The metabolism and role of free fatty acids in key physiological processes in insects of medical, veterinary and forensic importance

Agata Kaczmarek1 and Mieczysława Boguś1,2

1 Witold Stefański Institute of Parasitology, Polish Academy of Sciences, Warsaw, Poland
2 Biomibo, Warsaw, Poland

ABSTRACT

Insects are the most widespread group of organisms and more than one million species have been described. These animals have significant ecological functions, for example they are pollinators of many types of plants. However, they also have direct influence on human life in different manners. They have high medical and veterinary significance, stemming from their role as vectors of disease and infection of wounds and necrotic tissue; they are also plant pests, parasitoids and predators whose activities can influence agriculture. In addition, their use in medical treatments, such as maggot therapy of gangrene and wounds, has grown considerably. They also have many uses in forensic science to determine the minimum post-mortem interval and provide valuable information about the movement of the body, cause of the death, drug use, or poisoning. It has also been proposed that they may be used as model organisms to replace mammal systems in research. The present review describes the role of free fatty acids (FFAs) in key physiological processes in insects. By focusing on insects of medical, veterinary significance, we have limited our description of the physiological processes to those most important from the point of view of insect control; the study examines their effects on insect reproduction and resistance to the adverse effects of abiotic (low temperature) and biotic (pathogens) factors.

INTRODUCTION

Due to varied feeding habits of insects, especially in the larval stage (sarcophagy, coprophagy, necrophagy), insects have considerable veterinary and medical impact as obligatory and facultative parasitoids, predators and myiasis-causing factors (Kamut & Jezierski, 2014; Scholl, Colwell & Cepeda-Palacios, 2018; Silveira et al., 2019). Several species, like mosquitoes, cockroaches or flies, are synanthropic and may be responsible for the mechanical transmission of pathogens to food and the human body (Higgs & Vanlandingham, 2016; Scholl, Colwell & Cepeda-Palacios, 2018; Gerhardt & Hribar, 2019; Huang, Higgs & Vanlandingham, 2019; Donkor, 2020). Other species are hematophagous

How to cite this article Kaczmarek A, Boguś M. 2021. The metabolism and role of free fatty acids in key physiological processes in insects of medical, veterinary and forensic importance. PeerJ 9:e12563 http://doi.org/10.7717/peerj.12563
and can disseminate vector-borne diseases, like malaria, Dengue or Chagas’ Disease (Majerowicz & Gondim, 2013).

In addition to their epidemiological importance, the flies from the Families Calliphoridae (blow flies), Sarcophagidae (flesh flies) and Muscidae (house flies) are also convenient tools for forensic studies, and can be used for detecting drugs or other toxic substances (entomotoxicology) (Byrd & Sutton, 2020; Hodecek, 2020), while the larvae of other species, such as Lucilia sericata (Diptera: Calliphoridae) or Protophormia terraenovae (Diptera: Calliphoridae), are also used as maggot therapy in the treatment of gangrene and wounds (Stadler, 2020; Zubir, Holloway & Noor, 2020). Some insects, mostly Drosophila melanogaster (Diptera: Drosophilidae) but also Galleria mellonella (Lepidoptera: Pyralidae), Apis mellifera (Hymenoptera: Apidae) and Bombyx mori (Lepidoptera: Bombycidae), are considered as model organisms in medical and veterinary research (Menzel, 2012; Abdelli, Peng & Keping, 2018; Nainu et al., 2020; Wojda et al., 2020; Younes et al., 2020; Beer & Helfrich-Forster, 2020).

Due to their negative impact on human and livestock health, there is a need to better understand the physiological processes governing their development and reproduction.

FFAs are a diverse group of lipids which play important roles in maintaining homeostasis and managing cellular processes. By restricting our scope to insects of medical, veterinary and forensic importance, the present article focuses on the key challenges faced by human populations exposed to these species and potential control methods. The ability of insects to adapt to cold conditions is key to their colonisation success, and the role of FFAs in these mechanisms should be highlighted. In addition, any potential disruption of this process might be employed to control the insect population. In addition, most of insects with medical, veterinary and forensic significance live in environments with high numbers of pathogenic microorganisms, such as decaying animal tissues or faeces, and previous studies have highlighted that insect cuticular FFAs significantly influence survival. As any manipulation of FFA synthesis or transport may be used to significantly decrease the insect population, any discussion of insect resistance should include data the role of FFAs. Moreover, a more thorough understanding of the role of FFAs in insect resistance and reproduction could serve as an effective tool for controlling insect-borne pathogens.

The presence and level of FFAs demonstrate considerable variation between insect developmental stages, even in the same species (Soulages & Wells, 1994; Gołębiowski et al., 2007; Gołębiowski et al., 2008; Gołębiowski et al., 2010; Gołębiowski et al., 2012b; Gołębiowski et al., 2013b; Gołębiowski et al., 2013a; Gołębiowski et al., 2015; Gołębiowski et al., 2016; Urbanek et al., 2012; Gutierrez et al., 2015; Paszkiewicz et al., 2016b; Sönmez, Güvenç & Gülel, 2016; Wrońska et al., 2018; Wojciechowska, Stepnowski & Gołębiowski, 2019; Cerkowniak et al., 2020; Giannetto et al., 2020; Kaczmarek et al., 2020a; Wojciechowska & Gołębiowski, 2020). Internal fatty acids are essential components of cell and organelle membranes; they are known to act as energy sources, and precursors for various waxes and pheromones, secondary metabolites and even defensive secretions (Blomquist & Bagnères, 2010; Ginzel et al., 2021).

The FFAs found in the cuticle are a diverse set of lipids whose content and composition vary considerably according to diet and climate. They perform a range of essential functions
associated with well-being of insects, particularly minimizing transpiration and protecting terrestrial insects from desiccation (Gibbs & Rajpurohit, 2010). Cuticular lipids also play important roles in biochemical, physiological and semiochemical processes. They are also used as cues for recognising species, nest mates and castes. In addition, they are considered as a precursor of pheromones needed for sexual attraction and epideictic activity, such as display behaviour, as well as territorial markers, alarm signals and defensive chemicals. They are also believed to support thermoregulation, predator–prey and parasitoid-host interactions, and to enable insect camouflage and mimicry (Blomquist & Bagnères, 2010). Most importantly for the purposes of this paper, the lipid profile of the insect cuticle can also determine the effectiveness of fungal invasion (Kerwin, 1982; Gołębiewski et al., 2020; Gołębiewski et al., 2008; Gołębiewski et al., 2011; Gołębiewski et al., 2012a; Gołębiewski et al., 2013a; Gołębiewski et al., 2014a; Gołębiewski et al., 2014b; Gołębiewski et al., 2015; Bogus et al., 2010; Bogus et al., 2017; Urbanek et al., 2012; Gutierrez et al., 2015; Paszkiewicz et al., 2016a; Wrońska et al., 2018; Kaczmarek et al., 2020a; Cerkowniak et al., 2020; Wojciechowska & Gołębiewski, 2020; Gołębiewski, Bojke & Tkaczuk, 2021; Kaczmarek & Bogus, 2021a; Kaczmarek & Boguś, 2021b; Kazek et al., 2021). Therefore, an understanding of the FFA profile could assist in the identification and control of insect pests. In addition, during their lifespan, the insect demonstrates changes in lipid composition related to its stage of development; these changes are influenced by body composition, lifestyle, diet, sex and the environment (Lease & Wolf, 2011; Gołębiewski, 2012; Gołębiewski et al., 2014b; Gołębiewski et al., 2016; Toprak et al., 2014; Kazek et al., 2019; Ewald et al., 2020; Seite et al., 2021; Kaczmarek et al., 2021).

Why the study needed
The past decades have seen a growth in interest in entomological physiology and morphology. Insects are important vectors of disease, causing infection via wounds and necrotic tissue; they can also act as parasitoids and predators, and can contribute to losses in agriculture. However, they also have potential medical value; for example, maggots can be used to treat gangrene and wounds as maggot therapy, a procedure approved by the Food and Drug Administration (FDA). Insects are also commonly used in forensic science; their presence can indicate the minimum post-mortem interval and provide valuable information about the movement of the body, cause of death, drug use, or poisoning. They have also been proposed as model organisms in research, as a replacement for mammal systems.

Lipid metabolism plays a crucial role in insects. As in other organisms, lipids perform various functions in insects, such as forming constituents of cellular structures, acting as signalling messengers, and serving as the most significant form of stored energy. These lipid reserves are fundamental in certain situations of high metabolic demand, such as flight and egg production. Also, the cuticle lipids, a complex mixture of hydrocarbons, wax esters and acylglycerols, play an essential role in insect fitness, both as a waterproof barrier and a means to regulate the penetration of pesticides and microorganisms; moreover, they also participate in chemical communication events.
Our present work describes the role of FFAs in cold adaptation, as a supply material during development, and as a resistance/susceptibility factor. It also reviews recent scientific reports on FFA transport, which is an important issue concerning all insects.

Who it is intended for
Our review is intended for researchers hoping to describe insect physiology and biochemistry; however, it includes aspects of insect biology that are relevant for those studying Entomology in general: it describes the role of FFAs in cold adaptation, as a supply material during holometabolous development, and as a resistance or susceptibility factor, and reviews recent scientific reports on FFA transport, which is applicable to all insects. In addition, insects can be used as models, which can be a potential alternative for researchers using vertebrate research models. Finally, our findings may be of interest for researchers studying the interactions between hosts and pathogens with the aim of creating innovative and effective biocontrol agents.

SURVEY METHODOLOGY
A range of approaches were to identify articles. Firstly, a search was performed on popular platforms such as Google Scholar and PubMed. The popular keywords were insect, free fatty acid and holometabolous/hemimetabolous, hematophagous, development, adaptation to cold, oleic acid, linoleic acid, thermal compensation - rapid cold-hardening (RCH), diapause, metabolism of lipids, transport of lipids, lipophorin, HDLp, LDLp, VHDLp, plasma membrane fatty acid binding protein (FABPpm), fatty acid translocase (FAT/CD36), fatty acid transport proteins (FATPs), Acetyl-CoA carboxylase (ACC), Fatty acid synthase (FAS), Very long-chain fatty acid elongase (ELOVL), Long-chain acyl-CoA synthetase (ACSL) Fatty acid desaturase (FAD), free fatty acid as a resistance factor. The search was refined by re-arranging the keywords as necessary. The search only included articles in English. After a large number of articles was identified, they were finalized for the review process by reading the abstract; following this, articles the most relevant to the topic were chosen for further analysis. Some papers regarded as having a good research contribution was further scrutinised to identify further references.

Classification of FFAs
FFAs can be classified into several groups with respect to their structure, physiological role and biological effects. The classification and examples of FFAs are presented in Table 1.

Fatty acids have a backbone made of carbon atoms and they vary in the number of carbon atoms, and in the number of double bonds between them. Short-chain fatty acids (SCFAs) are fatty acids with up to 5 carbon atoms, medium-chain fatty acids (MCFAs) have 6 to 12, long-chain fatty acids (LCFAs) 13 to 21, and very long chain fatty acids (VLCFAs) are fatty acids with more than 22 carbon atoms. Fatty acids are classified according to the presence and number of double bonds in their carbon chain. Saturated fatty acids (SFAs) contain no double bonds, monounsaturated fatty acids (MUFAs) contain one, and polyunsaturated fatty acids (PUFAs) contain more than one double bond. Unsaturated fatty acids can also be classified as cis (bent form) or trans (straight form), depending on...
### Table 1  Classification of FFAs with examples in insects.

| Definition | Examples of FFAs | Examples in Insects | Literature data |
|------------|------------------|---------------------|-----------------|
| **Length of FAs** | | | |
| **Short-chain fatty acids (SCFAs)** | up to 5 carbon atoms | C2:0; Ethanoic acid; Acetic acid; CH₃COOH | Apis mellifera gut microbiota | Zheng et al. (2017b) |
| | | C3:0; Propionic acid; Propanoic acid; CH₃CH₂COOH | Gilliamella apicola | |
| | | C4:0; Butyric acid; Butanoic acid; CH₃(CH₂)₂COOH | | |
| **Medium-chain fatty acids (MCFAs)** | 6 to 12 carbon atoms | C6:0; Hexanoic acid; Caproic acid; CH₃(CH₂)₄COOH | Hermetia illucens, Oecophylla smaragdina Zophobas morio, Tenebrio molitor, Gryllus bimaculatus | Ewald et al. (2020); Jayanegara et al. (2020) |
| | | C8:0; Octanoic acid; Caprylic acid; CH₃(CH₂)₆COOH | | |
| | | C10:0; Decanoic acid; Capric acid; CH₃(CH₂)₈COOH | | |
| | | C12:0; Dodecanoic acid; Lauric acid; CH₃(CH₂)₁₀COOH | | |
| **Long-chain fatty acids (LCFAs)** | 13 to 21 carbon atoms | C14:0; Tetradecanoic acid; Myristic acid; CH₃(CH₂)₁₂COOH | Tenebrio molitor | Paul et al. (2017); Zheng et al. (2017a) |
| | | C16:0; Hexadecanoic acid; Palmitic acid; CH₃(CH₂)₁₄COOH | | |
| | | C18:0; Octadecanoic acid; Stearic acid; CH₃(CH₂)₁₆COOH | | |
| **Very long chain fatty acids (VLCFAs)** | more than 22 carbon atoms | C24:0; Tetracosanoic acid; Lignoceric acid; CH₃(CH₂)₂₂COOH | Tenebrio molitor | Zheng et al. (2017a) |
| | | C26:0; Hexacosanoic acid; Cerotic acid; CH₃(CH₂)₂₄COOH | | |
| | | C28:0; Octacosanoic acid; Montanic acid; CH₃(CH₂)₂₆COOH | | |
| | | C30:0; Triacontanoic acid; Melissic acid; CH₃(CH₂)₂₈COOH | | |
| | | C32:0; Dotriacontanoic acid; Lacceroic acid; CH₃(CH₂)₃₀COOH | | |
| | | C34:0; Tetratriacontanoic acid; Gheidoic acid; CH₃(CH₂)₳₂COOH | | |
| | | C35:0; Pentatriacontanoic acid; Ceroplastic acid; CH₃(CH₂)₳₃COOH | | |

(continued on next page)
Table 1 (continued)

| Saturation          | Definition                                  | Examples of FFAs                                                                 | Examples in Insects                                      | Literature data                                                  |
|---------------------|---------------------------------------------|----------------------------------------------------------------------------------|----------------------------------------------------------|-----------------------------------------------------------------|
| Saturation          | no C=C double bonds                         | C16:0; Hexadecanoic acid, Palmitic acid; CH_{16}(CH_{2})_{15}COOH                 | Galleria mellonella                                      | Wrońska et al. (2018);                                        |
|                     |                                             | C18:0; Octadecanoic acid; Stearic acid; CH_{18}(CH_{2})_{16}COOH                  |                                                         | Sarcophaga argyrostoma;                                         |
|                     |                                             |                                                                                   |                                                         | Blatta orientalis;                                                |
|                     |                                             |                                                                                   |                                                         | Blattella germanica;                                             |
|                     |                                             |                                                                                   |                                                         | Kaczmarek et al. (2020);                                         |
|                     | saturated                                   |                                                                                   |                                                         | Paszkiewicz et al. (2016b);                                     |
|                     |                                             |                                                                                   |                                                         | Paszkiewicz et al. (2016a);                                     |
|                     |                                             |                                                                                   |                                                         | Kaczmarek et al. (2020);                                         |
|                     |                                             |                                                                                   |                                                         | Calliphora vicina;                                               |
|                     |                                             |                                                                                   |                                                         | Gołębiewski et al. (2012a);                                     |
|                     |                                             |                                                                                   |                                                         | Gołębiewski et al. (2012b);                                     |
|                     |                                             |                                                                                   |                                                         | Kazek et al. (2021);                                             |
|                     |                                             |                                                                                   |                                                         | Lucilia sericata;                                                |
|                     |                                             |                                                                                   |                                                         | Kaczmarek et al. (2021);                                         |
|                     |                                             |                                                                                   |                                                         | Dermestes ater;                                                  |
|                     |                                             |                                                                                   |                                                         | Cerhowski et al. (2020);                                         |
| Unsaturated         | one or more C=C double bonds                 | C16:1; cis- Δ9, n = 7 (9Z)-hexadec-9-enoic acid; Palmitoleic acid; CH_{16}(CH_{2})_{14}CH=CH(CH_{2})_{7}COOH | Anopheles messeae, Ochlerotatus caspius, O. flavescens, O. euedes, O. cataphylla, Aedes cinereus | Gladyshev et al. (2011);                                        |
|                     |                                             |                                                                                   |                                                         | Tenebrio molitor;                                                |
|                     |                                             |                                                                                   |                                                         | Benzertiha et al. (2019);                                        |
|                     |                                             |                                                                                   |                                                         | Trachyderma philistina;                                          | (Nancy Taha Mohamed PhD, 2020)                                    |
|                     | monounsaturated fatty acids (MUFAs)         | One C=C double bonds                                                             |                                                         | Michaud & Denlinger (2006);                                     |
|                     |                                             |                                                                                   |                                                         | Rakankanteng et al. (2019);                                     |
|                     |                                             |                                                                                   |                                                         | Blauf et al. (2014);                                             |
|                     |                                             |                                                                                   |                                                         | McAfee et al. (2018);                                           |
|                     |                                             |                                                                                   |                                                         | Tang et al. (2019);                                              |
|                     | polyunsaturated fatty acids (PUFAs)         | More than one C=C double bonds                                                    |                                                         | Stanley-Samuelson & Dadd (1983);                                |
|                     |                                             |                                                                                   |                                                         | Blomquist, Borgeon & Vundla (1991);                             |
|                     |                                             |                                                                                   |                                                         | Guíl-Guerrero et al. (2018);                                    |
|                     |                                             |                                                                                   |                                                         | Hassan, Ahmed & Kim (2019);                                     |
|                     |                                             |                                                                                   |                                                         | Vatanparast, Lee & Kim (2020);                                  |
|                     |                                             |                                                                                   |                                                         | Scharnweber et al. (2020);                                      |
|                     |                                             |                                                                                   |                                                         | Stanley & Kim, (2020);                                          |
|                     |                                             |                                                                                   |                                                         | Broschwitz et al. (2021);                                       |
|                     |                                             |                                                                                   |                                                         | Duarte et al. (2021);                                           |
|                     |                                             |                                                                                   |                                                         | Kim & Stanley (2021);                                           |
|                     |                                             |                                                                                   |                                                         | Nishidono et al. (2021)                                         |

(continued on next page)
### Table 1 (continued)

| Description                        | Definition                                                                 | Examples of FFAs                                                                 | Examples in Insects Literature data |
|------------------------------------|---------------------------------------------------------------------------|---------------------------------------------------------------------------------|-------------------------------------|
| **Length of FFAs**                 |                                                                           |                                                                                 |                                     |
| Short-chain fatty acids (SCFA)     | up to 5 carbon atoms                                                     | C2:0 Ethanoic acid Acetic acid CH3COOH C3:0 Propionio acid CH3CH2COOH C4:0 Butanoic acid CH3(CH2)2COOH | honeybee (Apis mellifera) gut microbe - Gilliamella apicola (Zheng et al. 2017a) |
| medium-chain fatty acids (MCFA)    | 6 to 12 carbon atoms                                                     | C6:0 Hexanoic acid Caproic acid CH3(CH2)2COOH C8:0 Octanoic acid Caprylic acid CH3(CH2)3COOH C10:0 Decanoic acid Capric acid CH3(CH2)4COOH C12:0 Dodecanoic acid Lauric acid CH3(CH2)5COOH | Hermetia illucens mealworms, Octophyla smaragdina krotos, Zophobas morio superworms, Tenebrio molitor mealworms, and Gryllus bimaculatus crickets (Ewald et al. 2020; Jayanegara et al. 2020) |
| long-chain fatty acids (LCFA)      | 13 to 21 carbon atoms                                                    | C14:0 Tetradecanoic acid Myristic acid CH3(CH2)13COOH C16:0 Hexadecanoic acid Palmitic acid CH3(CH2)14COOH C18:0 Octadecanoic acid Stearic acid CH3(CH2)17COOH | Tenebrio molitor I. (Paul et al. 2017; Zheng et al. 2017b), B. germanica (Pei et al. 2021), Chilecomadina valdiviana (Herrera, Barros-Parada & Bergmann, 2019) |
| very long chain fatty acids (VLCFA) | more than 22 carbon atoms                                                | C24:0 Tetraicosanoic acid Lignoceric acid CH3(CH2)23COOH C26:0 Hexacosanoic acid Cerotic acid CH3(CH2)26COOH | Tenebrio molitor (Zheng et al. 2017b), Coptotermes formosanus (Chen, Henderson & Laine, 1999), B. orientalis (Gutierrez et al., 2015), Drosophila melanogaster (Wicker Thomas et al. 2015), Apis mellifera (Bharathwaaj et al. 2018) |
| **Saturation**                     |                                                                           |                                                                                 |                                     |
| Saturated                          | no C=C double bonds                                                      | C16:0 Hexadecanoic acid Palmitic acid CH3(CH2)14COOH C18:0 Octadecanoic acid Stearic acid CH3(CH2)17COOH | (Goldbrowski et al., 2006; Goldbrowski et al., 2012a; Goldbrowski et al., 2012b; Wrońska et al. 2018; Kaczmarek et al., 2020a; Kaczmarek et al., 2020b; Kaczmarek et al., 2021) |
| Unsaturated                        | one or more C=C double bonds                                             |                                                                                 |                                     |
| cis                                | the two hydrogen atoms adjacent to the double bond stick out on the same side of the chain |                                                                                 |                                     |
| trans                              | the adjacent two hydrogen atoms lie on opposite sides of the chain       |                                                                                 |                                     |
| monounsaturated fatty acids (MUFA) | One C=C double bonds                                                     | C16:1, cis-Δ9, n–7 (9Z)-hexadec-9-enolic acid Palmiolic acid CH3(CH2)13:CH=CH(CH2)7COOH C18:1, cis-Δ9, n–7 (9Z)-Octadec-9-enolic Oleic acid CH3(CH2)13:CH=CH(CH2)7COOH | (Michaud & Denlinger, 2006; Banskotang et al. 2010; Blaul et al. 2014a;McAfee et al. 2018; Tang et al. 2019) |
| Polyunsaturated fatty acids (PUFA) | More than one C=C double bonds                                           | C18:2, cis,cis-Δ9,Δ12, n–6 (9Z,12Z)-Octadec-9,12-dienoic acid Linoleic acid CH3(CH2)13:CH=CHCH=CH(CH2)7COOH C18:3, cis,cis,cis-Δ9,Δ12,Δ15, n–3 (9Z,12Z,15Z)-Octadec-9,12,15-trienoic acid Δ9-Linolenic acid CH3(CH2)13:CH=CHCH=CHCH=CH(CH2)7COOH C20:4, cis,cis,cis,cis-Δ5,Δ8,Δ11,Δ14, n–6 (5Z,8Z,11Z,14Z)-Eicosatetraenoic acid Arachidonic acid CH3(CH2)20:CH=CHCH=CHCH=CHCH=CH=CH(CH2)7COOH | Stanley-Samuelson & Dadd (1983); Blomquist, Bargeon & Vanda, 1991; Guit-Guerrero et al. (2018); Hasan et al. (2019); Yatamparan et al. (2020); Scharnowski et al. (2020); Stanley & Kim (2020); Brouillet et al. (2021); Duarte et al. (2021); Kim & Stanley (2021); Nishadono et al. (2021) |
whether hydrogen is bound on the same, or on the opposite side of the molecule. Most naturally occurring unsaturated fatty acids are found in cis form. Trans fatty acids (TFAs) can be divided in two groups: artificial TFAs (industrial) and natural TFAs (ruminant) (Tvrzicka et al., 2011; Yoon et al., 2018).

**FFAs during the development of insects**

**Holometabolous development**

Lipid accumulation and mobilisation also plays particularly important roles in the radical reconstruction of body plan and biochemistry in holometabolous insects. Holometabolous metamorphosis is characterised by four developmental stages: egg, larva, pupa and adult. While most females lay eggs and are thus oviparous, Sarcophagidae might be larviparous, meaning that the egg develops internally, and the females give birth to first-instar larvae. A few insect groups, such as louse flies (Hippoboscidae) and tsetse flies (Glossinidae), are pupiparous: the developing larvae are retained within the maternal body until they are ready to pupate. Larviparous and pupiparous species produce lower numbers of offspring per female compared with oviparous and ovoviviparous species (Gerhardt & Hribar, 2019).

Holometabolous insects have the advantage that they develop through specialised stages: the larva for feeding and growth, and adult form for reproduction (Horne, Haritos & Oakeshott, 2009). Moreover, larvae and adults do not compete for the same food, because they have been adapted to different ecological niches (Terra & Ferreira, 2020).

The lipid content of holometabolous insects increases steadily during larval development to match the metabolic requirements of the larva, and allows the accumulation of energy reserves for metamorphosis (Lease & Wolf, 2011). Nutritional deficiencies during larval feeding and development result in smaller adult size, lower resistance to environmental stress and reduced reproductive capacity (Nestel et al., 2016; Pascacio-Villafan et al., 2016); in addition, in the Lepidoptera, lipid deficiencies during the larval stage might result in incorrect male behaviour, decreased reproductive investment (Vande Velde, Schtickzelle & Van Dyck, 2013) and adult fitness (Boggs & Freeman, 2005), as well as compromised immune system function and pathogen resistance (Lee et al., 2006a).

The fatty acid content of black soldier fly larvae *Hermetia illucens* (Diptera: Stratiomyidae), which are able to feed on a variety of organic materials and are considered alternative sources of both protein and fat in feeds used in aquaculture (Diener, Zurbrugg & Tockner, 2009; Wang & Shelomi, 2017), is strongly correlated with diet and larval weight; larvae with a higher weight contained a higher percentage of saturated fatty acids and a lower percentage of unsaturated fatty acids, such as eicosapentaenoic (EPA) and docosahexaenoic acid (DHA) (Li et al., 2016; Ewald et al., 2020). The different fatty acid profiles of black soldier flies and larvae and prepupae may be related to the modulation of lipid metabolism-related gene expression during larval development (Giannetto et al., 2020).

During metamorphosis, most larval tissues degenerate and adult structures are synthesized *de novo* from imaginal discs (Truman & Riddiford, 2019). This process is dependent upon the levels of energy reserves, such as lipids, and precursors accumulated during larval growth. The presence of lower amounts of internal FFAs during the pupal stage might be connected with the disintegration of the larval fat body in the pupal stage (Kurata,
In addition, chemical analyses of cuticular compounds, including FFAs, in insects and other arthropods are often used to estimate the post-mortem index in criminal investigations, and are considered substitutes for traditional morphological examinations and/or DNA-based methods (Gołębiowski et al., 2014a; Kranz et al., 2017; Kaczmarek et al., 2020b).

