in the tyrosine content. At ecdysis the vacuoles disappear as they release tyrosine into the hemolymph (after McDermid and Locke, 1983).
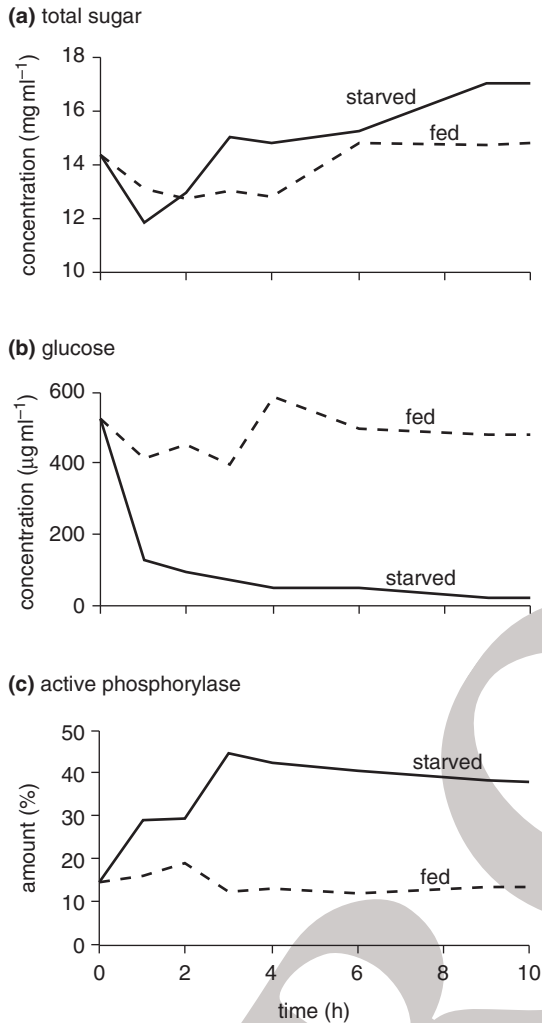
(a) total sugar

(b) glucose

(c) active phosphorylase

Figure 6.7 The effects of starvation on carbohydrate metabolism in a well-fed final-stage larva of *Manduca* (after Gies *et al.*, 1988). (a) Concentration of total sugars, mainly trehalose, in the hemolymph. (b) Concentration of glucose in the hemolymph. (c) Percentage of active glycogen phosphorylase in the fat body.

In caterpillars, and probably in other insects, glycogen accumulates in the fat body during periods of active feeding. This store becomes depleted during sustained activity or over a molt, when the insect is not feeding, or if it is starved. For example, the glycogen content of the fat body of a well-fed migratory locust, *Locusta* (Orthoptera), is about 20 mg g^{-1} fresh weight. Of this, 75% is consumed after two hours of flight. In *Manduca* (Lepidoptera) larvae, the hemolymph concentration of trehalose is maintained by conversion of glycogen to trehalose in the fat body (Fig. 6.7).

6.2.4 Mobilization of energy stores

Starvation and high activity levels stimulate the release of energy reserves from the fat body. During starvation, stored triglycerides can be metabolized through the hormonal stimulation of lipases. Mobilized lipids are ultimately transported to various target tissues, where the energy is released by β-oxidation of fatty acids, thereby allowing for continued growth and survival. The fat body is the principal tissue involved in starvation-induced autophagy, a process which degrades and recycles macromolecules and organelles. A unique feature of the larval fat cells of dipterans is that the larval fat cells which are brought forward into the adult serve as an energy reservoir that can be used during starvation stress and are critical to the maturation of the ovaries.