The cuticular lipid content in the imago varies according to age. Research on Sarcophaga bullata (Diptera: Sarcophagidae), has shown that FFAs constitute 26% all cuticular lipids in newly emerged flies and 45% in seven-days-old and suggest that lipid synthesis or transport to the cuticle surface is incomplete in newly-emerged adults. There are also morphological differences of the cuticles of newly-emerged adults, which are pliable and paler coloured then older ones; transport of FFAs occurs primarily through the unhardened cuticle, and this process is essentially completed by the time the adult cuticle is fully hardened (Jackson, Arnold & Regnier, 1974). Also, in Drosophila females, the lipid content increased with age, and this correlates with increased resistance to starvation (Service, 1987).

Adult insects that do not feed rely on these reserves to support life and reproduction; however, some holometabolous insects, such as blood-feeding mosquitos, require meals to increase protein or lipid levels to enable, or even enhance, reproductive success (Arrese & Soulages, 2010). Egg development involves a substantial mobilization of reserves from the fat body to the ovaries. Lipids are potent sources of energy for oocyte maturation in females and also account for the formation of membranes; for example, in the mosquito Culex quinquefasciatus (Diptera: Culicidae), ~90% of the energy used by the developing embryo originates from lipids (Van Handel, 1993) and in tobacco hornworm Manduca sexta (Lepidoptera: Sphingidae), a novel host model for the study of fungal virulence and drug efficacy, lipids represent around 40% of the dry weight of a mature oocyte (Soulages & Wells, 1994; Lyons et al., 2020). Although oocytes are able to synthesize fatty acids de novo, this contribution does not account for more than 1% of egg lipid content (Arrese & Soulages, 2010) and the vast majority of the lipid accumulated in oocytes originates in the fat body and is transported to the ovaries by lipophorin (Ziegler & Van Antwerpen, 2006; Santos et al., 2011; Lu et al., 2018).

In Aedes aegypti (Diptera: Culicidae), feeding females with sugar before a blood meal resulted in lipid accumulation in the fat body, suggesting that de novo lipogenesis was active in these insects; in addition, amino acids derived from the blood meal were also used for de novo lipogenesis, which improved oogenesis efficiency (Ziegler & Ibrahim, 2001; Zhou, Pennington & Wells, 2004). Research demonstrated that lipid metabolism in the fat body of female Ae. aegypti during vitellogenesis is an extremely dynamic process (Pinch et al., 2021). Studies have shown that lipid levels in the fat body of female mosquitoes decrease significantly over the first 36 h post blood meal (PBM) (Hou et al., 2015; Wang et al., 2017). This decrease corresponded with a decrease in lipid droplet size (Wang et al., 2017). In turn, another study found maximal lipid accumulation in the developing oocytes at 30 h PBM (Briegel, Gut & Lea, 2003). These accumulated lipids constitute up to 30–40% of oocyte dry weight (Troy, Anderson & Spielman, 1975; Briegel, 1990; Van Handel, 1993).

The adults of several parasitoid species, such as parasitoid wasps, which are also considered as indicators in forensic science (Rivers, 2016), demonstrate little possibility to
accumulate energy supplies and were believed to have no enzymes which synthesize fatty acids de novo (Visser & Ellers, 2008). Due to their parasitic lifestyle, parasitic wasps were assumed to receive sufficient amounts of lipids from their hosts during larval development making the ability to synthesize fatty acids redundant, finally leading to the loss of the evolutionary trait (Visser et al., 2010). However, recent studies have shown that wasps from the Nasonia group are able to synthesize palmitic and stearic acid from α-D-glucose (Prager, Bruckmann & Ruther, 2019; Ruther, Prager & Pokorny, 2021) and linoleic acid from oleic acid (Broschwitz et al., 2021). This confirms that these insects possess the enzymatic machinery to synthesize not only the primary products of fatty acid biosynthesis, but also to introduce double bonds at positions 9 and 12 to produce oleic acid and linoleic acid; more importantly, it is not the case that these insects lack lipogenesis due to environmental compensation, as suggested by several previous studies (Visser et al., 2010; Visser et al., 2012).

**Hemimetabolous insects**

The life cycle of hemimetabolous insects includes three developmental stages: egg, nymph (several instars) and adult. The early-stage of hemimetabolous insects is characterised by proportionally lower lipid contents than adults, which is contrary situation than in holometabolous insects. The differences in lipid content in immature and adults occur in holometabolous and hemimetabolous insects might be connected with different morphological changes occurs in the growth and reproduction phase in both insect insects (Lease & Wolf, 2011). In holometabola the intense periods of growth and the development of reproductive, in other word periods of energy accumulation and use is observed, and thus affect energy storage. In hemimetabolous insects, this kind of shifts are observed also, however there are not direct changes from an immature insect to an adult insect (Chapman, 1998). On the other hand, metamorphosis in the holometabola includes a stage characterised by the breakdown of larval tissue and formation of adult tissue; this nonfeeding stage is fuelled completely by energy reserves, which accumulate steadily during larval development (Downer & Matthews, 1976; Lease & Wolf, 2011). This abrupt transition between energy accumulation (as a larva) and energy use (as a pupa, preparing to be an adult) might underlie the higher relative lipid content of holometabolous larvae compared with hemimetabolous larvae (Lease & Wolf, 2011).

A higher FFA content was also observed for adults than nymphs for cockroaches: *Blatta orientalis, Blaptica dubia* (both Blattodea: Blaberidae), *Blatella germanica, Blaberus discoidalis* and *Blatta lateralis* (all Blattodea: Blaberidae) (Gutierrez et al., 2015; Kulma et al., 2016) and the highest concentration was observed for C16:0, C18:1, C18:2 and C18:0 in both development stage (Gutierrez et al., 2015; Kulma et al., 2016; Paszkiewicz et al., 2016a; Paszkiewicz et al., 2016b; Kaczmarek et al., 2020a). Moreover, the different distribution of cuticular FFAs in wings and thoraces of adults *B. germanica* and *B. orientalis* was observed. Although these species have similar whole body FFA content, the higher concentration of FFAs in wings and thoraces was observed in *B. germanica* than in *B. orientalis* (Kaczmarek et al., 2020a).
The metabolism of dietary lipids is important for kissing bugs, as it allows the storage of lipid resources in peripheral tissues. After large blood meal the fifth-instar nymphs of Panstrongylus megistus (Hemiptera: Reduviidae) control the digestion of lipid process. The few days after the blood meal the regulation of mobilization of lipids from the lumen and consequently, their transfer to the hemolymph and storage in fat body is still well-regulated (Canavoso, Frede & Rubiolo, 2004). The ingested triglicerides (TAGs) are hydrolysed to FA in the P. megistus midgut lumen (Canavoso, Frede & Rubiolo, 2004). The lipid loading of lipophorin at the midgut is connected with the nutritional status of the insect, being mediated by specific binding sites located at the cell membrane of enterocytes (Fruttero, Rubiolo & Canavoso, 2009).

The lipid transfer to developing oocytes of P. megistus is accomplished by endocytosis of lipophorin, and by the classic extracellular lipophorin-shuttle mechanism. In addition, lipids in the oocyte lipid droplets can originate from endocytosed vitellogenin (Fruttero et al., 2011). Considering that in P. megistus, lipophorin only constitutes about 3% of the total protein content of ovarian tissue, while lipids comprise almost 40% of the dry weight of a mature egg, it is possible that most of the lipids will be transferred from lipophorin to the oocytes by a selective mechanism operating at the cell surface without lipoprotein internalization. In addition, since significant vitellogenin endocytosis occurs during vitellogenesis, its role in lipid deposition in oocytes should not be disregarded (Fruttero et al., 2011).

The hematophagous hemimetabolous insect, Rhodnius prolixus (Hemiptera: Reduviidae) feeds exclusively on large and infrequent blood meals. After feeding, the adult female slowly digests the blood for approximately 14 days, providing diet-derived lipids that are transported through the hemolymph to the fat body and ovary (Grillo, Majerowicz & Gondim, 2007). In the fat body, the amount of stored lipid increases during the first days after a blood meal, decreasing only after approximately 15 days, when digestion is almost complete (Pontes et al., 2008). Blood meal also triggered de novo lipid synthesis in fat body of R. prolixus (Saraiva et al., 2021). The storage of TAGs in fat body cells is promoted by insulin receptors (IR). The knockdown of RhoprIR (R. prolixus IR) resulted in a lower potential to utilize hemolymph-derived fatty acids, which could reduce the levels of TAG and lipid droplet sizes in the fat body and, in turn, impair ovary development and reproductive capacity (Silva-Oliveira et al., 2021). Oocytes accumulate lipids and other yolk components during the meal-induced oogenesis cycle (Gondim, Oliveira & Masuda, 1989; Santos et al., 2008; Santos et al., 2011) and lipids that were incorporated into the ovaries were primarily used to synthesize TAG, which in insect oocytes are stored in lipid droplets (Ziegler & Van Antwerpen, 2006). After oviposition in eggs of R. prolixus, the TAG content (70.4%) was slightly higher than in mature oocytes (60%), while the diacylglycerol (DAG) content (9.6%) was lower than in 2.0 mm oocytes (13.9%). These differences illustrated a reorganisation of lipid composition in the later stages of oocyte maturation, after chorion deposition, where about 40% of TAG reserves is used during embryogenesis (Santos et al., 2011). This result, that less than half of the TAG content in the egg was consumed before hatching was similar to that of eggs of other arthropods, where a large portion of the egg lipids are still present in the hatchlings, for example in C. quinquefasciatus, where 46% of
l lipids are consumed during embryogenesis (Van Handel, 1993). On the seventh day after oviposition, about half of the TAG in the egg was associated with the embryo, which is the same amount of lipids found in newly hatched nymphs. In R. prolixus part of the substances storage in the yolk, i.e., proteins, glycogen and lipids, are detected in the digestive tract of the nymphs and are used as nutrients during the initial days after hatching (Santos et al., 2008; Santos et al., 2011). The research on unfed nymph of R. prolixus has shown that fifteen days after emergence, about 30% of the TAG originated from the egg is still present, and describes that after hatching, lipids found in the nymph are slowly used by the insect in an efficient and controlled mechanism (Santos et al., 2011).

In Dipetalogaster maxima (Hemiptera: Reduviidae) oenocytes, the highest amounts of FFAs were detected at both stages of atresia. Taking into account that follicular atresia involves remarkable changes in both ovarian morphology and oocyte resorption, it is likely that FFAs detected at atretic stages arose from the breakdown of TAG reserves. The extent to which such FFAs provide energy to support the instauration and progression of the degenerative process or recycle to circulation remains to be established (Leyria et al., 2014). Research pointed the role of juvenile hormone in mediation in lipid transfer and storage in the oocytes of D. maxima (Ramos et al., 2021) and also speculated about possibility of bidirectional lipophorin-mediated transfer in insect from the oocyte to the hemolymph during atresia. Moreover, the role of lipophorin oocyte receptors seems be crucial in this process, especially that some results suggest that oocyte plasma membrane proteins, unrelated to the low-density lipoprotein receptor (LDLR) superfamily, can function as nonendocytic lipophorin receptors to regulate the lipid transfer process (Leyria et al., 2014).

**FFAs as a fuel for flight**

Lipids serve as the main source of energy in long-term flying insects (Briegel, Knusel & Timmermann, 2001; Wang et al., 2009; Lopez et al., 2014). Generally, carbohydrates are used as fuel in the initial stages of flight, with the fuel source being switched to fats during longer flight. The use of carbohydrates is governed by the hormone octopamine, which also increases trehalose concentration in the hemolymph as part of stress responses. During the first few minutes of flight, octopamine also induces the first release of DAG from the fat body, however, the subsequent, more prolonged phase of TAG mobilization occurs through the action of adipokinetic hormone (AKH). As a result, the concentration of DAG in the hemolymph increases and constitutes the principal fuel for flight (Toprak, 2020). Briefly, longer flight stimulates the release of AKH from the corpus cardiacum. AKH acts directly on the fat body and induces lipid mobilization in the adipose (fat body) cells, which ultimately results in the release of DAG from TAG stores (Skowronek, Wójcik & Strachecka, 2021) Adipokinetic Hormone Receptor (AKHR) knockdown leads to TAG accumulation in fat body and flight muscles, and reduced hemolymph lipid levels after starvation in R. prolixus, also indicating the requirement of AKHR in TAG mobilization (Zandawala et al., 2015). TAG molecules are transported by lipophorin to flight muscles, where they are digested to FFAs, which are oxidised for energy generation (Van Der Horst et al., 2002; Jenni-Eiermann & Srygley, 2018). The source of energy for flight can differ between insect
species, for example Dipteran species, like *D. melanogaster* usually use firstly glycogen as the primary source of energy for flight and then, lipid reserves to maintain long-term flight after several hours (*Wigglesworth, 1949; Briegel, Knusel & Timmermann, 2001; Kaufmann & Briegel, 2004*), while aphids primarily use lipids (*Liquido & Irwin, 1986; Xueke et al., 2017*).

Lipids are also involved as an energy source by triatomine bugs during flight. The presence of lipid droplets in flight muscle has been reported in at least three vectors of Chagas disease including *Triatoma infestans* (Hemiptera: Reduviidae), *R. prolixus*, and *D. maxima* (*Ward, Candy & Smith, 1982; Cavagnari et al., 2000*).

Although *D. maxima* is not a strong flyer, research indicate the presence of fatty acid binding protein (FABP), abundant mitochondria, and lipid stores in the flight muscles, which suggests the presence of beta oxidation of fatty acids as a main energy source for the triatomine thoracic muscle, and could be related to its dispersal capacity (*Cavagnari et al., 2000*).

Research has shown that the flight in *R. prolixus* induced both changes in the muscle content of lipid and glycogen and the increase of hemolymph lipid. However, no changes in the hemolymph carbohydrate in insects flown for a short time were observed (*Ward, Candy & Smith, 1982; Canavoso, Stariolo & Rubiolo, 2003*).

Similar changes (decrease of flight muscle lipids, 60% decrease in fat body lipid content and increase lipid level in hemolymph) was observed in *P. megistus* (Hemiptera: Reduviidae) after 45 min of flight (*Canavoso, Stariolo & Rubiolo, 2003*). The research indicated that the changes in lipid content in hemolymph is connected with low-density lipophorin particle (LDLp), and flight promoted the partial interconversion of lipophorins and therefore, both high-density lipoprotein HDLp and LDLp were observed (*Canavoso, Stariolo & Rubiolo, 2003*).

**FFAs and adaptation to adverse temperatures**

Most insects are ectothermic organisms, for whom physiological sources of heat are of relatively small or quite negligible significance in controlling body temperature and so they gain heat from their environment. Therefore, insects have had to develop mechanisms to allow them to survive in environments with both long-term low temperature variations associated with seasonal changes and short-term daily or local fluctuations. Preventing cellular damage due to low temperatures (cold shock) is a major challenge for insects living in temperate zones. Extended periods of low temperature are one of the conditions for the insect entering a photoperiod-induced diapause (metabolic suppression); to prevent or decrease the effect of cold shock after short-term temperature changes, the insect can use various thermal compensation strategies, such as rapid cold-hardening (RCH), a quick response that can occur at any stage of the life cycle (*Michaud & Denlinger, 2006; Zhu et al., 2016*).

**Thermal compensation - Rapid cold-hardening (RCH)**

The term *thermal compensation* defines processes that allow adaptation to low temperatures while maintaining a high level of metabolism enabling movement and nutrition and allowing the development of the organism.
RCH is a cold-hardening mechanism that overwintering insects possess throughout their lifespan, although the degree of protection imparted by RCH varies with life stage (Chen, Denlinger & Lee, 1987).

The whole-body glycerol content of Sarcophaga crassipalpis (Diptera: Sarcophagidae) increases three-fold during RCH, similarly to the level of glycerol in diapausing insect, which suggests that it plays a protective role in this process. Apart from glycerol, various other lipids are also involved in damage prevention. There is known to be a positive correlation between body lipid content and cold tolerance in Drosophila spp. (Hoffmann et al., 2001); in addition, Coleman and co-workers, based on a study in which C. vicina was fed with a protein-poor diet containing water and sugar, propose that the insect may derive its cold tolerance from its increased lipid content (Coleman, Bale & Hayward, 2015).

FFAs are also an important group involved in cold protection, especially in a process known as homeoviscous adaptation, where the FFA composition is adjusted to maintain the liquid crystalline state at lower temperatures (Sinensky, 1974). Several biochemical mechanisms are employed to help insects survive RCH. For example, membrane fluidity can be enhanced by increasing the proportion of unsaturated fatty acids in the cell membrane, and the ratio of 16-carbon fatty acids relative to 18-carbon fatty acids can be altered, as short-chain fatty acids have lower melting points than long-chain fatty acids; in addition, the position of the moieties within glycerophospholipids can be changed to alter membrane fluidity. Furthermore, the amount of unsaturated and/or short-chain fatty acids in the membrane can be increased, and the polar head groups of membrane phospholipids can be restructured; glycerophosphoethanolamines promote membrane disorder at low temperatures, which also enhances membrane fluidity (Teets & Denlinger, 2013; Teets, Gantz & Kawarasaki, 2020).

In many insects, such as D. melanogaster, fast and slow cold hardening causes changes in membrane fatty acid composition, increased fatty acid unsaturation and decreased length of fatty acid chains (Overgaard et al., 2006; Colinet et al., 2016). An increase in the concentration of oleic acid in response to, or in preparation for, low-temperature may maintain proper fluidity of the membrane without sacrificing the delicate balance needed to allow sensitive membrane proteins to continue their optimum function. Increasing proportions of oleic acid have been observed in Hepialus xiaojinensis (Lepidoptera: Hepialidae) (Zhu et al., 2016), the ghost moths, which act as hosts for the Chinese caterpillar fungus Ophiocordyceps sinensis, which has a long history of use in traditional Chinese medicine (TCM) for its anti-inflammatory and immunomodulatory effects, among others (Zhou et al., 2009; Ng & Wang, 2010; Meng et al., 2015). In S. crassipalpis, the pivotal role during RCH and the diapause is played by oleic acid, mostly because is energetically more favorable to manufacture than, for example double bonded fatty acids. It is possible, therefore, that insects that prefer oleic acid in preparation for low temperatures may be preserving finite energy reserves while still gaining the benefit of a wide window of fluidity (Michaud & Denlinger, 2006). In the model organisms for cold research –freeze-tolerant fly Eurosta solidaginis (Diptera: Tephritidae) and the freeze-avoiding moth Epiblema scudderiana (Lepidoptera: Tortricidae) increased proportions of unsaturated fatty acids during the winter is observed; however, whereas total lipid content did not change in
E. solidaginis, a decrease in total lipids was observed in E. scudderiana, a species sensitive to freezing, over the winter, suggesting the use of reserves to maintain basal metabolism (Joanisse & Storey, 1996).

In S. crassipalpis, cold treatment resulted in a 17% increase of total phospholipid fatty acid content; in addition, a decrease of other fatty acids was observed, with the exception of C16:0, which remained the same. These changes are characteristic of RCH; however, in the diapause process, the level of C16:0 changes but C16:1 remains the same (Michaud & Denlinger, 2006). Elsewhere, in D. melanogaster has been demonstrated an increase of polyunsaturated linoleic acid and decrease of monounsaturated (18:1) and saturated (14:0) phospholipid fatty acid as a response to RCH. These caused a significant increase in the overall degree of unsaturation and may improve the ability to harden during RCH (Overgaard et al., 2005).

In ghost moth, H. xiaojinensis, most unsaturated and long chain FFAs were maintained at higher levels in the hemolymph of cold-acclimated larvae than controls; C16:0 was found to be the most abundant fatty acid in the fat body and the only one whose level changed after cold acclimation, with a reduction of 23%, possibly due to reduced de novo synthesis of fatty acids or enhanced transition to other fatty acids (Zhu et al., 2016). Cell membrane fluidity has also been found to increase in response to RCH in the cells of S. bullata fat bodies (Lee et al., 2006b). In addition to insects (Khani et al., 2007), faster mobilisation of unsaturated fatty acids compared to saturated acids has been observed in mammals and birds (Raclot, 2003; Price, Krokfors & Guglielmo, 2008) as a general adaptation to cold.

**Diapause**

The insect diapause is dynamic state of low metabolic activity, genetically determined, with the neurohormonal system as mediator. Diapause occurs at a species-specific stage of ontogenesis and its expression is regulated by various environmental signals that precede and reliably predict the arrival of unfavourable conditions. The cause–effect relationship between diapause and cold-resistance in arthropods is still debated, and both phenomena may not be directly related, depending on the species and even the population. The main stimulus inducing winter diapause in arthropods is the decrease in day length after summer. Once induced, diapause cannot be immediately terminated even if favourable conditions for development occur (Tougeron, 2019).

The diapause process in C. vicina is associated with cold tolerance, and diapausing larvae were more cold tolerant than same-age (nondiapausing) pupae (Saunders & Hayward, 1998). Moreover, C. vicina adults exposed to warmer autumn conditions during diapause induction will produce larvae with a reduced cold hardiness capacity, which could negatively impact winter survival. Given that maternal regulation of diapause is common among temperate insects, this could be a widespread phenomenon (Coleman, Bale & Hayward, 2014).

Diapause is characterised by long-term upregulation of heat shock proteins, which prevents protein denaturation and repairs denatured proteins (Hayward et al., 2005), as well as increased glycerol levels. Glycerol acts as an antifreeze agent in insects, lowers the supercooling point of the organism and stabilizes membranes and proteins.
(Chen, Denlinger & Lee, 1987; Lee et al., 1987; Tsvetkova & Quinn, 1994; Tang & Pikal, 2005). However, it is important to mention that glycerol is not the only antifreeze agent in insects: freeze tolerance is also conferred by trehalose and antifreeze proteins (AFPs). Trehalose is a versatile sugar molecule that can accumulate to high levels in freeze-tolerant and freeze-avoiding insects, where it functions as a cryoprotectant and supercooling agent. Similarly, AFPs lower the freezing temperature and prevent the formation of ice crystals; interestingly, these are present at high levels in both freeze-tolerant insects and some freeze-avoiding insects in winter (Wen et al., 2016).

The process of diapause also influences the amount of lipid reserves in insects, which are used in both catabolic energy production and anabolic processes, including cell membrane maintenance and remodelling (Hahn & Denlinger, 2011). Insects often accumulate lipid stores during diapause-destined or overwintering stages (Hahn & Denlinger, 2011). As most overwintering insects end winter with substantially fewer lipid stores than they began with, it is likely that lipids are a primary source of overwintering fuel (Hahn & Denlinger, 2011).

Diapausing mosquito *Culex pipiens* (Diptera: Culicidae) females accumulate more lipid droplets during diapause preparation and overwintering diapause maintenance than during the nondiapause phase (Zhang et al., 2019). Energy metabolism is crucial for the survival of diapausing insects throughout winter: energy demands are fueled by lipid stores, and *C. pipiens* females begin to utilize TAGs stores, convert stored fat to FFAs, and transport these fatty acids to the mitochondria to meet energetic needs (Zhang et al., 2019). Research has shown that the genes coding for fatty acid synthase-1,-3 and fatty acid binding protein are upregulated, which contributes to the accumulation of TAGs in the fat body (Sim & Denlinger, 2013); after diapause, these lipid reserves are used for egg production (Zhou & Miesfeld, 2009).

The increase of lipid content of diapause compared with non-diapause eggs and 30% more lipid content in larvae entering diapause than their nondiapause counterparts was observed also for the tiger mosquito, *Aedes albopictus* (Diptera: Culicidae) (Reynolds et al., 2012). The substantial differences in lipid metabolism observed within the embryo occur as a consequence of the diapause program, with some differences taking place both before the actual onset of diapause and during the diapause state. For example, research has shown the elevated expression of the lipid storage droplet protein 2 gene (*lsd2*) during embryonic development, which might likely contribute to the higher amounts of lipid noted in diapausing individuals. The changes in the transcript abundance of genes that regulate lipid storage (*lsd2*), lipolysis (*lip2*, *lip3*, and *lip4*), β-oxidation (*acs*, *cpt*, *acd4*, and *acd5*), and unsaturated fatty acid synthesis (*desat*, and *face*), contribute to increased amounts of lipids in diapause embryos. The upregulation of two genes involved in fatty acid synthesis and modification, Δ(9)-*desaturase*, and *fatty acyl-CoA elongase*, was observed in diapausing larvae, which might suggest roles for their gene products in generating unsaturated fatty acids to enhance membrane fluidity at low temperatures and generating precursors to the surface hydrocarbons needed to resist desiccation, respectively (Reynolds et al., 2012).

The gall moth *E. scudderiana* is freeze-avoidant; its lipolysis-related enzyme activity increases in winter, suggesting a shift to lipid metabolism. By contrast, lipolysis enzyme
activity decreases over winter in the goldenrod gall fly *E. solidaginis*, a freeze-tolerant species (*Joanisse & Storey, 1996*). This indicates either a shift to non-lipid fuels or that the rate of lipid metabolism is slowed. However, both species demonstrate an upregulation of 5′adenosine monophosphate-activated protein kinase (AMPK) during winter, implying a shift towards lipolysis (*Rider et al., 2011*). Flesh flies show the opposite pattern where lipids are depleted early in diapause followed by a shift to other substrates; for example, *S. crassipalpis* larvae destined for pupal diapause contain nearly twice the lipid content as non-diapausing larvae. A rapid decline of lipid content was observed at the beginning of the pupal diapause, but after 40 days, the pupae switched from lipid to non-lipid energy reserves, and the lipid content stabilized and remained nearly constant until adult eclosion (*Adedokun & Denlinger, 1985*). Research into diapausing *S. crassipalpis* pupae also revealed an increase in the concentration of fatty acid C18:1 in the cell membrane, while those of other fatty acid decreased; however, the level of C16:1 remained the same, and as a consequence, the ratio of unsaturated to saturated fatty acids in diapausing individuals increased (*Michaud & Denlinger, 2006*), which is a common adaptation to low temperatures in insects (*Harwood & Takata, 1965; Valder, Hopkins & Valder, 1969; Bridges & Watts, 1975; Ohtsu et al., 1993; Kostal & Simek, 1998; Tomčala et al., 2006*).

The cosmopolitan wasp *Nasonia vitripennis* (Hymenoptera: Pteromalidae), whose broad host range, rate of parasitism and seasonal prevalence afford it great potential as an indicator of time of death in forensic investigations (*Voss, Spafford & Dadour, 2009*), has been found to contain corresponding levels of glycerol to its host. *N. vitripennis* larvae fed on diapausing *S. crassipalpis* pupae contained four times more glycerol than parasitoids consuming non-diapausing hosts, and the wasp larvae which contained high levels of glycerol also exhibited greater cold tolerance (*Rivers, Lee & Denlinger, 2000*).

Several hormones have contributed in lipid metabolism during diapause, like AKH, insulin, neuropeptide F (NPF) and short Neuropeptide F (sNPF) or Diapause Hormone-Pheromone Biosynthesis Activating Neuropeptide (DH-PBAN) (*Toprak, 2020*).

AKHs do not contribute to diapause-associated alterations in metabolism. They are produced in response to AMPH activation in insects, which leads to the release of DAG into hemolymph from TAG stores in the fat body. This takes place via a cyclic cAMP and calcium signalling cascade during diapause maintenance (*Sinclair & Marshall, 2018; Toprak, 2020*).

Another important hormone involves in diapause is insulin. The relationship between diapause-dependent lipid accumulations and insulin has been shown in *Drosophila* (*Tatar & Yin, 2001* and *C. pipiens* (*Sim & Denlinger, 2013*). Additionally, silencing insulin receptor (InR) in non-diapausing females inhibits ovary development, which simulates the diapause state (*Sim & Denlinger, 2008*). As expected, the insulin effect occurs mainly during feeding, i.e., before the initiation of the diapause. For example, adult females of *C. pipiens* increase feeding with sugar instead of blood in the prediapause period and accumulate much greater lipid reserves compared to non-diapausing counterparts (*Robich & Denlinger, 2005*). In this manner, specific insulin-like peptides (ILPs), such as ILP1, contribute to the diapause regulation-related lipid accumulation in *C. pipiens* (*Robich & Denlinger, 2005*). Notably,
juvenile hormones and ecdysone interfere with insulin signalling in terminating diapause (Denlinger, Yocum & Rinehart, 2012).

Lipid metabolism during diapause is also dependent on NPF, a functional homolog of mammalian Orexigenic Neuropeptide Y, and sNPF, which is conserved across protostomes, but not present in vertebrates. These peptides are hormones that inhibit peristalsis and the release of digestive enzymes, and preserve nutrition; they are involved in feeding behaviour, nutritional homeostasis and insulin signalling (Fadda et al., 2019; Toprak, 2020; Skowronek, Wójcik & Strachecka, 2021). In Drosophila larvae, it has been found that the accumulation of lipid sources for diapause preparation is dependent *inter alia* on NPF activation: overexpression of NPF leads to prolonged feeding, and NPF-deficient mutant larvae feed less (Fadda et al., 2019).

**Metabolism of FFAs**

*Preference of dietary FFAs by insects*

The fatty acid profiles of insects can differ depending on different growth stages, temperatures and nutritional regimes. Insects are able to take up dietary C20:5, which has been found to alter the overall fatty acid profile of tissue phospholipids in lengthy feeding experiments (Stanley-Samuelson & Dadd, 1981; Stanley-Samuelson & Dadd, 1984; Gadellha et al., 1995). Research has shown that some insect species have dietary preferences regarding FFAs. For example, the adult yellow fever mosquitoes *Ae. aegypti* (Bosch, Geier & Boeckh, 2000), *Anopheles gambiae* (Diptera: Culicidae) (Smallegange et al., 2009), and *T. infestans* (Barrozo & Lazzari, 2004) are attracted by specific FFAs (combined with L-lactic acid); and also, some FFAs might discourage some flies (Mullens, Reifenrath & Butler, 2009) and mosquitoes (Skinner et al., 1970). This preference towards certain FFAs could change during life, for example *D. melanogaster* larvae prefer unsaturated FFAs whereas the adults prefer saturated FFAs (Fougeron et al., 2011).

*Absorption and storage of lipids*

Lipids are absorbed from food through the middle intestine and transferred from the intestine to the hemolymph in the form of diglycerides (DGs). At this stage, DGs bind to HDL (produced from the apoliprotein in the fat body) and then to LDL. Lipids are transported in the body by lipophorin (Skowronek, Wójcik & Strachecka, 2021). The absorption of FFAs is presented schematically on Fig. 1 The *R. prolixus* gut is compartmentalized into three segments that perform different functions during blood digestion, with fatty acid adsorption taking place in the posterior midgut (Grillo, Majerowicz & Gondim, 2007; Ribeiro et al., 2014). When consumed, DAGs from the hemolymph are bound by LDL and hydrolyzed to fatty acids, which are transported to fat body cells (Grillo, Majerowicz & Gondim, 2007). A different pattern was observed in *P. megistus*, where significant digestion takes place in the anterior midgut (Canavoso, Frede & Rubiolo, 2004).

After absorption, FFAs are immediately bound to binding proteins to avoid toxic effects induced by a rise in intracellular FFA concentration, and to allow their rapid metabolic flow to utilization pathways or storage sites (Glatz, Luiken & Bonen, 2010; Toprak et al., 2020).
Figure 1 The absorption and transport of FFAs in insect. FFA, free fatty acid; FABP, fatty acid binding protein; FATP, fatty acid transport protein; LP, lipophorin; LP_R, lipophorin receptor; HDLp, high-density lipophorin particle; LDLp, low-density lipophorin particle; VHDLp, very high lipophorin particle.
Lipids absorbed from the midgut are generally stored in fat body cells. Fat body tissues are major sites for nutrient storage, energy metabolism, innate immunity and detoxification. Recent studies have revealed that the fat body plays a central role in the integration of hormonal and nutritional signals to regulate larval growth, body size, circadian clock, pupal diapause, longevity, feeding behaviour, and courtship behaviour, partially by releasing fat body signals to remotely control the brain. In addition, the fat body has emerged as a fascinating model for studying metabolic disorders and immune diseases (Lehmann, 2018; Li, Yu & Feng, 2019; Toprak, 2020; Toprak et al., 2020; Skowronek, Wójcik & Strachecka, 2021).

The adipocytes, i.e., cells involved in lipid metabolism, are able to store lipid as TAGs, these being strongly hydrophobic neutral lipid droplets with high energy content (Arrese et al., 2001; Arrese & Soulages, 2010; Skowronek, Wójcik & Strachecka, 2021). The ability to mobilize stored TAG reserves is important for the survival of insects under energy-demanding conditions (Lehmann, 2018). The start of lipid mobilisation is indicated by the release of AKH from the corpora cardiaca, which binds to AKH-receptors in adipocytes, leading to the generation of the secondary messenger 3′,5′-cyclic monophosphate (cAMP) and the phospholipase C (PLC) and Ca\(^{2+}\) cascades (Toprak, 2020; Toprak, Dogan & Hegedus, 2021). cAMP induces cAMP-dependent protein kinase, leading to activation of the lipolytic transcription factor foxO, which is believed to act on lipase genes (Baumbach et al., 2014); this is accompanied by the hydrolysis of phosphatidylinositol 4,5-bisphosphate (PIP2) to inositol 1,4,5-trisphosphate (IP3) by PLC, which binds to inositol 1,4,5- triphosphate receptor (IP3R); this results in activation of the channel and an elevation in cytosolic Ca\(^{2+}\) levels (Toprak et al., 2020). Thus, AKH activity results in lipolysis accompanied by an increase in the cytosolic levels of Ca\(^{2+}\) in adipocytes (Toprak et al., 2020).

An important aspect of the proper functioning of lipid metabolism is calcium ion homeostasis (Ca\(^{2+}\)). Many functions in the insect organism, including diapause, metamorphosis, hunger sensing, and receiving signals from neurotransmitters require a certain level of Ca\(^{2+}\) to be maintained. In addition, studies have shown that cytosolic Ca\(^{2+}\) levels correspond with the levels of triglycerides in lipid droplets, and the process of lipolysis and lipogenesis are dependent on the Ca\(^{2+}\) in invertebrates (Skowronek, Wójcik & Strachecka, 2021; Toprak, Dogan & Hegedus, 2021). Most of the data on the involvement of insect endoplasmic reticulum Ca\(^{2+}\) channels in lipid metabolism are related to IP3R, which induce lipolysis in insect adipocytes (Toprak, Dogan & Hegedus, 2021). The loss of IP3R leads to elevated levels of triglycerides with enlarged lipid droplets in the fat body and hyperphagia in D. melanogaster adults (Subramanian et al., 2013). In line with this, fat body-specific knockdown of IP3R leads to an increase in lipid droplet size and triglyceride accumulation in adult flies (Bi et al., 2014). On the other hand, AKH-induced lipolysis has been reported only in adults of D. melanogaster as manipulation of cytosolic Ca\(^{2+}\) levels in the larval fat body does not have a significant effect on larval fat stores (Baumbach et al., 2014; Galikova et al., 2015). In contrast, insects, such as Leptinotarsa decemlineata (Coleoptera: Chrysomelidae), accumulate greater amounts of lipid at the larval stage, which show impaired lipid metabolism upon silencing Ca\(^{2+}\)-signaling genes (Doğan et al., Kaczmarek and Boguś (2021), PeerJ, DOI 10.7717/peerj.12563
There, the dynamics of lipid metabolism in relation to Ca^{2+} might be different depending on the species. Dogan et al. investigated the key binding proteins, finding calmodulin, calcineurin, and regucalcin in the *L. decemlineata* fat body. This indicates additional adaptation of this tissue to lipid metabolism (Dogan et al., 2021).

**Transport of lipids**

In insects, lipid transfer to the tissues is mediated by lipophorin, the major circulating lipoprotein (Van der Horst, Roosendaal & Rodenburg, 2009). Lipophorins are synthesised in the fat body and secreted to the circulation. Here, they perform several cycles of lipid loading and unloading, without internalization or further degradation of the apolipoprotein matrix (Fruttero, Leyria & Canavoso, 2017).

Lipophorins were purified from the hemolymph of various insect vectors, including the *T. infestans*, *R. prolixus*, *Glossina morsitans* (Diptera: Glossinidae), *Ae. aegypti*, *C. quinquefasciatus*, *Anopheles albimanus* (Diptera: Culicidae), *An. gambiae*, *Simulium vittatum*. *Musca domestica* (Diptera: Muscidae) and *Lucilia cuprina* (Diptera: Calliphoridae) (Bianchi, Capurro & Marinotti, 1987; Trowell et al., 1994; Pennington & Wells, 2002; Gondim et al., 2018). The major function and examples of lipophorin are presented in Table 2.

In *P. megistus*, the process of lipophorin binding in the midgut is dependent on the nutritional status of the insect, with a higher binding activity being observed three days after blood feeding (Fruttero, Rubiolo & Canavoso, 2009). Interestingly, during this period, about 50% of dietary lipids had been digested in the midgut lumen, allowing a significant rate of lipid absorption and transfer to lipophorin (Canavoso, Frede & Rubiolo, 2004). A similar result was observed in *R. prolixus* (Grillo, Pontes & Gondim, 2003), where a very high capacity to bind lipophorin in the midgut was observed on the second day after feeding. The lipophorin binding capacity of the organ decreased and at day 10, when digestion was close to the end (Grillo, Pontes & Gondim, 2003). The high rate of lipid transfer to lipophorin observed in both species suggests that digestion of dietary lipids is an important factor influencing lipophorin binding and consequently, the ability of the tissue to export lipids to the circulation.

The principal circulating lipoprotein in the hemolymph of resting insects is HDLp (1.063–1.21 g/ml), and under physiological conditions characterised by intense energy demands, such as flight or oogenesis, this lipophorin increases its lipid content by binding additional DAG at the surface of the adipocytes. However, mosquito lipophorins have a unique characteristic: they carry TAG rather than DAG as the principle neutral lipid (Ford & Van Heusden, 1994). Either way, the binding of DAG or TAG to the lipophorin results in the production of LDLp, (1.006–1.063 g/ml), which can carry the DAG, or TAG, through the haemolymph to the peripheral tissues (Blacklock & Ryan, 1994; Arrese & Soulages, 2010; Fruttero, Leyria & Canavoso, 2017; Toprak et al., 2020).

Literature data suggests the additional presence of very high-density lipophorin (VHDLp) (Kawooya & Law, 1988; Kawooya, Osir & Law, 1988); this is formed when lipophorin is taken up by oocytes, deposited in yolk bodies, and stripped from its lipids by
Table 2  The function of lipophorin and examples of its occurrence in insects.

| Description     | Function                                                                 | Examples in insects | Literature data                                      |
|-----------------|---------------------------------------------------------------------------|---------------------|----------------------------------------------------|
| HDLp            | reach midgut or fat body to acquire fatty acid, delivers pheromones to the cuticle and specialized pheromone glands, hydrocarbons to the epicuticle, fat body, and ovaries and retinoids to yet undetermined locations | Aedes aegypti       | Capurro, de Bianchi & Marinotti (1994); Cheon et al. (2001) |
| LDLp            | take up lipids released from the midgut/fat body cells and transport them to the fat body or to selectively unload its lipid cargo at target tissues without endocytosis and lysosomal degradation | Anopheles gambiae   | Atella et al. (2006)                               |
|                 |                                                                          | Blattella germanica | Sevala et al. (1999); Young et al. (1999)           |
|                 |                                                                          | Culex quinquefasciatus | Kumar & Paily (2011)                               |
|                 |                                                                          | Dipetalogaster maxima | Leyria et al. (2014)                               |
|                 |                                                                          | Drosophila melanogaster | Palm et al. (2012)                                 |
|                 |                                                                          | Glossina morsitans   | Ochanda et al. (1991)                               |
|                 |                                                                          | Lucilia cuprina      | Trowell et al. (1994)                               |
|                 |                                                                          | Musca domestica      | De Bianchi, Capurro & Marinotti (1987); Schal et al. (2001) |
|                 |                                                                          | Panstrongylus megistus | Fruettero, Rubiolo & Canavoso (2009); Fruettero et al. (2011) |
|                 |                                                                          | Rhodnius prolixus    | Grillo, Pontes & Gondim (2003); Entringer et al. (2013) |
|                 |                                                                          | Sarcophaga bullata   | Gysen et al. (1988)                                 |
|                 |                                                                          | Simulium vittatum    | Pennington & Wells (2002)                           |
|                 |                                                                          | Triatoma infestans   | Fichera & Brenner (1982)                            |
| VHDLp           | transport precursors from the fat body to the ovaries for the deposition of lipid yolk droplets; the constituents of the protein yolk body | Aedes aegypti       | Sun et al. (2000)                                  |
|                 |                                                                          | Rhodnius prolixus    | Santos et al. (2011)                               |
|                 |                                                                          | Triatoma infestans   | Rimoldi et al. (1989); Rimoldi et al. (1996)       |

Lipase. This transformation results in the formation of higher density lipophorin particles (~1.238 g/ml) (Liu & Ryan, 1991; Ziegler & Van Antwerpen, 2006).

The presence of VHDL, a hexameric protein, was detected in various tissues of *T. infestans* throughout the last nymphal and adult stages, and in egg extracts (Rimoldi et al., 1996). Hemolymph VHDL reaches a maximum value before the last moult; it abruptly declines in males and females just after emergence but increases again during adult life. Fat body VHDL decreases slowly and continuously during nymph growth, reaching a minimum
value prior to moulting: the values can be as much as two-fold lower in the first week of adult life; its level then follows accumulation and depletion cycles which differ between males and females (Gonzalez, Soulages & Brenner, 1991; Rimoldi et al., 1996).

Most insect lipophorins have two structural apolipoproteins, apolipoprotein I (apoLp-I, Mr ∼230–250 kDa) and apolipoprophorin II (apoLp-II, ∼70–85 kDa) (Fruttero, Leyria & Canavoso, 2017). ApoLp-I and apoLp-II are integral components of the lipophorin particle, and cannot be removed without destruction of lipophorin particle integrity (Van der Horst & Ryan, 2012). It is recognized that apoLp-I and apoLp-II are the product of the same gene, and that the two proteins arise through post-translational cleavage of their common precursor protein (Weers et al., 1993). ApoLp-II/I is a homolog of the mammalian apoB and belongs to the same superfamily of large lipid transfer proteins (LLTP) (Van Der Horst & Rodenburg, 2010).

ApoLp-I and ApoLp-II are responsible for transport of dietary cholesterol in R. prolixus (Entringer, Majerowicz & Gondim, 2021). They have been found to mediate lipid transfer to developing eggs and manage the distribution of the imported lipid in developing embryos in An. gambiae and Anopheles aquasalis (Diptera: Culicidae) (Atella et al., 2006; Dias-Lopes et al., 2016). In the tsetse fly G. morsitans, RNA interference (RNAi) against GmmapoLp-II/I resulted in decreased hemolymph lipid levels in females and delayed oocyte development (Benoit et al., 2011). In D. melanogaster, DmapoLp-II/I was shown to be the major lipid transport protein in the larval hemolymph (Palm et al., 2012). Lipoprotein serves as a carrier for the transport of hydrocarbons from the site of synthesis (oenocyte) to the site of deposition (cuticle) in the American cockroach Periplaneta americana (Blattodea: Blattidae) and it is speculated that after synthesis in the oenocytes, the lipids bind to apoLps and are released into the hemolymph; they subsequently shuttle to the epidermis where they bind to lipoprotein receptors, and are finally transported to the cuticle surface via pore canals (Haruhito & Haruo, 1982; Chapman, 1998).

A third apolipoprotein particle is the low molecular weight apolipophorin-III ApoLpIII; Mr 18–20 kDa), homologous to mammalian apoE (Weers & Ryan, 2006), which circulates free in the hemolymph and is taken up by the HDLp when it acquires DAGs from the fat body; ApoLpIII expands the surface of the lipophorin particle during lipid loading (Van der Horst et al., 2002). In insects that use lipid as a fuel for flight, such as M. sexta, ApoLpIII is present in adult hemolymph as a lipid-free protein (Van der Horst & Ryan, 2012). The decreased expression of apoLp-III was observed during diapause in the mosquito, Ae. albopictus (Reynolds et al., 2012). ApoLp-III plays also an important role in the innate immune system (Zdybicka-Barabas & Cytrynska, 2013; Staczek et al., 2018; Maravilla et al., 2020). In G. mellonella this apolipoprotein stimulates the expression of antimicrobial peptides and proteins, regulates nodulation and opsonization in cellular immunity, and may act as a pattern recognition protein (Wiesner et al., 1997). Moreover, apoLp-IIIGM binds to the surface of gram-negative bacteria, resulting in the deformation of the bacterial membrane (Zdybicka-Barabas et al., 2013; Zdybicka-Barabas et al., 2014). Apolipophorin-III acts as a positive regulator of Plasmodium development in Anopheles stephensi (Diptera: Culicidae) and An. gambiae (Gupta et al., 2010; Dhawan et al., 2017).
Lipophorin and lipophorin receptor genes activation was observed in the Ae. aegyptii fat body as a response to Plasmodium infection. The fat bodies were found to demonstrate a similar pattern of lipophorin and lipophorin receptor activation on the mRNA level in response to Plasmodium infection as observed with Gram-positive bacteria or fungal infections; however, interestingly, Gram-negative bacterial infection did not change the level of transcription of either gene, which might suggest that the Toll/REL1 pathway is involved in the regulation of both Lp and LpRfb transcripts during immune challenge (Cheon et al., 2006).

The interaction of lipophorin with tissues is mediated by specific receptors and in many insects, Lipophorin receptors have been characterised as members of the low-density lipoprotein receptor gene superfamily (Entringer et al., 2013).

The transported lipids are hydrolysed into FFAs and glycerol at the surface of the recipient cell by a membrane bound lipase, and the FFAs are transported into the cell via fatty acid binding proteins. They can be either hydrolysed to FFAs by membrane-bound lipophorin lipases (Arrese et al., 2001; Sinclair & Marshall, 2018) or taken up by endocytosis of the lipoprotein-DG complex (Rodenburg & Van Der Horst, 2005) In contrast to vertebrates, HDLp is recycled for additional lipid transport in insects; this increases the efficiency of lipid transport and reduces its overall cost (Van Der Horst et al., 2002).

**Lipophorin receptors**

In R. prolixus, the transfer of lipids from the posterior midgut to lipophorin is mediated by specific binding sites in the midgut cell membrane. The midgut capacity to bind lipophorin varies according to the time after a meal: it is very high during the second day after a meal, when a high rate of lipid transfer to lipophorin is also observed, and the number of lipophorin receptors in midgut cell membranes may be an important mechanism for controlling lipid flux in R. prolixus (Grillo, Majorowicz & Gondim, 2007). The ectopic β-chain of ATP synthase (βATPase) was recently described as a possible non-endocytic lipophorin receptor in the anterior midgut of the hematophagous insect P. megistus (Fruttero et al., 2014; Fruttero et al., 2017; Fruttero et al., 2019).

In some insects, the lipophorin receptor (LpR), which binds to lipophorin and accepts its lipid cargo, plays an essential role in female fecundity by mediating the incorporation of lipophorin in developing oocytes (Van Der Horst et al., 2002; Ciudad, Belles & Piulachs, 2007; Parra-Peralbo & Culi, 2011; Palm et al., 2012; Lu et al., 2018). The examples of lipophorin receptors in insect are presented in Table 3.

The increase in LpR transcript expression during vitellogenesis has been reported in D. maxima (Ramos et al., 2021). In Ae. aegypti they are two splice variants of LpR gene products specific to the fat body (AaLpRfb) and ovary (AaLpRov) (Cheon et al., 2001; Seo et al., 2003); these two distinct isoforms of lipophorin receptors, which are derived from a single gene, are differentially expressed in oocytes and the fat body (Seo et al., 2003). The expression of the fat body-specific AaLpRfb transcript is restricted to the post-vitellogenic period, during which production of yolk protein precursors is terminated and the fat body is transformed into a storage depot of lipid, carbohydrate and protein (Seo et al., 2003).
Table 3  Examples of lipophorin receptors in insects.

| Insect               | Name       | Place of detection                | Literature data                      |
|----------------------|------------|-----------------------------------|--------------------------------------|
| Aedes aegypti        | AaLpRov    | ovaries                           | Cheon et al. (2001)                  |
|                      | AaLpRfb    | fat body                          | See et al. (2003)                    |
| Blattella germanica  | BgLpR      | fat body and ovarian               | Ciudad, Belles & Piulachs (2007)     |
| Culex quinquefasciatus | LpR       | fat body                          | Kumar & Paily (2011)                 |
| Dipetalogaster maxima | LpR1, LpR2| muscle                            | Ramos et al. (2021)                  |
| Galleria mellonella  | LpR_Gm     | fat body                          | Kim et al. (2021)                    |
| Glossina morsitans morsitans | GmmLpR | midgut, fat body, milk gland, spermatheca and head | Lee et al. (2003) |
| Leucophaea maderae   | LemLpR     | ovaries                           | Tufail et al. (2009)                 |
| Panstrongylus megistus | β-ATPase  | ovaries                           | Fruttero, Leyria & Canavoso (2017)   |
| Rhodnius prolixus    | LpR        | ovaries                           | Entringer et al. (2013);             |
|                      |            | midgut                            | Leyria, Orchard & Lange (2020)       |
|                      |            | fat body                          | Grillo, Pontes & Gondim (2003)       |
|                      |            |                                   | Pontes, Grillo & Gondim (2002)       |

In *D. melanogaster*, although the knockdown of LpR did not affect the lipid content of the fat body and hemolymph, it impaired the uptake of neutral lipids in the oocytes and imaginal discs, suggesting an organ-specific role (*Parra-Peralbo & Culi, 2011*). In *P. megistus* no differences in the expression of the putative lipophorin receptor β-ATPase were observed between fed and fasted insects; however, the nutritional condition influenced the histological features of the fat body (*Fruttero et al., 2019*).

Different amounts of Lp receptors in the fat body and ovary was also observed in *R. prolixus*, where $^{125}$I-Lp demonstrated higher specific binding to the oocyte membrane than to the fat body membrane. This outcome might be a result of the increased amount of lipophorin receptors on the oocytes or to differences in the receptor properties between the fat body and oocytes (*Entringer et al., 2013*).

In *Drosophila*, PUFA are selectively incorporated into the acyl chains of lipophorin phospholipids and effectively transported to the central nervous system by endocytosis, mediated by the lipophorin receptor (*Matsuo et al., 2019*). In *Drosophila* also, the muscle-specific knockdown of *LpR1* or *LpR2* genes resulted in mitochondrial dysfunction and reduced proteostasis, which contributed to muscle aging (*kyeong et al., 2021*).

**Intracellular transport of FFA**

Import of FFAs by cells can take place by two main mechanisms working in parallel. When the extracellular FFA concentration is high, they often enter the cell by rapid free diffusion, *flip–flopping* across the lipid component of the membrane bilayer along the resulting FFA gradient (*Hamilton & Kamp, 1999; Hamilton, 2007*). However, in many cell types and organs, transport occurs primarily through a saturable mechanism mediated by FFA-binding protein (*Hamilton, 1998; Schaffer, 2002; Doege & Stah, 2006*). Three main types of FFA binding proteins are believed to exist (*Stahl, 2004; Doege & Stah, 2006; Glatz, Luiken & Bonen, 2010; Toprak et al., 2020*): plasma membrane fatty acid binding protein (FABPpm), which acts as an integral membrane protein, fatty acid translocase...
(FAT/CD36), and fatty acid transport proteins (FATPs), a large family of multifunctional proteins. Selected examples of intracellular transporters in insects are presented in Table 4

**Fatty acid binding protein (FABP)**

Fatty acid binding protein (FABP) is an evolutionarily-conserved membrane-bound protein that facilitates the uptake of extracellular long chain fatty acids; in adipocytes, localization of FABP into the plasma membrane causes specific and saturable uptake of long chain fatty acids (Schaffer & Lodish, 1994). Some reports clearly demonstrate the presence of FABPs in the midgut epithelium of the investigated insect, hence suggesting a function in dietary lipid uptake (Holtof et al., 2019). Once the FAs pass through the plasma membrane, they are bound by FABPs and transported to different compartments, such as lipid droplets, the endoplasmic reticulum or the mitochondria, depending on the physiological needs of the insect. FABPs might be also involved in trafficking amongst these compartments (Toprak et al., 2020). Examples of FABPs in insects are presented in Table 3

*fabp* expression was upregulated in early diapausing *C. pipiens* females, and the level of expression increased during diapause. In the early stage of diapause, FABP might be involved in mobilizing TAG for storage in the fat body, while in the late stage, FABP may play a role in mobilizing and distributing fatty acids for use in generating energy. The hypothesis that FABP mobilizes fatty acids in late diapause is also supported by the strong upregulation of the putative lipase genes (Sim & Denlinger, 2009; Gondim et al., 2018).

A form of FABP was also purified from the cytosolic fraction of the triatomine *D. maximus*. The protein has an apparent molecular mass of 14 kDa, and its N-terminus is unblocked, and the obtained sequence indicates that this FABP belongs to the heart type, characteristic of organisms which obtain energy from fatty acid beta oxidation (Cavagnari et al., 2000).

In adult *Drosophila*, FABP is very strongly expressed in the adult eye, hindgut, fat body, heart (Dourlen et al., 2015). Beyond its role in fatty acid transport, FABP has also been implicated as a modulator of sleep in *D. melanogaster* (Gerstner et al., 2011).

FABP has also been detected in the flight muscle of the migratory locust *Schistocerca gregaria* (Orthoptera: Acrididae) (Haunerland et al., 1992); this insect is not only an economically damaging pest for a wide range of crops but it is also a source of therapeutic sterols (Cheseto et al., 2015). In addition, knockdown of the gene associated with the expression of FABP in *S. gregaria* impairs the ability to fly (Rajapakse et al., 2019).