The AKH family of peptides are critical for regulating the supply of energy to tissues, such as the flight muscles to maintain long-distance flight. Depending on the insect species, lipids, carbohydrates, proline or a combination of these substrates are released from the fat body during times of metabolic need. Peptides that primarily mobilize lipids are referred to as adipokinetic hormone, while peptides whose predominant role is to mobilize carbohydrates are known as hypertrehalosemic hormones (HrTH). The HrTH mobilize carbohydrates by mobilizing trehalose. The adipokinetic and hypertrehalosemic functions of AKH peptides are similar to the metabolic responses induced by the vertebrate hormone, glucagon. In some insects AKH peptides stimulate the synthesis of proline, while in the tsetse fly (*Glossina morsitans*) and Coleoptera, proline is released into the hemolymph to provide fuel for the flight muscles.
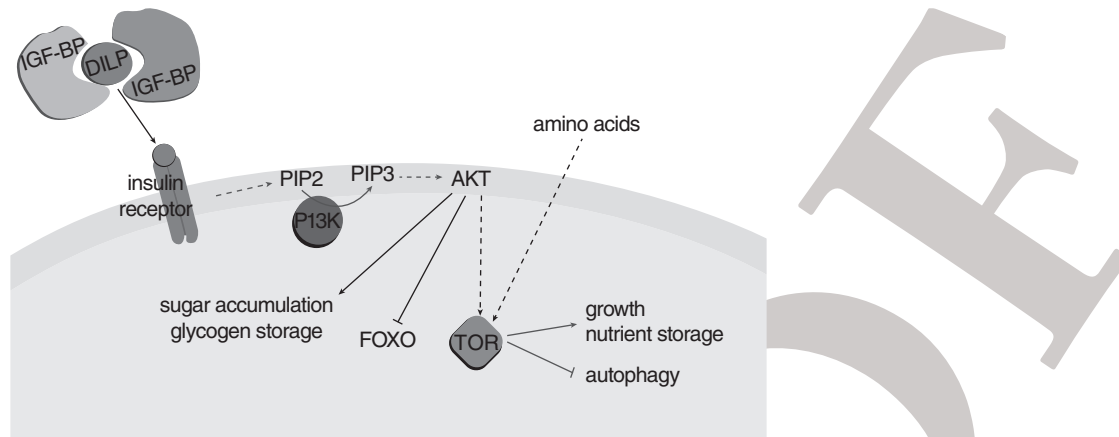
Figure 6.8 Insulin/IGF signaling (IIS) and the Target of Rapamycin (TOR) signaling in the fat cell serves as a nutrient-sensing system to maintain energy homeostasis. The release of *Drosophila* insulin-like polypeptide (DILP) from the insulin-like growth factor binding proteins (IGF-BPs) allows the DILPs to be accessible to the Insulin receptor and activates the IIS pathway. The IIS pathway promotes growth through the control of protein synthesis and autophagy via TOR, contributes to energy homeostasis by regulating carbohydrate storage and enhances translation by repressing FOXO. TOR signaling can also be activated by free amino acids present in the cell. FOXO can act as a translational repressor.

In addition to AKH signaling, the insulin signaling pathway regulates nutrient uptake, storage and metabolism. In insects, the insulin and insulin-like growth factor (IGF) signaling pathways function as a single pathway, the insulin/IGF pathway (IIS). In the IIS pathway both IGFs and ILPs bind to a single receptor, the insulin receptor (InR) (Fig. 6.8). In *D. melanogaster* ILP accessibility is regulated by IGF-binding proteins (IGF-BPs), which sequester the ILPs and protect them from degradation. Release of ILP from the complex allows binding to InR and activation of the IIS pathway. The IIS pathway promotes nutrient storage by inserting glucose transporters into the cell membrane to increase accumulation of sugars, phosphorylation of glycogen synthase to increase glycogen storage and by inactivation of the translational repressor FOXO (Fig. 6.8).

6.2.5 Larval energy stores in adults

In holometabolous insects distinct developmental stages are tightly linked to feeding (larva and most adults) and non-feeding periods (pupae and some adults). In *D. melanogaster*, and probably other Diptera, the larval fat cells generated by the remodeling of the fat body during metamorphosis (Section 6.1.5) are present in the newly eclosed adult. Within 24 hours, 85% of the larval fat cells are destroyed within the adult by the process of programmed cell death. Presumably the role of the fat cells is to provide an energy reserve to support the adult prior to feeding. In *D. melanogaster*, for example, the adults do not feed for the first eight hours.

For Lepidoptera, stable carbon isotope studies indicate that all the essential amino acids in the eggs deposited by adult females are derived from larval feeding, whereas non-essential amino acids are produced from the adult diet. Presumably, some of the essential amino acids are derived from storage proteins, but this has not been demonstrated directly.