**Fatty acid translocase (FAT/CD36)**

The FAT/CD36 protein was initially identified in the olfactory receptor neurons of Lepidoptera and Diptera. Examples of this proteins in insects are presented in Table 3. It is thought to play a role in odour detection by interacting with extracellular proteins such as odorant binding proteins (OBP) (Xu et al., 2020; Zhang et al., 2020). It has been proposed that *Ae. aegypti* odorant binding protein 22 (AeOBP22) might bind long-chain fatty acids (C15-C20) for example arachidonic acid, and that this process is enhanced by a conformational change in the C-terminal tail that generates a high affinity binding site (Jones, Wang & Murphy, 2019; Wang et al., 2020).
Table 4 Examples of lipophorin receptors in insects.

| Insect                        | Function of protein                                                                 | Literature data                                                                 |
|-------------------------------|------------------------------------------------------------------------------------|----------------------------------------------------------------------------------|
| **Fatty acid binding protein** |                                                                                   |                                                                                  |
| (FATB)                        |                                                                                   |                                                                                  |
| Aedes aegyptii                | function not established yet                                                      | Zheng, Blair & Bradley (2013)                                                   |
| Aedes albopictus              | lipid storage before diapause                                                      | Reynolds et al. (2012)                                                          |
| Anopheles gambiae             | function not established yet                                                      | Esteves & Ehrlich (2006); Zheng, Blair & Bradley (2013)                         |
| Apis mellifera                | retinoic acid binding                                                             | Evans & Wheeler (1999); Esteves & Ehrlich (2006); Zheng, Blair & Bradley (2013) |
| Culex pipiens                 | fat storage during early diapause                                                  | Sim & Denlinger (2009)                                                          |
| Dipetalogaster maxima         | transport of FFAs in the thoracic muscles during flight                            | Cavagnari et al. (2000)                                                         |
| Drosophila melanogaster       | mediated signalling in both sleep/ wake and memory-related processes               | Gerstner et al. (2011)                                                          |
| Panstrongylus megistus        | transfer of FFAs to developing oocytes by a non-endocytic mechanism and then segregation into lipid droplets | Fruttero et al. (2011)                                                          |
| Schistocerca gregaria         | transport of FFAs to the flight muscle during flight                               | Wu & Haunerland (2001); Rajapakse et al. (2019)                                  |
| **Fatty acid translocase**    |                                                                                   |                                                                                  |
| (FAT/CD36)                    |                                                                                   |                                                                                  |
| Aldrichina grahami            | an important component of protecting olfactory function                            | Han et al. (2020)                                                               |
| Aulacocentrum confusum        | function not established yet                                                      | Li et al. (2021)                                                               |
| Bombyx mori                   | selective carotenoid transport for cocoon coloration; transport of FFAs in the larvae midgut | Sakudoh et al. (2010); Zhang et al. (2020)                                         |
| Calliphora stygia             | function not established yet                                                      | Leitch et al. (2015)                                                          |
| Cotesia vestalis              | function not established yet                                                      | Liu et al. (2020)                                                              |
| Drosophila melanogaster       | involved in the oviposition response to C6–C9 fatty acids                          | Scheuermann & Smith (2019)                                                      |
| Galleria mellonella           | function not established yet                                                      | Li et al. (2021)                                                               |
| Hermetia illucens             | mediates responses to lipid pheromones                                            | Xu et al. (2020)                                                               |
| Microplitis mediator          | involved in perceiving plant volatiles and sex pheromones                         | Shan et al. (2020)                                                             |
| Phormia regina                | might solubilize and deliver palmitic, stearic, oleic, and linoleic acids to the midgut during feeding | Ishida, Ishibashi & Leal (2013)                                                |

(continued on next page)
### Table 4 (continued)

| Insect                   | Function of protein                                                                 | Literature data                          |
|--------------------------|--------------------------------------------------------------------------------------|------------------------------------------|
| **Rhodnius prolixus**    | function not established yet                                                         | Ribeiro et al. (2014)                    |
| **Fatty acid transport protein (FATP)** |                                                                                      |                                          |
| **Anopheles gambiae**    | functionally implicated in cuticular hydrocarbons biosynthesis in oenocytes          | Grigoraki et al. (2020a), Grigoraki et al. (2020b) |
| **Apis mellifera**       | transport of fatty acids for the production of ethyl oleate from the fat body to the honey crop/oesophagus, could be responsible for the transport/removal of ethyl oleate | Castillo et al. (2012)                    |
| **Bombus terrestris**    | mediate uptake of extracellular FFAs in the pheromone gland                           | Buček et al. (2016)                      |
| **Drosophila melanogaster** | transport of FFAs; synthesis of VLCFA; mediating in FFAs uptake into the nervous system | Rittschof & Schirmeier (2018); Van Den Brink et al. (2018); Poidevin et al. (2021) |
| **Musca domestica**      | FFAs uptake in the midgut                                                            | Barroso et al. (2021)                     |
| **Rhodnius prolixus**    | function not established yet                                                         | Alves-Bezerra et al. (2016)              |

The two OBP *D. melanogaster* proteins expressed in the leg sensilla, viz. OBP57d and OBP57e, are involved in the oviposition response to C6–C9 fatty acids. Flies knocked down for either of these two OBPs showed an altered preference for the tested fatty acid compared with control flies (Scheuermann & Smith, 2019).

Although OBP was initially found in the olfactory appendages, these proteins were later discovered in other chemosensory and non-chemosensory organs, such as the midgut (Rihani, Ferveur & Briand, 2021). Fluorescent binding assays revealed that in forensic important blowfly *Phormia regina* (Diptera: Calliphoridae) OBP (PregOBP56a) binds palmitic, stearic, oleic, and linoleic acids, indicating that PregOBP56a might solubilize and deliver fatty acids to the midgut during feeding (Ishida, Ishibashi & Leal, 2013). Similarly, OBP expression has also been detected in the midgut of *R. prolixus* (Ribeiro et al., 2014).

Besides OBPs, another important group of FAT/CD36 are sensory neuron membrane proteins (SNMPs) (Cassau & Krieger, 2020). A transcriptomic study on the antennae of adult *Aldrichina grahami* (Diptera: Calliphoridae), a necrophagous insect with forensic significance, demonstrated differences in the composition and expression of SNMP genes between sex and tissue type. Such differences are likely to greatly influence insect behaviour around a corpse. In addition, a better understanding of the function of candidate olfactory genes may provide a greater insight into the molecular mechanisms of olfactory detection of forensically-important fly species; such information would be of value in when determining the period before minimum post-mortem inference (PMImin) (Han et al., 2020).

In *Drosophila*, SNMP1 was shown to facilitate the detection of lipid-derived pheromones by their cognate receptors in olfactory cilia; structure–activity dissection indicates that the ectodomain of SNMP1 plays an essential role in cilia localization and pheromone-evoked responses (Gomez-Diaz et al., 2016). In addition, both SNMP1 and SNMP2 have been
detected in the chemosensory tissues, particularly in the antennae of the hemimetabolous desert locust *S. gregaria* (*Jiang et al., 2016*). The fact that neuronal-expressed SNMPs and CD36 share analogous functions in insects and vertebrates suggests that the olfactory mechanisms used in the detection of lipophilic odorants may be evolutionarily conserved (*Cassau & Krieger, 2020*).

In the Lepidoptera, research has shown the presence of three classes of SNMP: SNMP1, which is restrictively expressed in adult antennae, SNMP2, which is broadly expressed in multiple tissues and SNMP3, which is generally concentrated in larval and the adult midgut, indicating a possible function in fatty acid transportation (*Zhang et al., 2020*). In the model organism *B. mori* (*Meng, Zhu & Chen, 2017; Abdelli, Peng & Keping, 2018*), it has been proposed that class B type I scavenger receptors belonging to the CD36 protein family might be involved in the active transport of dietary fatty acids across the midgut membrane; this would play a role in elective carotenoid transport for cocoon coloration (*Sakudoh et al., 2010*).

**Fatty acid transport protein (FATP)**

Fatty acid transport protein (FATP) is an evolutionarily-conserved membrane-bound protein that facilitates the uptake of extracellular long chain fatty acid (LCFA) isoforms, which are widely expressed, but with distinct tissue specificity. Their activity is associated with fatty acyl-coenzyme A (CoA) synthetases, which catalyse the formation of CoA-derivatives, an activation step essential for the subsequent metabolic transformation of FAs (*Glatz, Luiken & Bonen, 2010*). Some research suggests that this protein plays a crucial role in lipid accumulation in insect oocytes (*Ziegler & Van Antwerpen, 2006*). Examples of FATP in insects are presented in Table 3.

The *Drosophila* genome encodes three FATP homologues, Fatp, CG3394 and CG44252. Of these, *Fatp* appears to be expressed in hemolymph–brain barrier (HBB)-forming glial cells, and it shows high homology to mouse and human FATP-1 and FATP-4; as such, this protein is considered as a good candidate for mediating fatty acid uptake into the nervous system (*Rittschof & Schirmeier, 2018*). In invertebrates, FATP expression is also tissue specific. In adult *Drosophila*, *fatp* is thought to be the major member of the family as it is very strongly expressed in the adult eye, hindgut, fat body, heart and carcass, whereas *fatp* paralogs, CG3394 and CG30194, are only moderately expressed in some of the tissues of the adult fly (*Dourlen et al., 2015*).

The two homologs of FATP, *viz.* MdFATP1 and MdFATP2, were found in *M. domestica* (*Barroso et al., 2021*). In *M. domestica* larvae, FATP1 may enhance the uptake of FAs at the apical membrane of midgut cells, as suggested by its occurrence at midgut microvillar-enriched membrane preparations along the midgut. On the other hand, FATP2, which has a predicted transmembrane domain, but is absent from microvillar-enriched membrane preparations, may be involved in the uptake of FAs through intracellular membranes, such as human FATP4 in the endoplasmic reticulum of enterocytes (*Stahl et al., 1999*). It is important to note the posterior midgut cells of *M. domestica*, where most of the FATP2 is expressed, have a well-developed endoplasmic reticulum (*Terra et al., 1988*). (*Terra et al., 1988*).
The honey bee, *Apis mellifora*, has been the source of a range of medicinal products, such as honey, propolis and bee venom for thousands of years. More recently, it has been used as an important model organism for studying the genetics of behaviour and cognition, as well as the regulation and maintenance of complex societies and their evolution (Oldroyd & Thompson, 2006; Sforcin, Bankova & Kuropatnicki, 2017; Webster, 2019; Al-Hatamleh et al., 2020; Duffy et al., 2020). Studies have also found the expression sites of FATP along the oesophagus to correspond with the intake of nectar by the bee, and the resulting exposure to ethanol. These proteins probably take part in the formation of ethyl oleate, by condensing oleic acid with ethanol and providing free fatty acids, or possibly removing the ethyl oleate from the regurgitate. A search in the honey bee peptide map for these genes resulted in the identification of peptides in the head of the adult worker and 33.6% of these genes were genes coding the FATP (Castillo et al., 2012).

Research suggests that FATP plays an essential role in bombykol biosynthesis in the silkworm *Bombyx mori*, a model animal used in toxicological research and for studying human disease: silkworm genes demonstrate high homology with certain genes related to human hereditary disease (Meng, Zhu & Chen, 2017; Abdelli, Peng & Keping, 2018). FATP stimulates both lipid accumulation and triacylglycerol synthesis via vectorial acylation during pheromonogenesis, thus allowing the uptake of extracellular fatty acids and their subsequent activation to CoA thioesters (Ohnishi et al., 2009).

In addition, a range of transcripts coding FATPs (FATP-1–FATP-3) was identified in the buff-tailed bumblebee, *Bombus terrestris* (Hymenoptera: Apidae), another important evolutionary model organism (Baer, 2003; Goulson, 2004; Wilfert et al., 2007; Rother et al., 2021). These were believed to code for FA transport-related proteins, some of which were homologous to *B. mori* FATPs, which mediate the uptake of extracellular FAs in the pheromone gland (Ohnishi et al., 2009). FATP-1 was abundantly and specifically expressed in the fat body, whereas FATP-2 and FATP-3 were expressed at comparable levels across the tissues, indicating that they play a role in the primary fatty acid metabolism rather than the biosynthesis of fatty acid-derived marking pheromones localized in the labial gland (Buček et al., 2016).

**Metabolism of FFAs**

After being absorbed, predigested lipid molecules are used as precursors for the synthesis of more complex structures that will be transported to other organs. Specifically, FFAs are either oxidized in the mitochondria (β-oxidation) for energy production or used to synthesize TAGs, DAGs and phospholipids (Toprak et al., 2020).

Once the FFAs are transported into the cells, they are activated by linking to CoA to generate fatty acyl-CoA (FA-CoA), an intermediate used for FA elongation and β-oxidation (Majerowicz & Gondim, 2013). The acetyl-CoA enters the mitochondrial Krebs cycle to generate energy in the presence of oxygen. β-Oxidation in the mitochondria involves sequential removal of acetyl-CoA and two pairs of hydrogen atoms from the FA-CoA to generate flavin adenine dinucleotide (FADH2) and nicotinamide adenine dinucleotide. Therefore, production of acetyl-CoA is a key intermediate for the interconversion of fats and carbohydrates. When the insect has enough energy, acetyl-CoA is removed from
the Krebs cycle and is transported from mitochondria to the cytosol; the acetyl-CoA is then able to enter the citric acid cycle. Notably, acetyl-CoA forms an ester with carnitine before it crosses the inner mitochondrial membrane, which facilitates the transport from mitochondria to the cytosol (Toprak et al., 2020).

Lipolysis is the process based on the constant hydrolysis of TAGs to fatty acids. In this process, the TAGs are first hydrolyzed to DGs and monoglycerides (MGs); these are further transformed into three fatty acid molecules and a glycerol molecule (Skowronek, Wójcik & Strachecka, 2021). All lipolysis is regulated by the protein perilipine, which prevents or stimulates the hydrolysis/phosphorylation of TAG. Its activity increases during starvation and the action of glucocorticoids, and decreases with food consumption. It stimulates phosphorylation and facilitates its translocation from the cytosol of the cell to the surface of the fat droplets, where TG hydrolysis occurs (Skowronek, Wójcik & Strachecka, 2021).

**Biosynthesis of FFAs**

Although the fatty acid profiles of insects are greatly altered by their diet (Kazek et al., 2019; Kaczmarek et al., 2021), there are some exceptions. The biosynthesis of palmitic, stearic, oleic acid seems to be widespread among insects, and correspondingly these fatty acids are the most abundant in their bodies (De Renobales et al., 1987; Stanley-Samuelson et al., 1988; Gołębiewski et al., 2013a; Malicka, Visser & Ellers, 2018; Broschwitz et al., 2021). The examples of enzymes engaged in FFAs synthesis in insects are presented in Table 5 and a schema of FFA synthesis is presented in Fig. 2.

Some hymenopteran insects, such as *N. vitripennis*, are able to synthesise palmitic and stearic acid from α-D-glucose (Prager, Bruckmann & Ruther, 2019; Ruther, Prager & Pokorny, 2021) and linoleic acid from oleic acid (Broschwitz et al., 2021). The synthesis of linoleic acid is observed in some insects, for example, some species from the Order Hemiptera (*Myzus cerasi, Myzus persicae, Prociphilus fraxini folli, Planococcus citri, Bemisia argentifolii*), Isoptera (*Zootermopsis angusticollis, Coptotermes formosanus, Reticulitermes flavipes*), Hymenoptera (*Nasonia vitripennis*), Neuroptera (*Chrysoperla carnea*) and Coleoptera (*Tribolium castaneum*) (Malicka, Visser & Ellers, 2018).

In female *Ae. aegypti*, sugar feeding before a blood meal resulted in lipid accumulation in the fat body, suggesting that *de novo* lipogenesis was active in these insects (Ziegler & Ibrahim, 2001; Zhou, Pennington & Wells, 2004). In these mosquitoes, amino acids derived from the blood meal were also used for *de novo* lipogenesis, which increased oogenesis efficiency (Zhou et al., 2004).

*De novo* lipogenesis may also occur in tissues other than the fat body. In the hematophagous hemipteran *T. infestans*, fatty acids and hydrocarbons are synthesized from acetate in the integument tissue, resulting in the production of cuticle lipids (Juarez & Brenner, 1989).

**Acetyl-CoA carboxylase (ACC)**
The first step in *de novo* fatty acid synthesis is the carboxylation of acetyl-CoA to produce malonyl-CoA, which is catalyzed by acetyl-CoA carboxylase (ACC). Following this, malonyl-CoA units are sequentially condensed with acetyl-CoA to synthesise long-chain
| Enzyme                                      | Function                                                                 | Insect                      | Literature data                          |
|--------------------------------------------|--------------------------------------------------------------------------|-----------------------------|------------------------------------------|
| Acetyl-CoA carboxylase (ACC)               | catalyze the carboxylation of acetyl-CoA to produce malonyl-CoA           | Aedes aegyti                | Alabaster et al. (2011)                   |
|                                            |                                                                          | Culex pipiens               | Sim & Denlinger (2009)                    |
|                                            |                                                                          | Drosophila melanogaster     | Parvy et al. (2012)                      |
|                                            |                                                                          | Glossina morsitans          | Dean Goldring & Read (1994)              |
|                                            |                                                                          | Rhodnius prolixus           | Saravia et al. (2021)                    |
|                                            |                                                                          | Sarcophaga nodosa           | Dean Goldring & Read (1993)              |
|                                            |                                                                          | Sarcophaga tibialis         | Konji, Olembo & Pearson (1984)           |
| Fatty acid desaturase (FAD)                |                                                                          | Aedes aegyti                | Sanders et al. (2003)                    |
|                                            |                                                                          | Aedes albopictus            | Reynolds et al. (2012)                   |
|                                            |                                                                          | Anopheles coluzzii          | Ferdous et al. (2021)                    |
|                                            |                                                                          | Anopheles gambiae           | Helmkampf, Cash & Gaidau (2015)          |
|                                            |                                                                          | Culex pipiens               | Sim & Denlinger (2009)                    |
|                                            |                                                                          | Drosophila melanogaster     | Wicker-Thomas, Henriet & Dallerac (1998); Dallerac et al. (2000) |
|                                            |                                                                          | Musca domestica             | Wang et al. (1982); Eigenheer et al. (2002) |
|                                            |                                                                          | Nasonia vitripennis         | Brandstetter & Ruther (2016); Semmelmann et al. (2019) |
|                                            |                                                                          | Rhodnius prolixus           | Majerowicz et al. (2017)                 |
|                                            |                                                                          | Sarcophaga crassispalpis    | Rinchert, Robich & Denlinger (2010)      |
| Fatty acid synthase (FAS)                  |                                                                          | Aedes aegyti                | Sanders et al. (2003); Alabaster et al. (2011); Martins et al. (2011) |
|                                            |                                                                          | Anopheles gambiae           | Grigoraki et al. (2020b)                 |
|                                            |                                                                          | Blattella germanica         | Juárez, Chafe & Blomquist (1992)         |
|                                            |                                                                          | Culex pipiens               | Sim & Denlinger (2009)                    |
|                                            |                                                                          | Lucilia sericata            | Thompson, Barlow & Douglas (1975)        |
|                                            |                                                                          | Musca domestica             | Gu et al. (1997)                         |
|                                            |                                                                          | Rhodnius prolixus           | Moriconi et al. (2019)                   |
|                                            |                                                                          | Triatoma infestans          | Juárez, Ayala & Brenner (1996); Juárez & Napolitano (2000); Calderón-Fernández et al. (2017) |
| Very long-chain fatty acid elongase (ELOVL)|                                                                          | Aedes aegyti                | Martins et al. (2011)                    |
|                                            |                                                                          | Aedes albopictus            | Urbanski et al. (2010); Reynolds et al. (2012) |

(continued on next page)
Table 5 (continued)

| Enzyme                                      | Function                                  | Insect                              | Literature data                                                                 |
|---------------------------------------------|-------------------------------------------|-------------------------------------|---------------------------------------------------------------------------------|
|                                             |                                            | **Anopheles. gambiae**               | Goltsev et al. (2009)                                                            |
|                                             |                                            | **Blattella germanica**              | Juárez (2004)                                                                   |
|                                             |                                            | **Drosophila melanogaster**          | Chertemps et al. (2005)                                                         |
|                                             |                                            | **Periplaneta americana**            | Vaz et al. (1988)                                                               |
|                                             |                                            | **Triatoma infestans**               | Juárez & Brenner (1989); Juarez, Ayala & Brenner (1996); Calderón-Fernández et al. (2017) |
| **Long-chain acyl-CoA synthetase (ACSL)**   | adds Coenzyme A to the long chain (C12-20) fatty acids | **Rhodnius prolixus**               | Majerowicz et al. (2017)                                                        |
|                                             |                                            | **Drosophila melanogaster**          | Zhang, Chen & Wang (2009); Zhang et al. (2011)                                  |

**Figure 2** The biosynthesis of FFAs in insect. ACC, acetyl-CoA carboxylase; FAS, fatty acid synthase; ACSL, long-chain acyl-CoA synthetase; FAD, fatty acid desaturase; VLC FFAs, very long chain free fatty acids.

Kaczmarek and Boguś (2021), *PeerJ*, DOI 10.7717/peerj.12563/fig-2

fatty acids (Toprak et al., 2020). Phylogenetic analysis has found that, similar to other arthropods but not vertebrates, insects have only one ACC gene (Alabaster et al., 2011; Parvy et al., 2012; Saraiva et al., 2021).

In R. prolixus females, the ACC (RhoprACC) transcript levels were similar in the anterior and posterior midgut, fat body and ovary on the fourth day after a blood meal, but higher in the flight muscles. In the fat body, gene expression was higher in fasted females and decreased after a blood meal. In the posterior midgut, it increased after feeding, and no variation was observed in the flight muscle. RhoprACC protein content analysis of the fat body revealed a similar profile to gene expression, with higher protein contents observed before feeding and in the first two days after a blood meal. De novo lipogenesis was very
low in starved females but increased during the initial days after a blood meal. The flight muscles had a very low capacity to synthesize lipids when compared to the fat body (Saraiva et al., 2021).

In *Ae. aegyptii*, ACC transcription in the fat body was stimulated by a blood meal. Research has shown that ACC-deficient mosquito females produced defective oocytes, which lacked an intact eggshell and gave rise to inviable eggs. This severe phenotype was restricted to the 1st gonotrophic cycle, suggesting that the eggshell defect was due to ACC deficiencies in the follicular epithelial cells, which are replaced after each gonotrophic cycle. On the other hand, the knockdown of FAS1 showed delayed blood meal digestion, suggesting that a feedback control mechanism may coordinate the rates of fat body lipid biosynthesis and midgut digestion during feeding. The knockdown of both ACC and FAS resulted in reduced number of laid eggs in both the 1st and 2nd gonotrophic cycles (Alabaster et al., 2011).

In the adult tsetse fly *G. morsitans*, ACC activity increased between two and three days after pupation in the abdomens of male and female flies. In in previously starved flies, a 50–70% increase in ACC specific activity was observed in the thorax, the abdominal cuticle and particularly the fat body within 20 h after a blood meal.

Fatty acid synthase (FAS)

Insect microsomal and cytosolic FASs were reported in the oenocyte-rich integument of insects. Studies on *B. germanica*, *M. domestica*, and *T. infestans* all confirmed that a microsomal FAS protein capable of adding methylmalonyl-CoA onto methyl-branched fatty acids more effectively than a cytosolic FAS (Juarez, Chase & Blomquist, 1992; Blomquist et al., 1995; Juarez, Ayala & Brenner, 1996).

Three FAS genes have been reported in the *R. prolixus* genome: RPRC000269, RPRC000123 and RPRC002909. It is worth noting that the fruit fly microsomal FAS (mFAS) of the oenocytes clusters is closely related to the *R. prolixus* cytosolic fat body FAS gene and more distantly to the other FAS gene expressed in the oenocytes (Majerowicz et al., 2017). The putative *R. prolixus* FAS gene (RPRC002909) is located immediately downstream from the putative fat body FAS gene (RPRC000269) in the supercontig sequence. Similarly, a similar arrangement is observed in *Drosophila*, with the genes CG3523 (fat body FAS) and CG3524 (mFAS) lying next to each other. This suggests that the mFAS gene, responsible for the synthesis of methyl-branched fatty acids, might have arisen as result of duplication of the fat body FAS gene, which is an orthologue of the FASN gene of mammals and other groups (Majerowicz et al., 2017).

Tissue-specific expression analysis of *B. germanica* FAS genes revealed that *BgFas1*, *BgFas3*, *BgFas4* and *BgFas7* were highly expressed in the integument, whereas *BgFas2* was dominantly expressed in the fat body (Pei et al., 2019). Research indicated also that RNAi knockdown of *BgFas1* caused a dramatic reduction of methyl-branched hydrocarbons, a slight decrease of straight-chain hydrocarbons for both internal and external hydrocarbons and also significant reduction of cuticular FFAs (Pei et al., 2019). Moreover, the *BgFas1* mRNA levels were correlated with insect molting cycles, and could be induced by long-term
mild dryness treatment. Furthermore, BgFas1 suppression accelerated water loss and led to the early death of cockroaches under desiccation (Pei et al., 2019).

The C. pipiens FAS gene, identified as fas-1, fas-2 and fas-3, was upregulated in early diapause: in addition, fas-1 and fas-2 are believed to be highly expressed in early diapause but are turned off in late diapause. By contrast, putative fas-3 remains highly expressed throughout diapause. These results suggest that fat accumulation is induced by the genes involved in fatty acid synthesis. RNA interference (RNAi) analysis revealed that the fas-1 gene and others (fas-3 and fabp) have important roles in fat storage during early diapause. When expression of these genes is suppressed, female mosquitoes fail to sequester the lipids needed for overwintering (Sim & Denlinger, 2009).

**Very long-chain fatty acid elongase (ELOVL)**

Both FAS products and fatty acids derived from the diet are further elongated into very long-chain fatty acids (VLCFA) by successive addition of two carbon units. Ten putative genes of elongases engaged in elongation of fatty acid into VLCFA (ELOVLs) were found in the genome of R. prolixus (Majerowicz et al., 2017). These include ELOVL7 family members, which elongate acyl-CoAs ranging in length from 16 to 20 carbons (Naganuma et al., 2011). This clade also includes an ELOVL gene of the mosquito Ae. albopictus, which is involved in controlling dehydration resistance in diapause eggs through regulation of the formation of hydrocarbons from VLCFA precursors (Urbanski et al., 2010).

**Fatty acid desaturase (FAD)**

FAD belongs to a superfamilly of oxygen-dependent membrane di-iron containing enzymes that share common features including a conserved tripartite histidine-rich motif coordinating two iron ions in the active centre. These enzymes catalyze the highly energy-demanding removal of hydrogen from an inactivated fatty acyl at a precise position along the hydrocarbon chain. The process involves a reactive oxo-intermediate formed by the activation of molecular oxygen. The net result of the desaturation reaction is the introduction of a double bond into the fatty acyl chain (and reduction of molecular oxygen to water) (Tupec et al., 2017). The insect FADs exhibit high functional diversity and three types of desaturases are involved in placing double bonds in long chain FAs: acyl-lipid, acyl-ACP and acyl-CoA desaturases (Malicka, Visser & Ellers, 2018).

Nine putative desaturase genes were identified in R. prolixus (Majerowicz et al., 2017). Research indicates that two genes (RPRC000617 and RPRC6553) were orthologous to other insect Δ9-desaturase genes, Daphnia and the human Δ9-desaturase gene. These genes encode highly-regulated enzymes that catalyze the formation of a carbon–carbon double bond at the ninth position from the carboxyl end of a saturated fatty acid. These enzymes contribute to the formation of the major monounsaturated components of most insect acylglycerols, which are essential for fat storage (Majerowicz et al., 2017). The Δ11 clade remained as an insect-specific family. Within this clade, six R. prolixus genes were grouped into four clusters. Although closely related to the Δ9-desaturases, Δ11 enzymes exhibit a wider substrate range and are involved in the production of sex pheromones in Lepidoptera (Blomquist et al., 2005; Majerowicz et al., 2017). In addition, one R. prolixus
gene (RPRC013818) encodes a putative member of the Δ4-desaturase family, which is a less diverse family (Majerowicz et al., 2017). These enzymes are mostly involved in sphingolipid Δ4 desaturation, a relevant process in cell cycle control during Drosophila spermatogenesis (Ternes et al., 2002).

**Long-chain acyl-CoA synthetase (ACSL)**

Long-chain acyl-CoA synthetases (ACSL) are believed to mediate in the synthesis of long-chain acyl-CoA esters from fatty acid.

In *R. prolixus*, two genes encoding ACSL isoforms (*RhoprAcs1* and *RhoprAcs2*) were detected. *RhoprAcs1* transcripts increased in posterior midgut on the second day after feeding, and *RhoprAcs2* was highly transcribed on the tenth day. The knockdown of *RhoprAcs1* did not result in noticeable phenotypes. However, *RhoprACSL2* deficient insects exhibited a 2.5-fold increase in triacylglycerol content in the fat body, and a 90% decrease in fatty acid β-oxidation. *RhoprAcs2* knockdown also resulted in a 20% increase in lifespan, delayed digestion, 30% reduced oviposition, and 50% reduction in egg hatching. Laid eggs and hatched nymphs showed remarkable alterations in morphology. The authors propose that *RhoprACSL2* is the main contributor for the formation of the intracellular acyl-CoA pool channeled for β-oxidation in the fat body, and is also required for normal reproduction (Alves-Bezerra et al., 2016).

In *D. melanogaster*, an ACSL isoform (dACSL) is required for normal embryonic segmentation and normal TAG accumulation in larvae (Zhang, Chen & Wang, 2009; Zhang et al., 2011). Both maternal and zygotic dAcsl are required for embryonic segmentation (Zhang et al., 2011). The Drosophila dACSL is required in the brain optic lobe for the decapentaplegic (Dpp, a BMP-like molecule, Dpp/BMP) production, for the formation of properly aligned glia and neurons, and for the accurate targeting of retinal axons (Zhang, Chen & Wang, 2009).

**Polyunsaturated fatty acids (PUFAs)**

Polyunsaturated fatty acids (PUFAs) are usually associated with biomembranes as phospholipid fatty acids. PUFAs are usually stored in the fat body or in other tissues where they are masked by triacylglycerols (Stanley-Samuelson & Dadd, 1983; Blomquist, Borgeon & Vundla, 1991). They are nutritionally essential for larval mosquitoes of *C. pipiens*, and arachidonic acid is essential for the adult to develop proper wing structure (Dadd & Kleinjan, 1979). The proportion and composition of 20:5, 20:4 and 20:3 vary according to life stage and tissue type (Howard & Stanley-Samuelson, 1996). They are considered to be precursors of leukotrienes, thromboxanes and prostaglandins (Stanley-Samuelson & Loher, 1986; Parnanen & Turunen, 1987; Bell & Sargent, 2003; Van Anholt et al., 2004).

One important group of PUFAs are the metabolites of arachidonic acid, also known as eicosanoids (Li et al., 2021; Zhang et al., 2021); these have a range of functions ranging from stimulating oviposition in crickets, and regulating the function of Malpighian tubules in mosquitoes and ants, to controlling thermoregulation in cicadas (Lord, Anderson & Stanley, 2002); arachidonic acid derivatives are also believed to play crucial roles in mediating cellular and humoral immunity in insects (Stanley & Kim, 2014;
Kim & Stanley, 2021). They also mediate nodulation and phagocytosis in the larval wax moth, G. mellonella (Mandato et al., 1997) important candidate for replacement mammalian models in immunological studies (Buyukguzel et al., 2007; Smith & Casadevall, 2021), and have been found to control the elongation of haemocytes isolated from tobacco hornworms, M. sexta (Miller, 2005), microaggregation reactions to bacterial challenge, this being an important step in nodulation (Miller & Stanley, 2001; Miller & Stanley, 2004; Phelps, Miller & Stanley, 2003), prophenoloxidase release from oenocytoids in the beetle armyworm Spodoptera exigua (Lepidoptera: Noctuidae) (Shrestha & Kim, 2008), behavioural fever responses to infection in the locust S. gregaria (Bundey et al., 2003) and biosynthesis of antibacterial proteins in the silkworm, B. mori (Morishima et al., 1997). In Sarcophaga argyrostoma (Diptera: Sarcophagidae), eicosanoids take part in NO and lysozyme biosynthesis after bacterial infection (Mohamed et al., 2018), and are important compounds in the LPS-dependent activation of the IMD pathway in S. peregrina (Yajima et al., 2003). Besides these important functions, most insects have relatively low PUFA concentrations; (Stanley & Kim, 2020) attribute this to their high sensitivity to oxygen damage, which might cause their peroxidation and, in turn, cellular damage. It is possible, therefore, that maintaining only a small reservoir of PUFAs may be an evolutionary strategy intended to reduce oxidative stress at the intracellular level (Stanley & Kim, 2020).

**Antimicrobial features of cuticular FFAs**

A number of studies based on various organisms have found FFA extracts to demonstrate antibacterial and antifungal effects (Harada et al., 2000; Wille & Kydonieus, 2003; Benkendorff et al., 2005; Liu et al., 2019). The activity of each FFA is influenced by its structure, especially the length of the carbon chain and the presence, number, orientation, and position of double bonds; in addition, a key role in the antibacterial activity of an FFA is played by the presence of a hydroxyl group (Zheng et al., 2005). Unsaturated FFAs are more active than saturated FFAs with the same carbon chain length (Zheng et al., 2005; Desbois et al., 2008) and unsaturated FFAs are more active against Gram-positive bacteria than Gram-negative bacteria (Galbraith et al., 1971). Additionally, FFAs with their double bonds in a cis orientation have greater antibacterial activity than FFAs with those in the trans orientation (Kabara et al., 1972; Feldlauffer et al., 1993).

In study of the effectiveness of various FFA mixtures against bacterial (Bacillus cereus (Bacillales: Bacillaceae), Bacillus subtilis (Bacillales: Bacillaceae), Enterococcus faecalis (Lactobacillales: Enterococcaceae), Citrobacter freundii (Enterobacteriales: Enterobacteriaceae), Pseudomonas aeruginosa (Pseudomonadales: Pseudomonadaceae) Pseudomonas fluorescens (Pseudomonadales: Pseudomonadaceae) and fungal strains: Paecilomyces lilacinus (Hypocreales: Ophiocordycipitaceae), Paecilomyces fumosoroseus (Hypocreales: Ophiocordycipitaceae), Lecanicillium lecanii (Hypocreales: Cordycipitaceae), M. anisopliae (Hypocreales: Clavicipitaceae), Beauveria bassiana [Tve-N39], B. bassiana [Dv-1/07] (Hypocreales: Clavicipitaceae). One mixture containing C14:0, C16:1, C16:0, C18:2, C18:1, and C18:0 fatty acids, one of four taken from Forcipomyia nigra (Diptera: Ceratopogonidae), was found to be significantly effective, especially toward B. cereus and E. faecalis; however, the highest antibacterial activity was demonstrated by C9:0, C10:0 and C16:1. In contrast,
C14:0, C16:0, C18:0 and C18:1 demonstrated rather poor antifungal activity and did not inhibit the growth of bacteria (Urbanek et al., 2012; Cerkowniak et al., 2013).

The fatty acid extract of L. sericata larvae (LFAs – Lucilia fatty acid) exhibited effective antibacterial activity against Staphylococcus aureus (Bacillales: Staphylococcaceae) and Streptococcus pneumoniae (Lactobacillales: Streptococcaceae) with minimal inhibitory concentrations (MICs) of 125 µg/mL and 100 µg/mL, respectively, with the bacterial wall and membrane being the main targets. Furthermore, the LFAs demonstrated a notable anti-biofilm activity against these two bacteria: the mixture both prevented biofilm formation and eradicated mature biofilms (Liu et al., 2019).

The free fatty acids present in insect lipids are biologically-active compounds. Certain short-chain fatty acids, such as caprylic acid, can block the absorption of phosphorus and thiamine by fungi, thereby preventing the development of mould spores. It has been found that cis-unsaturated fatty acids possess strong inhibitory properties (Barnes & Moore, 1997; Wang et al., 2002). The cuticular FFAs play an important role as a resistance factor of fungal infection by the flies C. vomitoria, C. vicina, Sarcoptophaga carnaria (Diptera: Sarcophagidae) and L. sericata (Gołębiewski et al., 2008; Gołębiewski et al., 2012a; Gołębiewski et al., 2013a; Gołębiewski et al., 2013b; Gołębiewski et al., 2014a; Gołębiewski et al., 2014b). Cuticular fatty acids are toxic and fungistatic but also may be stimulatory; for example, palmitoleic acid enhances mycelial growth, but is toxic to conidia of Erynia variabilis (Entomophthorales: Entomophthoraceae) (Kerwin, 1984), while the toxic effects of palmitoleic acid can be mitigated by the presence of a sufficient concentration of oleic acid.

The larvae of C. vicina are resistant to infection by the entomopathogenic cosmopolitan soil fungus Conidiobolus coronatus (Entomophthorales: Ancylistaceae) (Gołębiewski et al., 2008). Histological examination of C. vicina larvae exposed to sporulating C. coronatus colonies found that conidia were unable to germinate on the fly cuticle, thus suggesting the presence of compounds inhibiting spore germination (Boguś et al., 2007). In fact, the cuticular fatty acid profile of C. vicina larvae significantly differs from those of Dendrolimus pini (Lepidoptera: Lasiocampidae) and G. mellonella, which are highly susceptible to fungal infection. The major difference is the presence of C14:0, C16:1 and C20:0 in the cuticle of C. vicina; these three fatty acids are absent from the cuticle of D. pini and only present in trace amounts in the G. mellonella cuticle (Gołębiewski et al., 2008). The FFAs C14:0, 16:0, 16:1, 18:0, 18:1, 18:2, 18:3, 20:0, and 20:1 demonstrated fungistatic activity against C. coronatus in vitro, resulting in reduced sporulation and lower hyphal biomass, a lower ability to infect G. mellonella larvae and reduced toxicity of the metabolites released into the culture medium by the fungus (Bogus et al., 2010); these results indicate that these fatty acids play a role in resisting fungal attack.

The effectiveness of the cocktail of protease, chitinase and lipase enzymes produced by C. coronatus to degrade the primary cuticular constituents (viz. proteins, chitin and lipids) has been found to correlate with the chemical profile of the cuticle. The chemical components with positive correlations may be used by the fungus as nutrients, whereas those with negative correlations might be engaged in insect resistance (Bogus et al., 2017; Wrońska et al., 2018; Kaczmarek et al., 2020a).
CONCLUSION

The present review describes the role of FFAs in the physiological processes taking place in insects of medical, veterinary and forensic importance. FFAs play key roles in the reproductive processes of these insects and their resistance to pathogens, and are hence of great interest in development of pest control methods. This is of particular importance for the studied species as they present considerable threats to human and animal health and can incur considerable economic losses.

Insects have gained considerable evolutionary success, and this is arguably due in no small part to their ability to build up an effective pathogen defence system comprising the cuticle and humoral immune system, and cellular defence reactions. Among the defences employed by the insect, FFAs are important factors which determine resistance or susceptibility to microbial infection; they are employed as cuticle compounds and as precursors of eicosanoids, which also play key roles in the mediation of insect cellular and humoral immunity. FFAs also represent significant energy sources, and supply material for pupae during metamorphosis. In addition, altering the ratio of saturated to unsaturated FFAs allows the insect to adapt to cold conditions; an important consideration in insects living in temperate zones during the winter. The present review also describes the properties of FFA-transport proteins, which also play important roles in all insects.

ADDITIONAL INFORMATION AND DECLARATIONS

Funding
The authors received no funding for this work.

Competing Interests
The authors declare there are no competing interests.

Author Contributions
- Agata Kaczmarek conceived and designed the experiments, performed the experiments, analyzed the data, prepared figures and/or tables, authored or reviewed drafts of the paper, and approved the final draft.
- Mieczysława Boguś conceived and designed the experiments, authored or reviewed drafts of the paper, and approved the final draft.

Data Availability
The following information was supplied regarding data availability:
- There was no raw data generated in this work.

REFERENCES

Abdelli N, Peng L, Keping C. 2018. Silkworm, Bombyx mori, as an alternative model organism in toxicological research. *Environmental Science and Pollution Research* 25:35048–35054 DOI 10.1007/s11356-018-3442-8.
Adedokun TA, Denlinger DL. 1985. Metabolic reserves associated with pupal diapause in the flesh fly, Sarcophaga crassipalpis. *Journal of Insect Physiology* 31:229–233 DOI 10.1016/0022-1910(85)90124-6.

Al-Hatamleh MAI, Boer JC, Wilson KL, Plebanski M, Mohamud R, Mustafa MZ. 2020. Antioxidant-based medicinal properties of stingless bee products: recent progress and future directions. *Biomolecules* 10:1–28 DOI 10.3390/biom10060923.

Alabaster A, Isole J, Zhou G, Lee A, Murphy A, Day WA, Miesfeld RL. 2011. Deficiencies in acetyl-CoA carboxylase and fatty acid synthase 1 differentially affect eggshell formation and blood meal digestion in Aedes aegypti. *Insect Biochemistry and Molecular Biology* 41:946–955 DOI 10.1016/j.ibmb.2011.09.004.

Alves-Bezerra M, Klett EL, De Paula IF, Ramos IB, Coleman RA, Gondim KC. 2016. Long-chain acyl-CoA synthetase 2 knockdown leads to decreased fatty acid oxidation in fat body and reduced reproductive capacity in the insect Rhodnius prolixus. *Biochimica Et Biophysica Acta - Molecular and Cell Biology of Lipids* 1861:650–662 DOI 10.1016/j.bbalip.2016.04.007.

Arrese EL, Canavoso LE, Jouni ZE, Pennington JE, Tsuchida K, Wells MA. 2001. Lipid storage and mobilization in insects: current status and future directions. *Insect Biochemistry and Molecular Biology* 31:7–17 DOI 10.1016/S0965-1748(00)00102-8.

Arrese EL, Soulages JL. 2010. Insect fat body: energy, metabolism, and regulation. *Annual Review of Entomology* 55:207–225 DOI 10.1146/annurev-ento-112408-085356.

Atella GC, Silva-Neto MAC, Golodne DM, Arefin S, Shahabuddin M. 2006. Anopheles gambiae lipophorin: characterization and role in lipid transport to developing oocyte. *Insect Biochemistry and Molecular Biology* 36:375–386 DOI 10.1016/j.ibmb.2006.01.019.

Baer B. 2003. Bumblebees as model organisms to study male sexual selection in social insects. *Behavioral Ecology and Sociobiology* 54:521–533 DOI 10.1007/s00265-003-0673-5.

Barnes SE, Moore D. 1997. The effect of fatty, organic or phenolic acids on the germination of conidia of Metarhizium flavoviride. *Mycological Research* 101:662–666 DOI 10.1017/S0953756296003152.

Barroso IG, Cardoso C, Ferreira C, Terra WR. 2021. Transcriptomic and proteomic analysis of the underlying mechanisms of digestion of triacylglycerols and phosphatides and absorption and fate of fatty acids along the midgut of Musca domestica. *Comparative Biochemistry and Physiology - Part D: Genomics and Proteomics* 39:100826 DOI 10.1016/j.cbd.2021.100826.

Barrozo RB, Lazzari CR. 2004. Orientation behaviour of the blood-sucking bug Triatoma infestans to short-chain fatty acids: synergistic effect of L-lactic acid and carbon dioxide. *Chemical Senses* 29:833–841 DOI 10.1093/chemse/bjh249.

Baumbach J, Hummel P, Bickmeyer I, Kowalczyk KM, Frank M, Knorr K, Hildebrandt A, Riedel D, Jäckle H, Kühnlein RP. 2014. A Drosophila in vivo screen identifies store-operated calcium entry as a key regulator of adiposity. *Cell Metabolism* 19:331–343 DOI 10.1016/j.cmet.2013.12.004.
Beer K, Helfrich-Förster C. 2020. Model and non-model insects in chronobiology. *Frontiers in Behavioral Neuroscience* **14**:601676 DOI 10.3389/fnbeh.2020.601676.

Bell JG, Sargent JR. 2003. Arachidonic acid in aquaculture feeds: current status and future opportunities. *Aquaculture* **218**:491–499 DOI 10.1016/S0044-8486(02)00370-8.

Benkendorff K, Davis AR, Rogers CN, Bremner JB. 2005. Free fatty acids and sterols in the benthic spawn of aquatic molluscs, and their associated antimicrobial properties. *Journal of Experimental Marine Biology and Ecology* **316**:29–44 DOI 10.1016/j.jembe.2004.10.001.

Benoit JB, Yang G, Krause TB, Patrick KR, Aksoy S, Attardo GM. 2011. Lipophorin acts as a shuttle of lipids to the milk gland during tsetse fly pregnancy. *Journal of Insect Physiology* **57**:1553–1561 DOI 10.1016/j.jinsphys.2011.08.009.

Benzertiha A, Kierończyk B, Rawski M, Kolodziejski P, Bryszak M, Józefiak D. 2019. Insect oil as an alternative to palm oil and poultry fat in broiler chicken nutrition. *Animals* **9** DOI 10.3390/ani9030116.

Bharathwaaj R, Nagarajan PK, Kabeel AE, Madhu B, Mageshbabu D, Sathyamurthy R. 2018. Formation, characterization and theoretical evaluation of combustion of biodiesel obtained from wax esters of A. Mellifera. *Alexandria Engineering Journal* **57**:1205–1215 DOI 10.1016/j.aej.2017.03.021.

Bi J, Wang W, Liu Z, Hueng X, Jiang Q, Liu G, Wang Y, Huang X. 2014. Seipin promotes adipose tissue fat storage through the ER Ca 2+-ATPase SERCA. *Cell Metabolism* **19**:861–871 DOI 10.1016/j.cmet.2014.03.028.

Blacklock BJ, Ryan RO. 1994. Hemolymph lipid transport. *Insect Biochemistry and Molecular Biology* **24**:855–873 DOI 10.1016/0965-1748(94)90015-9.

Blaul B, Steinbauer R, Merkl P, Merkl R, Tschochner H, Ruther J. 2014. Oleic acid is a precursor of linoleic acid and the male sex pheromone in Nasonia vitripennis. *Insect Biochemistry and Molecular Biology* **51**:33–40 DOI 10.1016/j.ibmb.2014.05.007.

Blomquist GJ, Barghères AG. 2010. Insect hydrocarbons biology, biochemistry, and chemical ecology. Cambridge: Cambridge University Press DOI 10.1016/CBO9780511711909.

Blomquist GJ, Bagnères AG. 2010. Insect hydrocarbons biology, biochemistry, and chemical ecology. Cambridge: Cambridge University Press DOI 10.1016/CBO9780511711909.

Blomquist GJ, Borgeson CE, Vundla M. 1991. Polyunsaturated fatty acids and eicosanoids in insects. *Insect Biochemistry* **21**:99–106 DOI 10.1016/0020-1790(91)90069-Q.

Blomquist GJ, Jurenka R, Schal C, Tittiger C. 2005. Biochemistry and molecular biology of pheromone production. *Comprehensive Molecular Insect Science* **3–6**:705–751 DOI 10.1016/B0-44-451924-6/00046-6.

Blomquist GJ, Tillman JA, Reed JR, Gu P, Vanderwel D, Choi S, Reitz RC. 1995. Regulation of enzymatic activity involved in sex pheromone production in the housefly, Musca domestica. *Insect Biochemistry and Molecular Biology* **25**:751–757 DOI 10.1016/0965-1748(95)00015-N.

Boggs CL, Freeman KD. 2005. Larval food limitation in butterflies: effects on adult resource allocation and fitness. *Oecologia* **144**:353–361 DOI 10.1007/s00442-005-0076-6.

Boguś MI, Czygier M, Gołębiowski M, Kędra E, Kucińska J, Mazgańska J, Samborski J, Wieloch W, Włóka E. 2010. Effects of insect cuticular fatty acids on in vitro
growth and pathogenicity of the entomopathogenic fungus Conidiobolus coronatus. *Experimental Parasitology* 125:400–408 DOI 10.1016/j.exppara.2010.04.001.

Boguś MI, Kedra E, Bania J, Szczepanik M, Czygier M, Jabłoński P, Pasztaleniec A, Samborski J, Mazgajska J, Polanowski A. 2007. Different defense strategies of Dendrolimus pini, Galleria mellonella, and Calliphora vicina against fungal infection. *Journal of Insect Physiology* 53:909–922 DOI 10.1016/j.jinsphys.2007.02.016.

Boguś MI, Włóka E, Wrońska A, Kaczmarek A, Kazek M, Zalewska K, Ligeża-Zuber M, Gołębiowski M. 2017. Cuticle hydrolysis in four medically important fly species by enzymes of the entomopathogenic fungus Conidiobolus coronatus. *Medical and Veterinary Entomology* 31:23–35 DOI 10.1111/mve.12202.

Bosch OJ, Geier M, Boeckh J. 2000. Contribution of fatty acids to olfactory host finding of female Aedes aegypti. *Chemical Senses* 25:323–330 DOI 10.1093/oxfordjournals.chemse.a014042.

Brandstetter B, Ruther J. 2016. An insect with a delta-12 desaturase, the jewel wasp nasonia vitripennis, benefits from nutritional supply with linoleic acid.. *Science of Nature* 103(5–6):40 DOI 10.1007/s00114-016-1365-0.

Bridges RG, Watts SG. 1975. Changes in fatty acid composition of phospholipids and triglycerides of Musca domestica resulting from choline deficiency. *Journal of Insect Physiology* 21:861–871 DOI 10.1016/0022-1910(75)90014-1.

Briegel H. 1990. Fecundity, metabolism, and body size in Anopheles (Diptera: Culicidae), vectors of malaria. *Journal of Medical Entomology* 27:839–850 DOI 10.1093/jmedent/27.5.839.

Briegel H, Gut T, Lea AO. 2003. Sequential deposition of yolk components during oogenesis in an insect, Aedes aegypti (Diptera: Culicidae). *Journal of Insect Physiology* 49(3):249–260 DOI 10.1016/s0022-1910(02)00272-x.

Briegel H, Knüsel I, Timmermann SE. 2001. Aedes aegypti: size, reserves, survival, and flight potential. *Journal of vector ecology. Journal of the Society for Vector Ecology* 26:21–31.

Broschwitz B, Prager L, Pokorny T, Ruther J. 2021. De novo biosynthesis of linoleic acid is widespread in parasitic wasps. *Archives of Insect Biochemistry and Physiology* 107(2):e21788 DOI 10.1002/arch.21788.

Bundey S, Raymond S, Dean P, Roberts SK, Dillon RJ, Charnley AK. 2003. Eicosanoid involvement in the regulation of behavioral fever in the desert locust, Schistocerca gregaria. *Archives of Insect Biochemistry and Physiology* 52:183–192 DOI 10.1002/arch.10081.

Buček A, Brabcová J, Vogel H, Prchalová D, Kindl J, Valterová I, Pichová I. 2016. Exploring complex pheromone biosynthetic processes in the bumblebee male labial gland by RNA sequencing. *Insect Molecular Biology* 25:295–314 DOI 10.1111/imb.12221.

Büyükgüzel E, Tunaz H, Stanley D, Büyükgüzel K. 2007. Eicosanoids mediate Galleria mellonella cellular immune response to viral infection. *Journal of Insect Physiology* 53:99–105 DOI 10.1016/j.jinsphys.2006.10.012.
Byrd J, Sutton L. 2020. Forensic entomology for the investigator. WIREs Forensic Science 2:e1370 DOI 10.1002/wfs2.1370.

Canavoso LE, Frede S, Rubiolo ER. 2004. Metabolic pathways for dietary lipids in the midgut of hematophagous Panstrongylus megistus (Hemiptera: Reduviidae). Insect Biochemistry and Molecular Biology 34:845–854 DOI 10.1016/j.ibmb.2004.05.008.

Capurro M de L, de Bianchi AG, Marinotti O. 1994. Aedes aegypti lipophorin. Comparative Biochemistry and Physiology–Part B: Biochemistry 108:35–39 DOI 10.1016/0305-0491(94)90161-9.

Canavoso LE, Stariolo R, Rubiolo ER. 2003. Flight Metabolism in Panstrongylus megistus (Hemiptera: Reduviidae): the role of Carbohydrates and lipids. Memorias Do Instituto Oswaldo Cruz 98:909–914 DOI 10.1590/S0074-02762003000700009.

Cassau S, Krieger J. 2020. The role of SNMPs in insect olfaction. Cell and Tissue Research DOI 10.1007/s00441-020-03336-0.

Castillo C, Chen H, Graves C, Maisonnasse A, Conte YLe, Plettner E. 2012. Biosynthesis of ethyl oleate, a primer pheromone, in the honey bee (Apis mellifera L.). Insect Biochemistry and Molecular Biology 42:404–416 DOI 10.1016/j.ibmb.2012.02.002.

Cavagnari BM, Scaraffia PY, Haller JF, Gerez De Burgos NM, Santomé JA. 2000. Presence of a fatty acid-binding protein and lipid stores in flight muscles of Dipetalogaster maximus (Hemiptera: Reduviidae). Journal of Medical Entomology 37:938–944 DOI 10.1603/0022-2585-37.6.938.

Cerkowniak M, Boguś MI, Włóka E, Stepnowski P, Gołębiowski M. 2020. The composition of lipid profiles in different developmental stages of Dermestes ater and Dermestes maculatus and their susceptibility to the entomopathogenic fungus Conidiobolus coronatus. Phytoparasitica 48:247–260 DOI 10.1007/s12600-020-00789-5.

Cerkowniak M, Puckowski A, Stepnowski P, Gołębiowski M. 2013. The use of chromatographic techniques for the separation and the identification of insect lipids. Journal of Chromatography B: Analytical Technologies in the Biomedical and Life Sciences 937:67–78 DOI 10.1016/j.jchromb.2013.08.023.

Chapman RF. 1998. The insects: structure and function, 4th edition. Cambridge: Cambridge University Press DOI 10.1098/rsif.2013.0304.