Direct demonstration of a role for larval fat cells as a nutrient reserve in the adult comes from starvation experiments. Immature adult *D. melanogaster* (within ten minutes of emergence)
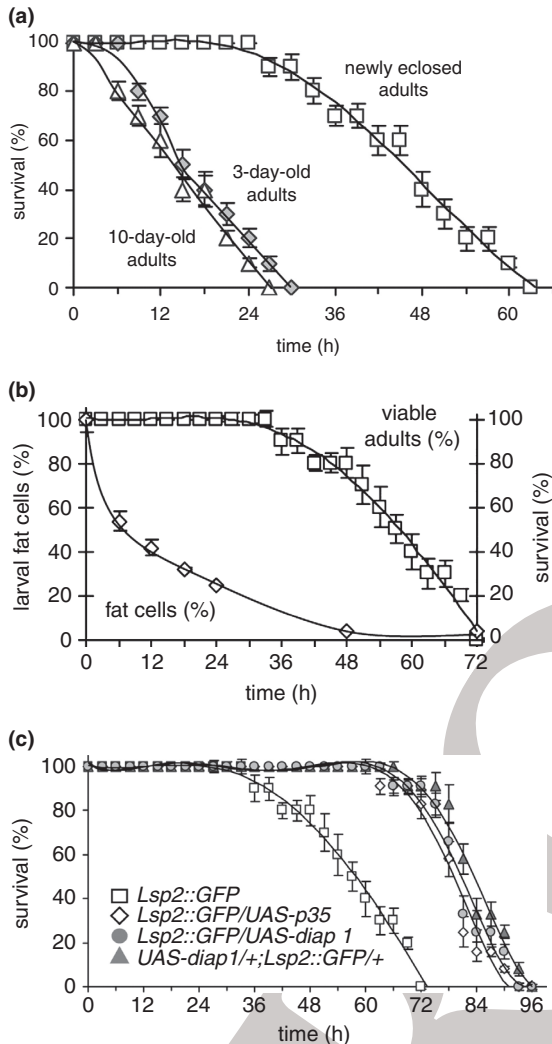
Figure 6.9 The role of larval fat cells in adult *Drosophila melanogaster*. (a) Survival of starved adults of different ages. (b) Number of larval fat cells in fed adults, and survival of starved adults over six days after eclosion. (c) Effect of retention of larval fat cells on survival of starved flies. Three genetic routes to prevent programmed cell death of larval fat cells were applied (diamond, circle, triangle), with wild-type controls (square). The LD50 for control flies was <60 hours and for genetically manipulated flies was 84 hours (reproduced from Aguila *et al.* 2007).

are more resistant to starvation than three-day-old feeding adults (Fig. 6.9a). These immature adults have nearly 100% of their larval fat cells, while in the three-day-old feeding adults the larval fat cells have undergone cell death and are absent (Fig. 6.9b). In transgenic flies, where programmed cell death is delayed, starvation resistance of the immature adult is further increased from 58 hours to 72 hours (Fig. 6.9c). Although this appears to be counter-intuitive, cell death is a mechanism for the rapid release of energy stores from fat cells into the hemolymph for uptake in other tissues (including ovaries to support the final steps in tissue maturation). Preservation of the fat cells maintains the energy reservoir for a measured mobilization in response to starvation. Thus, the larval fat cells serve as a nutrient reservoir that can be mobilized in response to stress to support the survival of the adult.

6.3 Function as an endocrine organ and nutritional sensor

The insect fat body has emerged as a dynamic tissue that functions as an endocrine organ to ensure proper energy homeostasis and as a sensor to integrate larval nutritional status with maturation signals for metamorphosis. The fat body coordinates the growth of multiple tissues with the energy demands of the organism and is involved in determining body size. For example, a reduction in the ability of the fat body to sense amino acids leads to a reduction in both cell growth and cell proliferation of other tissues, such as the larval salivary glands and imaginal discs.

6.3.1 The fat body as an endocrine organ

In holometabolous insects the larval stage is characterized by rapid growth of larval tissues (e.g., fat body, salivary glands, Malpighian tubules, trachea, muscle and epidermis) by increasing cell

size via endomitosis, and the cellular proliferation of the precursors to the adult tissues (imaginal discs) using the mitotic cell cycle. The insect fat body has a central role in fueling this growth through its participation in intermediary metabolism (i.e., generation of ATP) and in coordinating growth with nutritional status through the production of growth factors.