Chen C-P, Denlinger DL, Lee RE. 1987. Cold-shock injury and rapid cold hardening in the flesh fly Sarcophaga crassipalpis. Physiological Zoology 60:297–304 DOI 10.1086/physzool.60.3.30162282.

Chen J, Henderson G, Laine RA. 1999. Lignoceric acid and hexacosanoic acid: Major components of soldier frontal gland secretions of the Formosan subterranean termite (Coptotermes formosanus). Journal of Chemical Ecology 25:817–824 DOI 10.1023/A:1020844817492.

Cheon HM, Sang WS, Bian G, Park JH, Raikhel AS. 2006. Regulation of lipid metabolism genes, lipid carrier protein lipophorin, and its receptor during immune challenge in the mosquito Aedes aegypti. Journal of Biological Chemistry 281:8426–8435 DOI 10.1074/jbc.M510957200.

Cheon HM, Seo SJ, Sun J, Sappington TW, Raikhel AS. 2001. Molecular characterization of the VLDL receptor homolog mediating binding of lipophorin in oocyte of the
mosquito Aedes aegypti. *Insect Biochemistry and Molecular Biology* 31:753–760 DOI 10.1016/S0965-1748(01)00068-6.

Calderón-Fernández GM, Moriconi DE, Dulbecco AB, Patricia Juárez M. 2017. Transcriptome Analysis of the Triatoma infestans (Hemiptera: Reduviidae) integument. *Journal of Medical Entomology* 54(6):1531–1542 DOI 10.1093/jme/tjx151.

Chertemps T, Duportets L, Labeur C, Wicker-Thomas C. 2005. A new elongase selectively expressed in Drosophila male reproductive system. *Biochemical and Biophysical Research Communications* 333:1066–1072 DOI 10.1016/j.bbrc.2005.06.015.

Cheseto X, Kuate SP, Tchouassi DP, Ndung'u M, Teal PEA, Torto B. 2015. Potential of the desert locust Schistocerca gregaria (Orthoptera: Acrididae) as an unconventional source of dietary and therapeutic sterols. *PLOS ONE* 10(5):e0127171 DOI 10.1371/journal.pone.0127171.

Ciudad L, Bellés X, Piulachs MD. 2007. Structural and RNAi characterization of the German cockroach lipophorin receptor, and the evolutionary relationships of lipoprotein receptors. *BMC Molecular Biology* 8 DOI 10.1186/1471-2199-8-53.

Coleman PC, Bale JS, Hayward SAL. 2014. Cross-generation plasticity in cold hardiness is associated with diapause, but not the non-diapause developmental pathway, in the blow fly Calliphora vicina. *Journal of Experimental Biology* 217:1454–1461 DOI 10.1242/jeb.098053.

Coleman PC, Bale JS, Hayward SAL. 2015. Meat feeding restricts rapid cold hardening response and increases thermal activity thresholds of adult blow flies, calliphora vicina (Diptera: Calliphoridae). *PLOS ONE* 10(7):e0131301 DOI 10.1371/journal.pone.0131301.

Colinet H, Renault D, Javal M, Berková P, Šimek P, Koštál V. 2016. Uncovering the benefits of fluctuating thermal regimes on cold tolerance of drosophila flies by combined metabolomic and lipidomic approach. *Biochimica Et Biophysica Acta - Molecular and Cell Biology of Lipids* 1861:1736–1745 DOI 10.1016/j.bbalip.2016.08.008.

Dadd RH, Kleinjan JE. 1979. Essential fatty acid for the mosquito Culex pipiens: Arachidonic acid. *Journal of Insect Physiology* 25:495–502 DOI 10.1016/S0022-1910(79)80008-6.

Dallerac R, Labeur C, Jallon JM, Knipple DC, Roelofs WL, Wicker-Thomas C. 2000. A L9 desaturase gene with a different substrate specificity is responsible for the cuticular diene hydrocarbon polymorphism in Drosophila melanogaster. *Proceedings of the National Academy of Sciences of the United States of America* 97(17):9449–9454 DOI 10.1073/pnas.150243997.

De Bianchi AG, Capurro MDL, Marinotti O. 1987. Lipophorin in the larval and adult stages of Musca domestica. *Archives of Insect Biochemistry and Physiology* 6:39–48 DOI 10.1002/arch.940060105.

Dean Goldring JP, Read JS. 1993. Insect acetyl-CoA carboxylase: Activity during the larval, pupal and adult stages of insect development. *Comparative Biochemistry and Physiology B* 106(4):855–858 DOI 10.1016/0305-0491(93)90041-3.
Dean Goldring JP, Read JS. 1994. Insect acetyl-CoA carboxylase: enzyme activity during adult development and after feeding in the tsetse fly, Glossina morsitans. *Comparative Biochemistry and Physiology B* 108:27–33 DOI 10.1016/0305-0491(94)90160-0.

Denlinger DL, Yocum GD, Rinehart JP. 2012. Hormonal control of diapause. In: *Insect Endocrinology*. Academic Press, 430–463 DOI 10.1016/B978-0-12-384749-2.10010-X.

De Renobales M, Cripps C, Stanley-Samuelson DW, Jurenka RA, Blomquist GJ. 1987. Biosynthesis of linoleic acid in insects. *Trends in Biochemical Sciences* 12:364–366 DOI 10.1016/0968-0004(87)90167-8.

Desbois AP, Lebl T, Yan L, Smith VJ. 2008. Isolation and structural characterisation of two antibacterial free fatty acids from the marine diatom, Phaeodactylum tricornutum. *Applied Microbiology and Biotechnology* 81:755–764 DOI 10.1007/s00253-008-1714-9.

Dhawan R, Gupta K, Kajla M, Kakani P, Choudhury TP, Kumar S, Kumar V, Gupta L. 2017. Apolipophorin-III acts as a positive regulator of Plasmodium development in Anopheles stephensi. *Frontiers in Physiology* 8:185 DOI 10.3389/fphys.2017.00185.

Dias-Lopes G, Borges-Veloso A, Saboia-Vahia L, Padrón G, De Faria Castro CL, Guimarães ACR, Britto C, Cuervo P, De Jesus JB. 2016. Proteomics reveals major components of oogenesis in the reproductive tract of sugar-fed Anopheles aquasalis. *Parasitology Research* 5:1977–1989 DOI 10.1007/s00436-016-4940-6.

Diener S, Zurbrügg C, Tockner K. 2009. Conversion of organic material by black soldier fly larvae: establishing optimal feeding rates. *Waste Management and Research* 27:603–610 DOI 10.1177/0734242X09103838.

Doege H, Stah A. 2006. Protein-mediated fatty acid uptake: novel insights from in vivo models. *Physiology* 21:259–268 DOI 10.1152/physiol.00014.2006.

Donkor ES. 2020. Cockroaches and food-borne pathogens. *Environmental Health Insights* 14:117863020913365 DOI 10.1177/1178630220913365.

Doğan C, Hänniger S, Heckel DG, Coutu C, Hegedus DD, Crubaugh L, Groves RL, Mutlu DA, Suludere Z, Bayram Ş, Toprak U. 2021. Characterization of calcium signaling proteins from the fat body of the Colorado Potato Beetle, Lepinotarsa decemlineata (Coleoptera: Chrysomelidae): implications for diapause and lipid metabolism. *Insect Biochemistry and Molecular Biology* 133:103549 DOI 10.1016/j.ibmb.2021.103549.

Dourlen P, Sujkowski A, Wessells R, Mollereau B. 2015. Fatty acid transport proteins in disease: new insights from invertebrate models. *Progress in Lipid Research* 60:30–40 DOI 10.1016/j.plipres.2015.08.001.

Downer RGH, Matthews JR. 1976. Patterns of lipid distribution and utilisation in insects. *Integrative and Comparative Biology* 16:733–745 DOI 10.1093/icb/16.4.733.

Duarte PM., Maciel E, Pinho M, Domingues MR, Calado R, Lillebø AI, Ameixa OMCC 2021. Omega-3 on the fly: long-legged fly Machaerium maritimae as a potential source of eicosapentaenoic acid for aquafeeds. *Journal of Insects as Food and Feed* 1–12 DOI 10.3920/jiff2020.0112.
Duffy C, Sorolla A, Wang E, Golden E, Woodward E, Davern K, Ho D, Johnstone E, Pfleger K, Redfern A, Iyer KS, Baer B, Blancafort P. 2020. Honey-bee venom and melittin suppress growth factor receptor activation in HER2-enriched and triple-negative breast cancer. *Npj Precision Oncology* 4(1):24 DOI 10.1038/s41698-020-00129-0.

Eigenheer AL, Young S, Blomquist GJ, Borgeson CE, Tillman JA, Tittiger C. 2002. Isolation and molecular characterization of *Musca domestica* delta-9 desaturase sequences. *Insect Molecular Biology* 11:533–542 DOI 10.1046/j.1365-2583.2002.00362.x.

Entringer PF, Grillo LAM, Pontes EG, Machado EA, Gondim KC. 2013. Interaction of lipophorin with *Rhodnius prolixus* oocytes: biochemical properties and the importance of blood feeding. *Memorias Do Instituto Oswaldo Cruz* 108:836–844 DOI 10.1590/0074-0276130129.

Entringer PF, Majerowicz D, Gondim KC. 2021. The fate of dietary cholesterol in the kissing bug *Rhodnius prolixus*. *Frontiers in Physiology* 12:654565 DOI 10.3389/fphys.2021.654565.

Esteves A, Ehrlich R. 2006. Invertebrate intracellular fatty acid binding proteins. *Comparative Biochemistry and Physiology - C Toxicology and Pharmacology* 142:262–274 DOI 10.1016/j.cbpc.2005.11.006.

Evans JD, Wheeler DE. 1999. Differential gene expression between developing queens and workers in the honey bee, *Apis mellifera*. *Proceedings of the National Academy of Sciences of the United States of America* 96:5575–5580 DOI 10.1073/pnas.96.10.5575.

Ewald N, Vidakovic A, Langeland M, Kiessling A, Sampels S, Lalander C. 2020. Fatty acid composition of black soldier fly larvae (*Hermetia illucens*) – Possibilities and limitations for modification through diet. *Waste Management* 102:40–47 DOI 10.1016/j.wasman.2019.10.014.

Fadda M, Hasakiogullari I, Temmerman L, Beets I, Zels S, Schoofs L. 2019. Regulation of feeding and metabolism by neuropeptide F and short neuropeptide F in invertebrates. *Frontiers in Endocrinology* 10:64 DOI 10.3389/fendo.2019.00064.

Feldlaufer MF, Knox DA, Lusby WR, Shimanuki H. 1993. Antimicrobial activity of fatty acids against *Bacillus larvae*, the causative agent of American foulbrood disease. *Apidologie* 24:95–99 DOI 10.1051/apido:19930202.

Ferdous Z, Fuchs S, Behrends V, Trasanidis N, Waterhouse RM, Vlachou D, Christophides GK. 2021. Anopheles coluzzii stearoyl-CoA desaturase is essential for adult female survival and reproduction upon blood feeding. *PLOS PLOS* 17(5):e1009486 DOI 10.1371/journal.ppat.1009486.

Fichera LE, Brenner RR. 1982. Isolation and characterization of the haemolymph lipoproteins of *Triatoma infestans*. *Comparative Biochemistry and Physiology--Part B: Biochemistry* 72:71–75 DOI 10.1016/0305-0491(82)90012-8.

Ford PS, Van Heusden MC. 1994. Triglyceride-rich lipoprotein in Aedes aegypti (Diptera: Culicidae). *Journal of Medical Entomology* 31:435–441 DOI 10.1093/jmedent/31.3.435.
Fougeron AS, Farine JP, Flaven-Pouchon J, Everaerts C, Ferveur JF. 2011. Fatty-acid preference changes during development in drosophila melanogaster. *PLOS ONE* 6(10):e26899 DOI 10.1371/journal.pone.0026899.

Fruttero LL, Demartini DR, Rubiolo ER, Carlini CR, Canavoso LE. 2014. β-chain of ATP synthase as a lipophorin binding protein and its role in lipid transfer in the midgut of Panstrongylus megistus (Hemiptera: Reduviidae). *Insect Biochemistry and Molecular Biology* 52:1–12 DOI 10.1016/j.ibmb.2014.06.002.

Fruttero LL, Frede S, Rubiolo ER, Canavoso LE. 2011. The storage of nutritional resources during vitellogenesis of Panstrongylus megistus (Hemiptera: Reduviidae): the pathways of lipophorin in lipid delivery to developing oocytes. *Journal of Insect Physiology* 57:475–486 DOI 10.1016/j.jinsphys.2011.01.009.

Fruttero LL, Leyria J, Canavoso LE. 2017. Lipids in insect oocytes: from the storage pathways to their multiple functions. In: *Results and problems in cell differentiation*. vol. 63. Cham: Springer, 403–434 DOI 10.1007/978-3-319-60855-6_18.

Fruttero LL, Leyria J, Moyetta NR, Ramos FO, Settembrini BP, Canavoso LE. 2019. The fat body of the hematophagous insect, panstrongylus megistus (Hemiptera: Reduviidae): histological features and participation of the β-chain of ATP synthase in the lipophorin-mediated lipid transfer. *Journal of Insect Science* 19(4):16 DOI 10.1093/jisesa/iez078.

Fruttero LL, Leyria J, Ramos FO, Stariolo R, Settembrini BP, Canavoso LE. 2017. The process of lipid storage in insect oocytes: the involvement of β-chain of ATP synthase in lipophorin-mediated lipid transfer in the Chagas’ disease vector Panstrongylus megistus (Hemiptera: Reduviidae). *Journal of Insect Physiology* 96:82–92 DOI 10.1016/j.jinsphys.2016.10.014.

Fruttero LL, Rubiolo ER, Canavoso LE. 2009. Biochemical and cellular characterization of lipophorin-midgut interaction in the hematophagous Panstrongylus megistus (Hemiptera: Reduviidae). *Insect Biochemistry and Molecular Biology* 39:322–331 DOI 10.1016/j.ibmb.2009.01.009.

Gadelhak GG, Pedibhotla VK, Rosario RMT, Thomas GD, Stanley-Samuelson DW. 1995. The influence of blood meals on accumulation of arachidonic acid by adult stable flies. *Comparative Biochemistry and Physiology –Part B: Biochemistry and 110*:613–621 DOI 10.1006/cbpb.1994.10181-S.

Galbraith H, Miller TB, Paton AM, Thompson JK. 1971. Antibacterial activity of long chain fatty acids and the reversal with calcium, magnesium, ergocalciferol and cholesterol. *Journal of Applied Bacteriology* 34:803–813 DOI 10.1111/j.1365-2672.1971.tb01019.x.

Gálíková M, Diesner M, Klepsatel P, Hehlert P, Xu Y, Bickmeyer I, Predel R, Kühnlein RP. 2015. Energy homeostasis control in drosophila adipokinetic hormone mutants. *Genetics* 201:665–683 DOI 10.1534/genetics.115.178897.

Gerhardt RR, Hrbar LJ. 2019. Flies (Diptera). In: Mullen GR, Durden LA, eds. *Medical and veterinary entomology (third edition)*. New York: Academic Press, 171–190.
Gerstner JR, Vanderheyden WM, Shaw PJ, Landry CF, Yin JCP. 2011. Fatty-acid binding proteins modulate sleep and enhance long-term memory consolidation in Drosophila. *PLOS ONE* **6**(1):e15890 DOI 10.1371/journal.pone.0015890.

Geysen J, Cardoen J, Van Eynde S, Geens C, De Loof A. 1988. Cellular and molecular markers of anteroposterior and dorsoventral organisation in the vitellogenic follicles of adult Sarcophaga bullata (Diptera) and dorsoventral orientation of follicles in the ovary. *Roux's Archives of Developmental Biology* **197**:101–109 DOI 10.1007/BF00375932.

Giannetto A, Oliva S, Cecon Lanes CF, De Araújo Pedron F, Savastano D, Bавiera C, Parrino V, Lo Paro G, Spanò NC, Cappello T, Maisano M, Maucerì A, Fasulo S. 2020. Hermetia illucens (Diptera: Stratiomydae) larvae and prepupae: biomass production, fatty acid profile and expression of key genes involved in lipid metabolism. *Journal of Biotechnology* **307**:44–54 DOI 10.1016/j.jbiotec.2019.10.015.

Gibbs AG, Rajpurohit S. 2010. Cuticular lipids and water balance. In: Blomquist GJ, Bagnères A-G, eds. *Insect hydrocarbons biology, biochemistry, and chemical ecology*. Cambridge: Cambridge University Press, 100–120 DOI 10.1017/CBO9780511711909.007.

Ginzel MD, Tittiger C, MacLean M, Blomquist GJ. 2021. Hydrocarbon pheromone production in insects. In: Blomquist GJ, Vogt RG, eds. *Insect pheromone biochemistry and molecular biology*. New York: Academic Press, 205–235 DOI 10.1016/b978-0-12-819628-1.00007-9.

Gladyshev MI, Sushchik NN, Yurchenko YA, Belevich OE, Kalacheva GS. 2011. Differences in the fatty acid compositions of blood-sucking mosquito larvae and imagoes and the water-to-land export of essential acids. *Doklady Biological Sciences* **441**:385–388 DOI 10.1134/S001249661106007X.

Glatz JFC, Luiken JJFP, Bonen A. 2010. Membrane fatty acid transporters as regulators of lipid metabolism: implications for metabolic disease. *Physiological Reviews* **90**:367–417 DOI 10.1152/physrev.00003.2009.

Gołębiowski M. 2012. Comparison of free fatty acids composition of cuticular lipids of Calliphora vicina larvae and pupae. *Lipids* **47**:1001–1009 DOI 10.1007/s11745-012-3702-1.

Gołębiowski M, Boguś MI, Paszkiewicz M, Stepnowski P. 2010. The composition of the free fatty acids from Dendrolimus pini exuviae. *Journal of Insect Physiology* **56**:391–397 DOI 10.1016/j.jinsphys.2009.11.009.

Gołębiowski M, Boguś MI, Paszkiewicz M, Stepnowski P. 2011. Cuticular lipids of insects as potential biofungicides: Methods of lipid composition analysis. *Analytical and Bioanalytical Chemistry* **399**:3177–3191 DOI 10.1007/s00216-010-4439-4.

Gołębiowski M, Boguś MI, Paszkiewicz M, Wieloch W, Włóka E, Stepnowski P. 2012a. The composition of the cuticular and internal free fatty acids and alcohols from Lucciaria sericata males and females. *Lipids* **47**:613–622 DOI 10.1007/s11745-012-3662-5.

Gołębiowski M, Bojke A, Tlaczuk C. 2021. Effects of the entomopathogenic fungi Metarhizium robertsi, Metarhizium flavoviride, and Isaria fumosorosea on
the lipid composition of Galleria mellonella larvae. *Mycologia* 113(3):525–535 DOI 10.1080/00275514.2021.1877520.

Gołębiowski M, Cerkowniak M, Boguś MI, Włóka E, Dawgul M, Kamysz W, Stepnowski P. 2013a. Free fatty acids in the cuticular and internal lipids of Calliphora vomitoria and their antimicrobial activity. *Journal of Insect Physiology* 59:416–429 DOI 10.1016/j.jinsphys.2013.02.001.

Gołębiowski M, Cerkowniak M, Boguś MI, Włóka E, Przybysz E, Stepnowski P. 2013b. Developmental changes in the sterol composition and the glycerol content of cuticular and internal lipids of three species of flies. *Chemistry and Biodiversity* 10:1521–1530 DOI 10.1002/cbdv.201200419.

Gołębiowski M, Cerkowniak M, Dawgul M, Kamysz W, Boguś MI, Stepnowski P. 2013c. The antifungal activity of the cuticular and internal fatty acid methyl esters and alcohols in Calliphora vomitoria. *Parasitology* 140:972–985 DOI 10.1017/S0031182013000267.

Gołębiowski M, Cerkowniak M, Ostachowska A, Boguś MI, Stepnowski P. 2016. Determination of cuticular and internal fatty acids of Chorthippus brunneus males and females using HPLC-LLSD and GC–MS. *Biomedical Chromatography* 30:1318–1323 DOI 10.1002/bmc.3688.

Gołębiowski M, Cerkowniak M, Urbanek A, Dawgul M, Kamysz W, Boguś MI, Sosnowska D, Stepnowski P. 2014a. Antimicrobial activity of untypical lipid compounds in the cuticular and internal lipids of four fly species. *Journal of Applied Microbiology* 116:269–287 DOI 10.1111/jam.12370.

Gołębiowski M, Cerkowniak M, Urbanek A, Dawgul M, Kamysz W, Boguś MI, Stepnowski P. 2015. Identification and antifungal activity of novel organic compounds found in cuticular and internal lipids of medically important flies. *Microbiological Research* 170:213–222 DOI 10.1016/j.micres.2014.06.004.

Gołębiowski M, Maliński E, Boguś MI, Kumirska J, Stepnowski P. 2008. The cuticular fatty acids of Calliphora vicina, Dendrolimus pini and Galleria mellonella larvae and their role in resistance to fungal infection. *Insect Biochemistry and Molecular Biology* 38:619–627 DOI 10.1016/j.ibmb.2008.03.005.

Gołębiowski M, Maliński E, Nawrot J, Szafranek J, Stepnowski P. 2007. Identification of the cuticular lipid composition of the Western Flower Thrips Frankliniella occidentalis. *Comparative Biochemistry and Physiology - B Biochemistry and Molecular Biology* 147:288–292 DOI 10.1016/j.cbpb.2007.01.016.

Gołębiowski M, Paszkiewicz M, Grubba A, Gąsiewska D, Boguś MI, Włóka E, Wieloch W, Stepnowski P. 2012b. Cuticular and internal n-alkane composition of Lucilia sericata larvae, pupae, male and female imagines: application of HPLC-LLSD and GC/MS-SIM. *Bulletin of Entomological Research* 102:453–460 DOI 10.1017/S0007485311000800.

Gołębiowski M, Urbanek A, Oleszczak A, Dawgul M, Kamysz W, Boguś MI, Stepnowski P. 2014b. The antifungal activity of fatty acids of all stages of Sarcophaga carnaria L. (Diptera: Sarcophagidae). *Microbiological Research* 169:279–286 DOI 10.1016/j.micres.2013.07.011.
Gołębiowski M, Urbanek A, Pietrzak A, Naczk AM, Bojke A, Tkaczuk C, Stepnowski P. 2020. Effects of the entomopathogenic fungus Metarhizium flavoviride on the fat body lipid composition of Zophobas morio larvae (Coleoptera: Tenebrionidae). *Science of Nature* **107**(1):7 DOI 10.1007/s00114-019-1662-5.

Goltsev Y, Rezende GL, Vranizan K, Lanzaro G, Valle D, Levine M. 2009. Developmental and evolutionary basis for drought tolerance of the Anopheles gambiae embryo. *Developmental Biology* **330**:462–470 DOI 10.1016/j.ydbio.2009.02.038.

Gomez-Díaz C, Bargeton B, Abuin L, Bukar N, Reina JH, Bartoi T, Graf M, Ong H, Ulbrich MH, Masson JF, Benton R. 2016. A CD36 ectodomain mediates insect pheromone detection via a putative tunnelling mechanism. *Nature Communications* **7**:11866 DOI 10.1038/ncomms11866.

Gondim KC, Atella GC, Pontes EG, Majerowicz D. 2018. Lipid metabolism in insect disease vectors. *Insect Biochemistry and Molecular Biology* **101**:108–123 DOI 10.1016/j.ibmb.2018.08.005.

Gondim KC, Oliveira PL, Masuda H. 1989. Lipophorin and oogenesis in Rhodnius prolixus: Transfer of phospholipids. *Journal of Insect Physiology* **35**:19–27 DOI 10.1016/0022-1910(89)90032-2.

González MS, Soulages J, Brenner RR. 1991. Changes in the hemolymph lipophorin and very high density lipoprotein levels during the fifth nymphal and adult stages of Triatoma infestans. *Insect Biochemistry* **21**:679–687 DOI 10.1016/0020-1790(91)90038-G.

Goulson D. 2004. *Bumblebees: their behaviour and ecology*. Oxford University Press DOI 10.5860/choice.41-3443.

Grigoraki L, Grau-Bove X, Carringtion-Yates H, Lycett GJ, Ranson H. 2020a. Cuticular hydrocarbon biosynthesis in malaria vectors: Insights from the adult oenocyte transcriptome. *bioRxiv* DOI 10.1101/2020.04.28.065938.

Grigoraki L, Grau-Bove X, Carringtion-Yates H, Lycett GJ, Ranson H. 2020b. Isolation and transcriptomic analysis of anopheles gambiae oenocytes enables the delineation of hydrocarbon biosynthesis. *eLife* **9**:e58019 DOI 10.7554/eLife.58019.

Grillo LAM, Majerowicz D, Gondim KC. 2007. Lipid metabolism in Rhodnius prolixus (Hemiptera: Reduviidae): role of a midgut triacylglycerol-lipase. *Insect Biochemistry and Molecular Biology* **37**:579–588 DOI 10.1016/j.ibmb.2007.03.002.

Grillo LAM, Pontes EG, Gondim KC. 2003. Lipophorin interaction with the midgut of Rhodnius prolixus: characterization and changes in binding capacity. *Insect Biochemistry and Molecular Biology* **33**:429–438 DOI 10.1016/S0965-1748(03)00007-9.

Gu P, Welch WH, Guo L, Schegg KM, Blomquist GJ. 1997. Characterization of a novel microsomal fatty acid synthetase (FAS) compared to a cytosolic FAS in the housefly, Musca domestica. *Comparative Biochemistry and Physiology B* **118**:447–456 DOI 10.1016/S0305-0491(97)00112-0.

Guil-Guerrero JL, Ramos-Bueno RP, González-Fernández MJ, Fabrikov D, Sánchez-Muros MJ, Barroso FG. 2018. Insects as Food: Fatty Acid Profiles, Lipid Classes, and sn-2 Fatty Acid Distribution of Lepidoptera Larvae. *European Journal of Lipid Science and Technology* **120**: DOI 10.1002/ejlt.201700391.
Güney G, Toprak U, Hegedus DD, Bayram Ş, Coutu C, Bekkaoui D, Baldwin D, Heckel DG, Hönniger S, Cedden D, Mutlu DA, Suludere Z. 2021. A look into Colorado potato beetle lipid metabolism through the lens of lipid storage droplet proteins. *Insect Biochemistry and Molecular Biology* 133:103473 DOI 10.1016/j.ibmb.2020.103473.

Gupta L, Noh JY, Jo YH, Oh SH, Kumar S, Noh MY, Lee YS, Cha SJ, Seo SJ, Kim I, Han YS, Barillas-Mury C. 2010. Apolipophorin-III mediates antiplasmodial epithelial responses in Anopheles gambiae (G3) mosquitoes. *PLOS ONE* 5(11):e15410 DOI 10.1371/journal.pone.0015410.

Gutierrez AC, Gołębiowski M, Pennisi M, Peterson G, García JJ, Manfrino RG, López Lastra CC. 2015. Cuticle fatty acid composition and differential susceptibility of three species of cockroaches to the entomopathogenic fungi *Metarhizium anisopliae* (Ascomycota, Hypocreales). *Journal of Economic Entomology* 108:752–760 DOI 10.1093/jee/tou096.

Hahn DA, Denlinger DL. 2011. Energetics of insect diapause. *Annual Review of Entomology* 56:103–121 DOI 10.1146/annurev-ento-112408-085436.

Hamilton JA. 1998. Fatty acid transport: difficult or easy? *Journal of Lipid Research* 39:467–481 DOI 10.1016/S0022-2275(20)33287-9.

Hamilton JA. 2007. New insights into the roles of proteins and lipids in membrane transport of fatty acids. *Prostaglandins Leukotrienes and Essential Fatty Acids* 77:355–361 DOI 10.1016/j.plefa.2007.10.020.

Hamilton JA, Kamp F. 1999. How are free fatty acids transported in membranes?—Is it by proteins or by free diffusion through the lipids? *Diabetes* 48:2255–2269 DOI 10.2337/diabetes.48.12.2255.

Han H, Liu Z, Meng F, Jiang Y, Cai J. 2020. Identification of olfactory genes of a forensically important blow fly, *Aldrichina grahami* (Diptera: Calliphoridae). *PeerJ* 8:e9581 DOI 10.7717/peerj.9581.

Harada KI, Suomalainen M, Uchida H, Masui H, Ohmura K, Kiviranta J, Niku-Paavola ML, Ikemoto T. 2000. Insecticidal compounds against mosquito larvae from Oscillatoria agardhii strain 27. *Environmental Toxicology* 15:114–119 DOI 10.1002/(SICI)1522-7278(2000)15:2<114::AID-TOX7>3.0.CO;2-P.

Haruhito K, Haruo C. 1982. Transport of hydrocarbons by the lipophorin of insect hemolymph. *Biochimica Et Biophysica Acta (BBA)/Lipids and Lipid Metabolism* 710:341–348 DOI 10.1016/0005-2760(82)90117-5.

Harwood RF, Takata N. 1965. Effect of photoperiod and temperature on fatty acid composition of the mosquito *Culex tarsalis*. *Journal of Insect Physiology* 11:711–716 DOI 10.1016/0022-1910(65)90153-8.

Hasan MA, Ahmed S, Kim Y. Biosynthetic pathway of arachidonic acid in Spodoptera exigua in response to bacterial challenge. *Insect Biochemistry and Molecular Biology* 111 DOI 10.1016/j.ibmb.2019.103179.

Haunerland NH, Andolfatto P, Chisholm JM, Wang Z, Chen X. 1992. Fatty-acid-binding protein in locust flight muscle: developmental changes of expression,
concentration and intracellular distribution. *European Journal of Biochemistry* 210:1045–1051 DOI 10.1111/j.1432-1033.1992.tb17510.x.

Hayward SAL, Pavlides SC, Tammaroello SP, Rinehart JP, Denlinger DL. 2005. Temporal expression patterns of diapause-associated genes in flesh fly pupae from the onset of diapause through post-diapause quiescence. *Journal of Insect Physiology* 51:631–640 DOI 10.1016/j.jinsphys.2004.11.009.

Helmkampf M, Cash E, Gadau J. 2015. Evolution of the insect desaturase gene family with an emphasis on social hymenoptera. *Molecular Biology and Evolution* 32:456–471 DOI 10.1093/molbev/msu315.

Herrera H, Barros-Parada W, Bergmann J. 2019. Linoleic acid and stearic acid are biosynthetic precursors of (7Z,10Z)-7,10-hexadecadienal, the major component of the sex pheromone of Chilecomadia valdiviana (Lepidoptera: Cossidae). *PLoS ONE* 14(4):e0215769 DOI 10.1371/journal.pone.0215769.

Higgs S, Vanlandingham DL. 2016. Influences of arthropod vectors on encephalitic arboviruses. In: *Neurotropic Viral Infections: Volume 2: Neurotropic Retroviruses, DNA Viruses, Immunity and Transmission*. 371–401 DOI 10.1007/978-3-319-33189-8_11.

Hodecek J. 2020. Revisiting the concept of entomotoxicology. *Forensic Science International: Synergy* 2:282–286 DOI 10.1016/j.fsisyn.2020.09.003.

Hoffmann AA, Hallas R, Sinclair C, Partridge L. 2001. Rapid loss of stress resistance in drosophila melanogaster under adaptation to laboratory culture. *Evolution* 55:436–438 DOI 10.1111/j.0014-3820.2001.tb01305.x.

Holtorf M, Lenaerts C, Cullen D, VandenBroeck J. 2019. Extracellular nutrient digestion and absorption in the insect gut. *Cell and Tissue Research* 377:397–414 DOI 10.1007/s00441-019-03031-9.

Horne I, Haritos VS, Oakeshott JG. 2009. Comparative and functional genomics of lipases in holometabolous insects. *Insect Biochemistry and Molecular Biology* 39:547–567 DOI 10.1016/j.ibmb.2009.06.002.

Hou Y, Wang XL, Saha TT, Roy S, Zhao B, Raikhel AS, Zou Z. 2015. Temporal coordination of carbohydrate metabolism during mosquito reproduction. *PLOS Genetics* 11(7):e1005309 DOI 10.1371/journal.pgen.1005309.

Howard RW, Stanley-Samuelson DW. 1996. Fatty acid composition of fat body and Malpighian tubules of the tenebrionid beetle, Zophobas latius: significance in eicosanoid-mediated physiology. *Comparative Biochemistry and Physiology - B Biochemistry and Molecular Biology* 115:429–437 DOI 10.1016/S0305-0491(96)00161-7.

Huang YJS, Higgs S, Vanlandingham DL. 2019. Arbovirus-mosquito vector-host interactions and the impact on transmission and disease pathogenesis of arboviruses. *Frontiers in Microbiology* 10:22 DOI 10.3389/fmicb.2019.00022.

Ishida Y, Ishibashi J, Leal WS. 2013. Fatty acid solubilizer from the oral disk of the blowfly. *PLoS ONE* 8(1):e51779 DOI 10.1371/journal.pone.0051779.

Jackson LL, Armold MT, Regnier FE. 1974. Cuticular lipids of adult fleshflies, Sarcophaga bullata. *Insect Biochemistry* 4:369–379 DOI 10.1016/0020-1790(74)90074-2.
Jayanegara A, Gustanti R, Ridwan R, Widyastuti Y. 2020. Fatty acid profiles of some insect oils and their effects on in vitro bovine rumen fermentation and methanogenesis. *Italian Journal of Animal Science* **19**:1311–1318 DOI 10.1080/1828051X.2020.1841571.

Jenni-Eiermann S, Srygley RB. 2018. Physiological aeroecology: anatomical and physiological adaptations for flight. In: Chilson P, Frick W, Kelly J, Liechti F, eds. *Aeroecology*. Cham: Springer, 87–118 DOI 10.1007/978-3-319-68576-2_5.

Jiang X, Pregitzer P, Grosse-Wilde E, Breer H, Krieger J. 2016. Identification and characterization of two sensory neuron membrane proteins (SNMPs) of the desert locust, schistocerca gregaria (orthoptera: Acrididae). *Journal of Insect Science* **16** DOI 10.1093/jisesa/iew015.

Jioannese DR, Storey KB. 1996. Fatty acid content and enzymes of fatty acid metabolism in overwintering cold-hardy gall insects. *Physiological Zoology* **69**:1079–1095 DOI 10.1086/physzool.69.5.30164247.

Jones DNM, Wang J, Murphy EJ. 2019. Complete NMR chemical shift assignments of odorant binding protein 22 from the yellow fever mosquito, Aedes aegypti, bound to arachidonic acid. *Biomolecular NMR Assignments* **13**(2):279 DOI 10.1007/s12104-019-09875-0.

Juárez MP, Ayala S, Brenner RR. 1996. Methyl-branched fatty acid biosynthesis in Triatoma infestans. *Insect Biochemistry and Molecular Biology* **26**:599–605 DOI 10.1016/S0965-1748(96)00021-5.

Juárez MP. 2004. Fatty Acyl-CoA elongation in Blatella germanica integumental microsomes. *Archives of Insect Biochemistry and Physiology* **56**:170–178 DOI 10.1002/arch.20007.

Juárez MP, Napolitano R. 2000. Effects of organic acids on lipid synthesis and ecdysis in Triatoma infestans eggs. *Comparative Biochemistry and Physiology - B Biochemistry and Molecular Biology* **125** DOI 10.1016/S0305-0491(00)00155-3.

Juárez P, Brenner RR. 1989. Fatty acid biosynthesis in the integument tissue of triatoma infestans. *Comparative Biochemistry and Physiology - Part B: Biochemistry and Genetics* **93**:763–772 DOI 10.1016/0305-0491(89)90043-6.

Juárez P, Chase J, Blomquist GJ. 1992. A microsomal fatty acid synthetase from the integument of Blattella germanica synthesizes methyl-branched fatty acids, precursors to hydrocarbon and contact sex pheromone. *Archives of Biochemistry and Biophysics* **293**:333–341 DOI 10.1016/0003-9861(92)90403-J.

Kabara JJ, Swieczkowski DM, Conley AJ, Truant JP. 1972. Fatty acids and derivatives as antimicrobial agents. *Antimicrobial Agents and Chemotherapy* **2**:23–28 DOI 10.1128/AAC.2.1.23.

Kaczmarek A, Boguś MI. 2021a. Fungi of entomopathogenic potential in Chytridiomycota and Blastocladiomycota, and in fungal allies of the Oomycota and Microsporidia. *IMA Fungus* **12**:29 DOI 10.1186/s43008-021-00074-y.

Kaczmarek A, Boguś MI. 2021b. The impact of the entomopathogenic fungus conidiospore conidiospores on the free fatty acid profile of the flesh fly sarcophaga argyrostoma. *Insects* **12**(11):970 DOI 10.3390/insects12110970.
Kaczmarek A, Boguś MI, Włóka E, Wrońska AK, Krawiel A, Kazek M, Żalewska K, Kłocinska-Biały K, Sobocińska M, Gliniewicz A, Mikulak E, Matławska M. 2020a. The interaction between cuticle free fatty acids (FFAs) of the cockroaches Blattella germanica and Blatta orientalis and hydrolases produced by the entomopathogenic fungus Conidiobolus coronatus. *PLOS ONE* 15(7):e0235785 DOI 10.1371/journal.pone.0235785.

Kaczmarek A, Wrońska AK, Boguś MI, Kazek M, Gliniewicz A, Mikulak E, Matławska M. 2021. The type of blood used to feed Aedes aegypti females affects their cuticular and internal free fatty acid (FFA) profiles. *PLOS ONE* 16:e0251100 DOI 10.1371/journal.pone.0251100.

Kaczmarek A, Wrońska AK, Kazek M, Boguś MI. 2020b. Metamorphosis-related changes in the free fatty acid profiles of Sarcophaga (Liopygia) argyrostoma (Robineau-Desvoidy, 1830). *Scientific Reports* 10(1):17337 DOI 10.1038/s41598-020-74475-1.

Kamut M, Jezierski T. 2014. Ecological, behavioural and economic effects of insects on grazing farm animals - a review. *Animal Science Papers and Reports* 32:107–119.

Kaufmann C, Briegel H. 2004. Flight performance of the malaria vectors Anopheles gambiae and Anopheles atroparvus. *Journal of Vector Ecology: Journal of the Society for Vector Ecology* 29:140–153.

Kawooya JK, Law JH. 1988. Role of lipophorin in lipid transport to the insect egg. *The Journal of Biological Chemistry* 263(18):8748–8753 DOI 10.1016/s0021-9258(18)68369-3.

Kawooya JK, Osir EO, Law JH. 1988. Uptake of the major hemolymph lipoprotein and its transformation in the insect egg. *The Journal of Biological Chemistry* 263(18):8740–8747 DOI 10.1016/s0021-9258(18)68368-1.

Kazek M, Kaczmarek A, Wrońska AK, Boguś MI. 2019. Diet influences the bacterial and free fatty acid profiles of the cuticle of Galleria mellonella larvae. *PLOS ONE* 14(2):e0211697 DOI 10.1371/journal.pone.0211697.

Kazek M, Kaczmarek A, Wrońska AK, Boguś MI. 2021. Dodecanol, metabolite of entomopathogenic fungus Conidiobolus coronatus, affects fatty acid composition and cellular immunity of Galleria mellonella and Calliphora vicina. *Scientific Reports* 11:15963 DOI 10.1038/s41598-021-95440-6.

Kerwin JL. 1982. Chemical control of the germination of asexual spores of Entomophthora culicis, a fungus parasitic on dipterans. *Journal of General Microbiology* 128:2179–2186 DOI 10.1099/00221287-128-9-2179.

Kerwin JL. 1984. Fatty acid regulation of the germination of Erynia variabilis conidia on adults and puparia of the lesser housefly, Fannia canicularis. *Canadian Journal of Microbiology* 30:158–161 DOI 10.1139/m84-025.

Khani A, Moharramipour S, Barzegar M, Naderi-Manesh H. 2007. Comparison of fatty acid composition in total lipid of diapause and non-diapause larvae of Cydia pomonella (Lepidoptera: Tortricidae). *Insect Science* 14:125–131 DOI 10.1111/j.1744-7917.2007.00134.x.
Kim A kyeong, Kwon DW, Yeom E, Lee KP, Kwon KS, Yu K, Lee KS. 2021. Lipophorin receptor 1 (LpR1) in Drosophila muscle influences life span by regulating mitochondrial aging. *Biochemical and Biophysical Research Communications* **568**:95–102 DOI 10.1016/j.bbrc.2021.06.080.

Kim Y, Stanley D. 2021. Eicosanoid signaling in insect immunology: new genes and unresolved issues. *Gene* **12**:1–15 DOI 10.3390/genes12020211.

Konji VN, Olembo NK, Pearson DJ. 1984. Enzyme activities in the fat body of the tsetse fly Glossina morsitans and the fleshfly Sarcophaga tibialis in relation to proline metabolism. *Insect Biochemistry* **14**:685–690 DOI 10.1016/0020-1790(84)90047-7.

Kostal V, Simek P. 1998. Changes in fatty acid composition of phospholipids and triacylglycerols after cold-acclimation of an aestivating insect prepupa. *Journal of Comparative Physiology - B Biochemical, Systemic, and Environmental Physiology* **168**:453–460 DOI 10.1007/s003600050165.

Kranz W, Carroll C, Dixon DA, Goodpaster JV, Picard CJ. 2017. Factors affecting species identifications of blow fly pupae based upon chemical profiles and multivariate statistics. *Insects* **8**(2):43 DOI 10.3390/insects8020043.

Kulma M, Plachý V, Kouršímská I, Vrabec V, Bubová T, Adámková A, Hučko B. 2016. Nutritional value of three Blattodea species used as feed for animals. *Journal of Animal and Feed Sciences* **25**:354–360 DOI 10.22358/jafs/67916/2016.

Kumar BA, Paily KP. 2011. Up-regulation of lipophorin (Lp) and lipophorin receptor (LpR) gene in the mosquito, Culex quinquefasciatus (Diptera: Culicidae), infected with the filarial parasite, Wuchereria bancrofti (Spirurida: Onchocercidae). *Parasitology Research* **108**:377–381 DOI 10.1007/s00436-010-2075-8.

Kurata S, Komano H, Natori S. 1989. Dissociation of Sarcophaga peregrina (flesh fly) fat body by pupal haemocytes in vitro. *Journal of Insect Physiology* **35**:559–565 DOI 10.1016/0022-1910(89)90144-3.

Lee KP, Cory JS, Wilson K, Raubenheimer D, Simpson SJ. 2006a. Flexible diet choice offsets protein costs of pathogen resistance in a caterpillar. *Proceedings of the Royal Society B: Biological Sciences* **273**:823–829 DOI 10.1098/rspb.2005.3385.

Lee RE, Damodaran K, Yi SX, Lorigan GA. 2006b. Rapid cold-hardening increases membrane fluidity and cold tolerance of insect cells. *Cryobiology* **52**:459–463 DOI 10.1016/j.cryobiol.2006.03.003.

Lee RE, Chen C ping, Meacham MH, Denlinger DL. 1987. Ontogenetic patterns of cold-hardiness and glycerol production in Sarcophaga crassipalpis. *Journal of Insect Physiology* **33**:587–592 DOI 10.1016/0022-1910(87)90074-6.
Lee CS, Han JH, Lee SM, Hwang JS, Kang SW, Lee BH, Kim HR. 2003. Wax moth, Galleria mellonella fat body receptor for high-density lipophorin (HDLp). *Archives of Insect Biochemistry and Physiology* 54:14–24 DOI 10.1002/arch.10095.

Lehmann M. 2018. Endocrine and physiological regulation of neutral fat storage in Drosophila. *Molecular and Cellular Endocrinology* 461:165–177 DOI 10.1016/j.mce.2017.09.008.

Leitch O, Papanicolaou A, Lennard C, Kirkbride KP, Anderson A. 2015. Chemosensory genes identified in the antennal transcriptome of the blowfly Calliphora stygia. *BMC Genomics* 16:255 DOI 10.1186/s12864-015-1466-8.

Leyria J, Fruttero LL, Aguirre SA, Canavoso LE. 2014. Ovarian nutritional resources during the reproductive cycle of the hematophagous Dipetalogaster maxima (Hemiptera: Reduviidae): Focus on lipid metabolism. *Archives of Insect Biochemistry and Physiology* 87:148–163 DOI 10.1002/arch.21186.

Leyria J, Orchard I, Lange AB. 2020. What happens after a blood meal? A transcriptome analysis of the main tissues involved in egg production in rhodnius prolixus, an insect vector of chagas disease. *PLOS Neglected Tropical Diseases*. e0008516 DOI 10.1371/journal.pntd.0008516.

Li Y-j, Chen H-C, Hong T-le, Yan M-W, Wang J, Shao Z-M, Wu F-A, Sheng S, Wang J. 2021. Identification of chemosensory genes by antennal transcriptome analysis and expression profiles of odorant-binding proteins in parasitoid wasp Aulacocentrum confusum. *Comparative Biochemistry and Physiology - Part D: Genomics and Proteomics* 40:100881 DOI 10.1016/j.cbd.2021.100881.

Liu Y, Du L, Zhu Y, Yang S, Zhou Q, Wang G, Liu Y. 2020. Identification and sex-biased profiles of candidate olfactory genes in the antennal transcriptome of the parasitoid wasp Cotesia vestalis. *Comparative Biochemistry and Physiology - Part D: Genomics and Proteomics* 34:100657 DOI 10.1016/j.cbd.2020.100657.

Liu J, Jiang J, Zong J, Li B, Pan T, Diao Y, Zhang Z, Zhang X, Lu M, Wang S. 2019. Antibacterial and anti-biofilm effects of fatty acids extract of dried Lucilia sericata larvae against Staphylococcus aureus and Streptococcus pneumoniae in vitro. *Natural Product Research* 35(10):1702–1705 DOI 10.1080/14786419.2019.1627353.

Liu H, Ryan RO. 1991. Role of lipid transfer particle in transformation of lipoprotein in insect oocytes. *Biochimica Et Biophysica Acta (BBA)/Lipids and Lipid Metabolism* 1085:112–118 DOI 10.1016/0005-2760(91)90238-D.
Lopez VM, McClanahan MN, Graham L, Hoddle MS. 2014. Assessing the flight capabilities of the goldspotted Oak borer (Coleoptera: Buprestidae) with computerized flight mills. *Journal of Economic Entomology* 107:1127–1135 DOI 10.1603/EC13525.

Lord JC, Anderson S, Stanley DW. 2002. Eicosanoids mediate manduca sexta cellular response to the fungal pathogen Beauveria bassiana: A role for the lipoxygenase pathway. *Archives of Insect Biochemistry and Physiology* 51:46–54 DOI 10.1002/arch.10049.

Lu K, Chen X, Li Y, Li W, Zhou Q. 2018. Lipophorin receptor regulates Nilaparvata lugens fecundity by promoting lipid accumulation and vitellogenin biosynthesis. *Comparative Biochemistry and Physiology - Part a : Molecular and Integrative Physiology* 219–220:28–37 DOI 10.1016/j.cbpa.2018.02.008.

Lyons N, Softley I, Balfour A, Williamson C, O’Brien HE, Shetty AC, Bruno VM, Diezmann S. 2020. Tobacco Hornworm (Manduca sexta) caterpillars as a novel host model for the study of fungal virulence and drug efficacy. *Virulence* 11:1075–1089 DOI 10.1080/21505594.2020.1806665.

Majerowicz D, Calderón-Fernández GM, Alves-Bezerra M, De Paula IF, Cardoso LS, Juárez MP, Atella GC, Gondim KC. 2017. Lipid metabolism in Rhodnius prolixus: lessons from the genome. *Gene* 596:27–44 DOI 10.1016/j.gene.2016.09.045.

Majerowicz D, Gondim KC. 2013. Insect lipid metabolism: insights into gene expression regulation. In: Mandal SS, ed. *Recent trends in gene expression*. Hauppauge, NY: Nova Science Publishers, 147–189.

Malcicka M, Visser B, Ellers J. 2018. An evolutionary perspective on linoleic acid synthesis in animals. *Evolutionary Biology* 45:15–26 DOI 10.1007/s11692-017-9436-5.

Mandato CA, Diehl-Jones W, Moore SJ, Downer RGH. 1997. The effects of eicosanoid biosynthesis inhibitors on prophenoloxidase activation, phagocytosis and cell spreading in Galleria mellonella. *Journal of Insect Physiology* 43:1–8 DOI 10.1016/S0022-1910(96)00100-X.

Maravilla E, Le DP, Tran JJ, Chiu MH, Prenner EJ, Weers PMM. 2020. Apolipophorin III interaction with phosphatidylglycerol and lipopolysaccharide: A potential mechanism for antimicrobial activity. *Chemistry and Physics of Lipids* 229:104909 DOI 10.1016/j.chemphyslip.2020.104909.

Martins GF, Ramalho-Ortigão JM, Lobo NF, Severson DW, Mcdowell MA, Pimenta PFP. 2011. Insights into the transcriptome of oenocytes from aedes aegypti pupae. *Memorias do Instituto Oswaldo Cruz* 106:308–315 DOI 10.1590/S0074-02762011000300009.

Matsuo N, Nagao K, Suito T, Juni N, Kato U, Hara Y, Umeda M. 2019. Different mechanisms for selective transport of fatty acids using a single class of lipoprotein in Drosophila. *Journal of Lipid Research* 60:1199–1211 DOI 10.1194/jlr.M090779.

McAfee A, Chapman A, Iovinella I, Gallagher-Kurtzke Y, Collins TF, Higo H, Madilao LL, Pelosi P, Foster LJ. 2018. A death pheromone, oleic acid, triggers hygienic behavior in honey bees (Apis mellifera L.). *Scientific Reports* 8(1):5719 DOI 10.1038/s41598-018-24054-2.

Meng Q, Yu HY, Zhang H, Zhu W, Wang ML, Zhang JH, Zhou GL, Li X, Qin QL, Hu SN, Zou Z. 2015. Transcriptomic insight into the immune defenses in the ghost
moth, Hepialus Xiaojinensis, During an Ophiocordyceps Sinensis fungal infection. *Insect Biochemistry and Molecular Biology* 64:1–15 DOI 10.1016/j.ibmb.2015.06.014.

**Meng X, Zhu F, Chen K.** 2017. Silkworm: a promising model organism in life science. *Journal of Insect Science* 17(5):97 DOI 10.1093/jisesa/iex064.

**Menzel R.** 2012. The honeybee as a model for understanding the basis of cognition. *Nature Reviews Neuroscience* 13:758–768 DOI 10.1038/nrn3357.

**Michaud MR, Denlinger DL.** 2006. Oleic acid is elevated in cell membranes during rapid cold-hardening and pupal diapause in the flesh fly, Sarcophaga crassipalpis. *Journal of Insect Physiology* 52:1073–1082 DOI 10.1016/j.jinsphys.2006.07.005.

**Miller JS.** 2005. Eicosanoids influence in vitro elongation of plasmatocytes from the tobacco hornworm, Manduca sexta. *Archives of Insect Biochemistry and Physiology* 59:42–51 DOI 10.1002/arch.20052.

**Miller JS, Stanley DW.** 2001. Eicosanoids mediate microaggregation reactions to bacterial challenge in isolated insect hemocyte preparations. *Journal of Insect Physiology* 47:1409–1417 DOI 10.1016/S0022-1910(01)00131-7.

**Miller JS, Stanley DW.** 2004. Lipopolysaccharide evokes microaggregation reactions in hemocytes isolated from tobacco hornworms, Manduca Sexta. *Comparative Biochemistry and Physiology - a Molecular and Integrative Physiology* 137:285–295 DOI 10.1016/j.cbpb.2003.10.003.

**Mohamed AA, Ali MM, Dorrah MA, Bassal TTM.** 2018. Mediation of inducible nitric oxide and immune-reactive lysozymes biosynthesis by eicosanoid and biogenic amines in flesh flies. *International Journal of Tropical Insect Science* 38:93–104 DOI 10.1017/S1742758417000315.

**Moriconi DE, Dulbecco AB, Juárez MP, Calderón-Fernández GM.** 2019. A fatty acid synthase gene (FASN3) from the integument tissue of Rhodnius prolixus contributes to cuticle water loss regulation. *Insect Molecular Biology* 850–861 DOI 10.1111/imb.12600.

**Morishima I, Yamano Y, Inoue K, Matsuo N.** 1997. Eicosanoids mediate induction of immune genes in the fat body of the silkworm, Bombyx mori. *FEBS Letters* 419:83–86 DOI 10.1016/S0014-5793(97)01418-X.

**Mullens BA, Reifenrath WG, Butler SM.** 2009. Laboratory trials of fatty acids as repellents or antifeedants against houseflies, horn flies and stable flies (Diptera: Muscidae). *Pest Management Science* 65:1360–1366 DOI 10.1002/ps.1823.

**Naganuma T, Sato Y, Sassa T, Ohno Y, Kihara A.** 2011. Biochemical characterization of the very long-chain fatty acid elongase ELOVL7. *FEBS Letters* 585:3337–3341 DOI 10.1016/j.febslet.2011.09.024.

**Nainu F, Rahmatika D, Bin EmranT, Harapan H.** 2020. Potential application of drosophila melanogaster as a model organism in COVID-19-related research. *Frontiers in Pharmacology* 11:588561 DOI 10.3389/fphar.2020.588561.

**Nancy Taha Mohamed PhD ASE-EWE.** 2020. Liquid Chromatography Of Hemolymph Of Adult Trachyderma Philistina (Coleoptera:Tenebrionidae)And Antitumor Effect Of Crude Hemolymph Against Different Cell Lines. *European Journal of Molecular & Clinical Medicine* 7:762–780.
Nestel D, Papadopoulos NT, Pascacio-Villafán C, Righini N, Altuzar-Molina AR, Aluja M. 2016. Resource allocation and compensation during development in holometabolous insects. *Journal of Insect Physiology* **95**:78–88 DOI 10.1016/j.jinsphys.2016.09.010.