Since the initial efforts to culture insect cells and tissues, the addition of fat body or fat-body conditioned medium was found to be an important requirement for in vitro cell proliferation and differentiation. For example, the maintenance of *D. melanogaster* imaginal discs in culture required fat-body conditioned medium in addition to insulin and a juvenile hormone analog. These supplements are also needed for optimal growth and normal cell division in cultured lepidopteran imaginal discs and *Manduca sexta* midgut stem cells.

The fat body of *D. melanogaster* produces at least two classes of growth factors: the imaginal disc growth factor family (IDGFs), and the adenosine deaminase-related growth factors (ADGFs). The ADGFs stimulate imaginal disc proliferation, and one of them, ADGF-D, is produced primarily by the fat body and brain. The IDGF family is produced by embryonic yolk cells and the fat body of the embryo and larva and might correspond to the mitogenic factors responsible for growth in fat-body conditioned media. IDGF1 and IDGF2 promote imaginal disc cell proliferation in vitro and are likely to act through the *Drosophila* insulin receptor to promote cell growth. It appears that control of larval cell growth, as well as the imaginal cell proliferation, is regulated by fat body mitogenic growth factors.

In addition to the secretion of growth factors, the fat body is a key player in the synthesis of the insect molting hormone, 20-hydroxyecdysone (20E). Although the precursors of 20E are synthesized in the prothoracic gland (Section 15.4.2), the final step in 20E synthesis occurs in the peripheral tissues, e.g.,

the fat body. Specifically, P450 monooxygenase CYP314A1 (Shade protein in *D. melanogaster*) hydroxylates alpha-ecdysone to form the active form of the hormone, 20E. Orthologs of the CYP314A1 gene have been found in Hymenoptera, Coleoptera, Lepidoptera and Diptera, but functional studies of these monooxygenases have only been carried out in dipterans and lepidopterans. Studies in *D. melanogaster* have shown that conversion of alpha-ecdysone to 20E during the larval and pupal stages occurs predominantly in the fat body, with other organs such as the Malpighian tubules and midgut contributing small amounts of monoxygenase activity.

6.3.2 Monitoring nutritional status

Two major signaling pathways, the insulin/IGF signaling (IIS) and the Target of Rapamycin (TOR) pathway are active in the fat body of *D. melanogaster* and are involved in maintaining a stable equilibrium between energy storage and utilization (Fig. 6.8). In insects, the IIS and TOR signaling pathways are integrated to regulate growth, nutrient storage and autophagy, a catabolic process used to degrade the cell's own components through the lysosomal machinery. Autophagy is a major mechanism by which a starving cell reallocates nutrients from unnecessary processes to more-essential processes. In addition to activation by IIS, the TOR signaling pathway can be activated by amino acids.

Several putative amino acid transporters have been identified in the fat body. One of these, Minidisks, is predominately expressed in the fat body and is necessary for imaginal disc proliferation in *D. melanogaster*. Another amino acid transporter, Slimfast, is required for proper growth of the endoreplicating cells, which make up most of the larval tissues. Fat body lacking Slimfast also have down-regulated TOR activity, thus connecting this amino acid transporter to the nutrient-sensing mechanism in the fat body.

Summary

- The fat body is in the hemocoel, and the proximity of the cells to the hemolymph facilitates the exchange of metabolites. The dominant cell type of the fat body is the trophocyte, but the fat body of some insects additionally have urate cells, mycetocytes or oenocytes.

- The fat body is of mesodermal origin. In hemimetabolous insects the fat body persists into adulthood. In holometabolous insects the fat body cells disaggregate at metamorphosis, and either the organ reforms from these cells in the adult, or the larval fat body cells are eliminated with the adult fat body cells generated *de novo*.

- The fat body is rich in lipids, especially triacylglycerols, and glycogen. It is also responsible for the synthesis of many hemolymph proteins and major storage proteins, including vitellogenin and arylphorins.

- Fat body cells have active insulin-like peptide and TOR signaling, which play central roles in mediating the regulated growth and nutrition of the insect.

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