Ng TB, Wang HX. 2010. Pharmacological actions of Cordyceps, a prized folk medicine. *Journal of Pharmacy and Pharmacology* **57**:1509–1519 DOI 10.1211/jpp.57.12.0001.

Nishidono Y, Niwa K, Kitajima A, Watanabe S, Tezuka Y, Arita M, Takabayashi J, Tanaka K. 2021. Îś-Linolenic acid in Papilio machaon larvae regurgitant induces a defensive response in Apiaceae. *Phytochemistry* **188**:112796 DOI 10.1016/j.phytochem.2021.112796.

Ochanda JO, Osir EO, Nguu EK, Olembo NK. 1991. Lipophorin from the tsetse fly, Glossina morsitans morsitans. *Comparative Biochemistry and Physiology–Part B: Biochemistry* **99**:811–814 DOI 10.1016/0305-0491(91)90146-5.

Ohnishi A, Hashimoto K, Imai K, Matsumoto S. 2009. Functional characterization of the Bombyx mori fatty acid transport protein (BmFATP) within the silkmoth pheromone gland. *Journal of Biological Chemistry* **284**:5128–5136 DOI 10.1074/jbc.M806072200.

Ohtsu T, Katagiri C, Kimura MT, Hori SH. 1993. Cold adaptations in Drosophila, qualitative changes of triacylglycerols with relation to overwintering. *Journal of Biological Chemistry* **268**:1830–1834 DOI 10.1016/S0021-9258(18)53929-6.

Oldroyd BP, Thompson GJ. 2006. Behavioural Genetics of the Honey Bee Apis mellifera. *Advances in Insect Physiology* **33**:1–49 DOI 10.1016/S0065-2806(06)33001-9.

Overgaard J, Sørensen JG, Petersen SO, Loeschcke V, Holmstrup M. 2005. Changes in membrane lipid composition following rapid cold hardening in Drosophila melanogaster. *Journal of Insect Physiology* **51**:1173–1182 DOI 10.1016/j.jinsphys.2005.06.007.

Overgaard J, Sørensen JG, Petersen SO, Loeschcke V, Holmstrup M. 2006. Reorganization of membrane lipids during fast and slow cold hardening in Drosophila melanogaster. *Physiological Entomology* **31**:328–335 DOI 10.1111/j.1365-3032.2006.00522.x.

Palm W, Sampaio JL, Brankatschk M, Carvalho M, Mahmoud A, Shevchenko A, Eaton S. 2012. Lipoproteins in Drosophila melanogaster-assembly, function, and influence on tissue lipid composition. *PLOS Genetics* **8**(7):e1002828 DOI 10.1371/journal.pgen.1002828.

Pärnänen S, Turunen S. 1987. Eicosapentaenoic acid in tissue lipids of Pieris brassicae. *Experientia* **43**:215–217 DOI 10.1007/BF01942859.

Parra-Peralbo E, Culi J. 2011. Drosophila lipophorin receptors mediate the uptake of neutral lipids in oocytes and imaginal disc cells by an endocytosis-independent mechanism. *PLOS Genetics* **7**(2):e1001297 DOI 10.1371/journal.pgen.1001297.

Parvy JP, Napal L, Rubin T, Poidevin M, Perrin L, Wicker-Thomas C, Montagne J. 2012. Drosophila melanogaster Acetyl-CoA-Carboxylase sustains a fatty acid-dependent remote signal to waterproof the respiratory system. *PLOS Genetics* **8**(8):e1002925 DOI 10.1371/journal.pgen.1002925.
Pascacio-Villafán C, Williams T, Birke A, Aluja M. 2016. Nutritional and non-nutritional food components modulate phenotypic variation but not physiological trade-offs in an insect. *Scientific Reports* 6:29413 DOI 10.1038/srep29413.

Paszkiewicz M, Gołębiowski M, Sychowska J, Boguś MI, Włóka E, Stepnowski P. 2016a. The effect of the entomopathogenic fungus Conidiobolus coronatus on the composition of cuticular and internal lipids of Blatta orientalis females. *Physiological Entomology* 41:111–120 DOI 10.1111/phen.12133.

Paul A, Frederich M, Megido RC, Alabi T, Malik P, Uyttenbroeck R, Francis F, Blecker C, Haubruge E, Lognay G, Danthine S. 2017. Insect fatty acids: A comparison of lipids from three Orthopterans and Tenebrio molitor L. larvae. *Journal of Asia-Pacific Entomology* 20:337–340 DOI 10.1016/j.aspen.2017.02.001.

Paszkiewicz M, Sikora A, Boguś MI, Włóka E, Stepnowski P, Gołębiowski M. 2016b. Effect of exposure to chlorpyrifos on the cuticular and internal lipid composition of Blattella germanica males. *Insect Science* 23:94–104 DOI 10.1093/jis/2.1.15.

Pei XJ, Chen N, Bai Y, Qiao JW, Li S, Fan YL, Liu TX. 2019. BgFas1: a fatty acid synthase gene required for both hydrocarbon and cuticular fatty acid biosynthesis in the German cockroach, Blattella germanica (L.). *Insect Biochemistry and Molecular Biology* 112:103203 DOI 10.1016/j.ibmb.2019.103203.

Pei X-J, Fan Y-L, Bai Y, Bai T-T, Schal C, Zhang Z-F, Chen N, Li S, Liu T-X. 2021. Modulation of fatty acid elongation in cockroaches sustains sexually dimorphic hydrocarbons and female attractiveness. *PLOS Biology* 19(7):e3001330 DOI 10.1371/journal.pbio.3001330.

Pennington JE, Wells MA. 2002. Triacylglycerol-rich lipophorins are found in the dipteran infraorder Culicomorpha, not just in mosquitoes. *Journal of Insect Science* 2:15 DOI 10.1093/jis/2.1.15.

Phelps PK, Miller JS, Stanley DW. 2003. Prostaglandins, not lipoxygenase products, mediate insect microaggregation reactions to bacterial challenge in isolated hemocyte preparations. *Comparative Biochemistry and Physiology - A Molecular and Integrative Physiology* 136:409–416 DOI 10.1016/S1095-6433(03)00199-5.

Pinch M, Mitra S, Rodriguez SD, Li Y, Kandel Y, Dungan B, Holguin FO, Attardo GM, Hansen IA. 2021. Fat and happy: profiling mosquito fat body lipid storage and composition post-blood meal. *Frontiers in Insect Science* 1:693168 DOI 10.3389/finsc.2021.693168.

Poidevin M, Mazuras N, Bontonou G, Delamotte P, Denis B, Devilliers M, Petit D, WickerThomas C, Montagne J. 2021. A Fatty Acid Anabolic Pathway in Specialized-Cells Remotely Controls Oocyte Activation in Drosophila. *bioRxiv* 2021.04.19.440456 DOI 10.1101/2021.04.19.440456.

Pontes EG, Leite P, Majerowicz D, Atella GC, Gondim KC. 2008. Dynamics of lipid accumulation by the body of Rhodnius prolixus: the involvement of lipophorin binding sites. *Journal of Insect Physiology* 54:790–797 DOI 10.1016/j.jinsphys.2008.02.003.
Pontes EG, Grillo LAM, Gondim KC. 2002. Characterization of lipophorin binding to the fat body of Rhodnius prolixus. *Insect Biochemistry and Molecular Biology* 32:1409–1417 DOI 10.1016/S0965-1748(02)00061-9.

Prager L, Bruckmann A, Ruther J. 2019. De novo biosynthesis of fatty acids from α-D-glucose in parasitoid wasps of the Nasonia group. *Insect Biochemistry and Molecular Biology* 115:103256 DOI 10.1016/j.ibmb.2019.103256.

Price ER, Krokfors A, Guglielmo CG. 2008. Selective mobilization of fatty acids from adipose tissue in migratory birds. *Journal of Experimental Biology* 211:29–34 DOI 10.1242/jeb.009340.

Raclot T. 2003. Selective mobilization of fatty acids from adipose tissue triacylglycerols. *Progress in Lipid Research* 42:257–288 DOI 10.1016/S0163-7827(02)00066-8.

Rajapakse S, Qu D, Ahmed AS, Rickers-Haunerland J, Haunerland NH. 2019. Effects of FABP knockdown on flight performance of the desert locust, Schistocerca gregaria. *Journal of Experimental Biology* 222(Pt 21):jeb203455 DOI 10.1242/jeb.203455.

Ramos FO, Leyria J, Nouzova M, Fruttero LL, Noriega FG, Canavoso LE. 2021. Juvenile hormone mediates lipid storage in the oocytes of Dipetalogaster maxima. *Insect Biochemistry and Molecular Biology* 133:103499 DOI 10.1016/j.ibmb.2020.103499.

Raksakantong P, Meeso N, Kubola J, Siriamornpun S. 2010. Fatty acids and proximate composition of eight Thai edible terricolous insects. *Food Research International* 350–355 DOI 10.1016/j.foodres.2009.10.014.

Reynolds JA, Poelchau MF, Rahman Z, Armbruster PA, Denlinger DL. 2012. Transcript profiling reveals mechanisms for lipid conservation during diapause in the mosquito, *Aedes albopictus*. *Journal of Insect Physiology* 58:966–973 DOI 10.1016/j.jinsphys.2012.04.013.

Ribeiro JMC, Genta FA, Sorgine MHF, Logullo R, Mesquita RD, Paiva-Silva GO, Majerowicz D, Medeiros M, Koerich L, Terra WR, Ferreira C, Pimentel AC, Bisch PM, Leite DC, Diniz MMP, da Junior JLSGV, Da Silva ML, Araujo RN, Gandara ACP, Brosson S, Salmon D, Bousbata S, González-Caballero N, Silber AM, Alves-Bezerra M, Gondim KC, Silva-Neto MAC, Atella GC, Araujo H, Dias FA, Polycarpo C, Vionette-Amaral RJ, Fampa P, Melo ACA, Tanaka AS, Balczun C, Oliveira JHM, Gonçalves RLS, Lazoski C, Riveria-Pomar R, Diambra L, Schaub GA, Garcia ES, Azambuja P, Braz GRC, Oliveira PL. 2014. An insight into the transcriptome of the digestive tract of the bloodsucking Bug, *Rhodnius prolixus*. *PLOS Neglected Tropical Diseases* 8:27 DOI 10.1371/journal.pntd.0002594.

Rider MH, Hussain N, Dilworth SM, Storey JM, Storey KB. 2011. AMP-activated protein kinase and metabolic regulation in cold-hardy insects. *Journal of Insect Physiology* 57:1453–1462 DOI 10.1016/j.jinsphys.2011.07.006.

Rihani K, Ferveur J-F, Briand L. 2021. The 40-year mystery of insect odorant-binding proteins. *Biomolecules* 11(4):509 DOI 10.3390/biom11040509.

Rimoldi OJ, Córsico B, González MS, Brenner RR. 1996. Detection and quantification of a very high density lipoprotein in different tissues of Triatoma infestans during the last nymphal and adult stages. *Insect Biochemistry and Molecular Biology* 26:705–713 DOI 10.1016/S0965-1748(96)00037-9.
Rimoldi OJ, Soulages JL, González SM, Peluffo RO, Brenner RR. 1989. Purification and properties of the very high density lipoprotein from the hemolymph of adult Triatomia infestans. *Journal of lipid research* **30**:857–864 DOI 10.1016/s0022-2275(20)38311-5.

Rinehart JP, Robich RM, Denlinger DL. 2010. Isolation of diapause-regulated genes from the flesh fly, Sarcophaga crassipalpis by suppressive subtractive hybridization. *Journal of Insect Physiology* **56** DOI 10.1016/j.jinsphys.2009.12.007.

Rittschof CC, Schirmieer S. 2018. Insect models of central nervous system energy metabolism and its links to behavior. *Glia* **66**:1160–1175 DOI 10.1002/glia.23235.

Rivers DB. 2016. Parasitic hymenoptera as forensic indicator species. In: Shetty BSK, Padubidri JR, eds. *Forensic analysis - from death to justice*. London: IntechOpen DOI 10.5772/62501.

Rivers DB, Lee RE, Denlinger DL. 2000. Cold hardiness of the fly pupal parasitoid Nasonia vitripennis is enhanced by its host Sarcophaga crassipalpis. *Journal of Insect Physiology* **46**:99–106 DOI 10.1016/S0022-1910(99)00106-7.

Robich RM, Denlinger DL. 2005. Diapause in the mosquito Culex pipiens evokes a metabolic switch from blood feeding to sugar gluttony. *Proceedings of the National Academy of Sciences of the United States of America* **102**:15912–15917 DOI 10.1073/pnas.0507958102.

Rodenburg KW, Van Der Horst DJ. 2005. Lipoprotein-mediated lipid transport in insects: analogy to the mammalian lipid carrier system and novel concepts for the functioning of LDL receptor family members. *Biochimica Et Biophysica Acta - Molecular and Cell Biology of Lipids* **1736**:10–29 DOI 10.1016/j.bbalip.2005.07.002.

Rother L, Kraft N, Smith DB, Jundi Bel, Gill RJ, Pfeiffer K. 2021. A micro-CT-based standard brain atlas of the bumblebee. *Cell and Tissue Research* DOI 10.1007/s00441-021-03482-z.

Ruther J, Prager L, Pokorny T. 2021. Parasitic wasps do not lack lipogenesis. *Proceedings of the Royal Society B: Biological Sciences* **288**(1951):20210548 DOI 10.1098/rspb.2021.0548.

Sakudoh T, Iizuka T, Narukawa J, Sezutsu H, Kobayashi I, Kuwazaki S, Banno Y, Kitamura A, Sugiyama H, Takada N, Fujimoto H, Kadono-Okuda K, Mita K, Tamura T, Yamamoto K, Tsuchida K. 2010. A CD36-related transmembrane protein is coordinated with an intracellular lipid-binding protein in selective carotenoid transport for cocoon coloration. *Journal of Biological Chemistry* **285**:7739–7751 DOI 10.1074/jbc.M109.074435.

Sanders HR, Evans AM, Ross LS, Gill SS. 2003. Blood meal induces global changes in midgut gene expression in the disease vector, Aedes aegypti. *Insect Biochemistry and Molecular Biology* **33**:1105–1122 DOI 10.1016/S0965-1748(03)00124-3.

Santos R, Mariano AC, Rosas-Oliveira R, Pascarelli B, Machado EA, Meyer-Fernandes JR, Gondim KC. 2008. Carbohydrate accumulation and utilization by oocytes of Rhodnius prolixus. *Archives of Insect Biochemistry and Physiology* **67**:55–62 DOI 10.1002/arch.20217.
Santos R, Rosas-Oliveira R, Saraiva FB, Majerowicz D, Gondim KC. 2011. Lipid accumulation and utilization by oocytes and eggs of Rhodnius prolixus. Archives of Insect Biochemistry and Physiology 77:1–16 DOI 10.1002/arch.20414.

Saraiva FB, Alves-Bezerra M, Majerowicz D, Paes-Vieira L, Braz V, Almeida MGMD, Meyer-Fernandes JR, Gondim KC. 2021. Blood meal drives de novo lipogenesis in the fat body of Rhodnius prolixus. Insect Biochemistry and Molecular Biology 133:103511 DOI 10.1016/j.ibmb.2020.103511.

Saunders DS, Hayward SAL. 1998. Geographical and diapause-related cold tolerance in the blow fly, Calliphora vicina. Journal of Insect Physiology 44:541–551 DOI 10.1016/S0022-1910(98)00049-3.

Schaffer JE. 2002. Fatty acid transport: the roads taken. American Journal of Physiology - Endocrinology and Metabolism 282:E239–E246 DOI 10.1152/ajpendo.00462.2001.

Schaffer JE, Lodish HF. 1994. Expression cloning and characterization of a novel adipocyte long chain fatty acid transport protein. Cell 79:427–436 DOI 10.1016/0092-8674(94)90252-6.

Schal C, Sevala V, Capurro MLD, Snyder TE, Blomquist GJ, Bagnères AG. 2001. Tissue distribution and lipophorin transport of hydrocarbons and sex pheromones in the house fly, Musca domestica. Journal of Insect Science 1:1–11 DOI 10.1673/031.001.1201.

Scharnweber K, Chaguaceda F, Dalman E, Tranvik L, Eklöv P. 2020. The emergence of fatty acidsâĂŤAquatic insects as vectors along a productivity gradient. Freshwater Biology 65:565–578 DOI 10.1111/fwb.13454.

Scheuermann EA, Smith DP. 2019. Odor-specific deactivation defects in a drosophila odorant-binding protein mutant. Genetics 213:897–909 DOI 10.1534/genetics.119.302629.

Scholl PJ, Colwell DD, Cepeda-Palacios R. 2018. Myiasis (Muscoidea, Oestroidea). In: Mullen GR, Durden LABT-M VE, Third E, eds. Medical and veterinary entomology. Cambridge: Academic Press, 383–419 DOI 10.1016/B978-0-12-814043-7.00019-4.

Séité S, Harrison MC, Sillam-Dussès D, Lupoli R, Van Dooren TJM, Robert A, Poissonnier L-A, Lemainque A, Renault D, Acket S, Andrieu M, Viscarra J, Sul HS, De Beer ZW, Bornberg-Bauer E, Vasseur-Cognet M. 2021. Extreme longevity of highly fecund termite queens achieved by mitochondrial and insulin upregulation without harmful lipid signatures or accumulation. ArXiv preprint. arXiv:2021.05.10.443390 DOI 10.1101/2021.05.10.443390.

Semmelmann F, Kabeya N, Malicka M, Bruckmann A, Broschwitz B, Straub K, Merkl R, Monroig O, Sterner R, Ruther J, Ellers J. 2019. Functional characterisation of two Îľ1- desaturases demonstrates targeted production of linoleic acid as pheromone precursor in Nasonia. Journal of Experimental Biology 222(Pt 10):jeb201038 DOI 10.1242/jeb.201038.

Seo SJ, Cheon HM, Sun J, Sappington TW, Raikhe AS. 2003. Tissue- and stage-specific expression of two lipophorin receptor variants with seven and eight ligand-binding repeats in the adult mosquito. Journal of Biological Chemistry 278:41954–41962 DOI 10.1074/jbc.M308200200.
Service PM. 1987. Physiological mechanisms of increased stress resistance in drosophila melanogaster selected for postponed senescence. *Physiological Zoology* 60:321–326 DOI 10.1086/physzool.60.3.30162285.

Sevala V, Shu S, Ramaswamy SB, Schal C. 1999. Lipophorin of female Blattella germanica (L.): Characterization and relation to hemolymph titers of juvenile hormone and hydrocarbons. *Journal of Insect Physiology* 45:431–441 DOI 10.1016/S0022-1910(98)00142-5.

Sforcin JM, Bankova V, Kuropatnicki AK. 2017. Medical benefits of honeybee products. *Evidence-Based Complementary and Alternative Medicine* 2017:2702106 DOI 10.1155/2017/2702106.

Shan S, Wang SN, Song X, Khashaveh A, Lu ZY, Dhiloo KH, Li RJ, Gao XW, Zhang YJ. 2020. Molecular characterization and expression of sensory neuron membrane proteins in the parasitoid Microplitis mediator (Hymenoptera: Braconidae). *Insect Science* 27:425–439 DOI 10.1111/1744-7917.12667.

Shrestha S, Kim Y. 2008. Eicosanoids mediate prophenoloxidase release from oenocytes in the beet armyworm Spodoptera exigua. *Insect Biochemistry and Molecular Biology* 38:99–112 DOI 10.1016/j.ibmb.2008.09.013.

Silva-Oliveira G, De Paula IF, Medina JM, Alves-Bezerra M, Gondim KC. 2021. Insulin receptor deficiency reduces lipid synthesis and reproductive function in the insect Rhodnius prolixus. *Biochimica Et Biophysica Acta - Molecular and Cell Biology of Lipids* 1866(2):158851 DOI 10.1016/j.bbalip.2020.158851.

Silveira LCP, Souza II, Tomazella VB, Mendez HAG. 2019. Parasitoid insects. In: Souza B, Vázquez LL, Marucci RC, eds. *Natural enemies of insect pests in neotropical agroecosystems: biological control and functional biodiversity*. Cham: Springer International Publishing, 97–109 DOI 10.1007/978-3-030-24733-1_9.

Sim C, Denlinger DL. 2008. Insulin signaling and FOXO regulate the overwintering diapause of the mosquito Culex pipiens. *Proceedings of the National Academy of Sciences of the United States of America* 105:6777–6781 DOI 10.1073/pnas.0802067105.

Sim C, Denlinger DL. 2009. Transcription profiling and regulation of fat metabolism genes in diapausing adults of the mosquito Culex pipiens. *Physiological Genomics* 39:202–209 DOI 10.1152/physiolgenomics.00095.2009.

Sim C, Denlinger DL. 2013. Juvenile hormone III suppresses forkhead of transcription factor in the fat body and reduces fat accumulation in the diapausing mosquito, Culex pipiens. *Insect Molecular Biology* 22:1–11 DOI 10.1111/j.1365-2583.2012.01166.x.

Sinclair BJ, Marshall KE. 2018. The many roles of fats in overwintering insects. *Journal of Experimental Biology* 221(Pt Suppl 1):jeb161836 DOI 10.1242/jeb.161836.

Sinensky M. 1974. Homeoviscous adaptation: a homeostatic process that regulates the viscosity of membrane lipids in Escherichia coli. *Proceedings of the National Academy of Sciences of the United States of America* 71:522–525 DOI 10.1073/pnas.71.2.522.

Skinner WA, Tong HC, Maibach HI, Skidmore D. 1970. Human skin-surface lipid fatty acids - Mosquito repellents. *Experientia* 26:728–730 DOI 10.1007/BF02232510.

Skowronek P, Wójcik I, Strachecka A. 2021. Fat body—multifunctional insect tissue. *Insects* 12 DOI 10.3390/insects12060547.
Smallegange RC, Qiu YT, Bukovinszkiné-Kiss G, Van Loon JJA, Takken W. 2009. The effect of aliphatic carboxylic acids on olfaction-based host-seeking of the malaria mosquito Anopheles gambiae sensu stricto. *Journal of Chemical Ecology* **35**:933–943 DOI 10.1007/s10886-009-9668-7.

Smith DFQ, Casadevall A. 2021. Fungal immunity and pathogenesis in mammals versus the invertebrate model organism Galleria mellonella. *Pathogens and Disease* **3**:ftab013 DOI 10.1093/femspd/ftab013.

Sönmez E, Güvenç D, Gülel A. 2016. The changes in the types and amounts of fatty acids of adult Acanthoscelides obtectus (Coleoptera, Bruchidae) in terms of age and sex. *International Journal of Fauna and Biological Studies* **3**:90–96.

Soulages JL, Wells MA. 1994. Metabolic fate and turnover rate of hemolymph free fatty acids in adult Manduca sexta. *Insect Biochemistry and Molecular Biology* **24**:79–86 DOI 10.1016/0965-1748(94)90125-2.

Stadler F. 2020. The maggot therapy supply chain: a review of the literature and practice. *Medical and Veterinary Entomology* **34**:1–9 DOI 10.1111/mve.12397.

Stahl A. 2004. A current review of fatty acid transport proteins (SLC27). *Pflugers Archiv European Journal of Physiology* **447**:722–727 DOI 10.1007/s00424-003-1106-z.

Stahl A, Hirsch DJ, Gimeno RE, Punreddy S, Pei G, Watson N, Patel S, Kotler M, Raimondi A, Tartaglia LA, Lodish HF. 1999. Identification of the major intestinal fatty acid transport protein. *Molecular Cell* **4**:299–308 DOI 10.1016/S1097-2765(00)80332-9.

Stanley D, Kim Y. 2014. Eicosanoid signaling in Insects: from discovery to plant protection. *Critical Reviews in Plant Sciences* **33**:20–63 DOI 10.1080/07352689.2014.847631.

Stanley D, Kim Y. 2020. Why most insects have very low proportions of C20 polyunsaturated fatty acids: the oxidative stress hypothesis. *Archives of Insect Biochemistry and Physiology* **103**(1):e21622 DOI 10.1002/arch.21622.

Stanley-Samuelson DW, Dadd RH. 1981. Arachidonic and other tissue fatty acids of Culex pipiens reared with various concentrations of dietary arachidonic acid. *Journal of Insect Physiology* **27**:571–578 DOI 10.1016/0022-1910(81)90103-7.

Stanley-Samuelson DW, Dadd RH. 1983. Long-chain polyunsaturated fatty acids: patterns of occurrence in insects. *Insect Biochemistry* **13**:549–558 DOI 10.1016/0020-1790(83)90014-8.

Stanley-Samuelson DW, Dadd RH. 1984. Polysaturated fatty acids in the lipids from adult Galleria mellonella reared on diets to which only one unsaturated fatty acid had been added. *Insect Biochemistry* **14**:321–327 DOI 10.1016/0020-1790(84)90067-2.

Stanley-Samuelson DW, Jurenka RA, Cripps C, Blomquist GJ, De Renobales M. 1988. Fatty acids in insects: composition, metabolism, and biological significance. *Archives of Insect Biochemistry and Physiology* **9**:1–33 DOI 10.1002/arch.940090102.

Stanley-Samuelson DW, Loher W. 1986. Prostaglandins in Insect Reproduction. *Annals of the Entomological Society of America* **79**:841–853 DOI 10.1093/aesaa/79.6.841.

Stączek S, Zdybicka-Barabas A, Mak P, Sowa-Jasień A, Kedracka-Krok S, Jankowska U, Suder P, Wydrych J, Grygorczuk K, Jakubowicz T, Cytryńska M. 2018. Studies on localization and protein ligands of Galleria mellonella apolipophorin III during
immune response against different pathogens. *Journal of Insect Physiology* 105:18–27 DOI 10.1016/j.jinsphys.2017.12.009.

Subramanian M, Metya SK, Sadaf S, Kumar S, Schwudke D, Hasan G. 2013. Altered lipid homeostasis in Drosophila InsP3 receptor mutants leads to obesity and hyperphagia. *DMM Disease Models and Mechanisms* 6:734–744 DOI 10.1242/dmm.010017.

Sun J, Hiraoka T, Dittmer NT, Cho KH, Raikhel AS. 2000. Lipophorin as a yolk protein precursor in the mosquito, Aedes aegypti. *Insect Biochemistry and Molecular Biology* 30:1161–1171 DOI 10.1016/S0965-1748(00)00093-X.

Tang X, Pikal MJ. 2005. The effect of stabilizers and denaturants on the cold denaturation temperatures of proteins and implications for freeze-drying. *Pharmaceutical Research* 22:1167–1175 DOI 10.1007/s11095-005-6035-4.

Tang C, Yang D, Liao H, Sun H, Liu C, Wei L, Li F. 2019. Edible insects as a food source: a review. *Food Production, Processing and Nutrition* 1 DOI 10.1186/s43014-019-0008-1.

Tatar M, Yin CM. 2001. Slow aging during insect reproductive diapause: why butterflies, grasshoppers and flies are like worms. In: *Experimental gerontology*. 36. 723–738 DOI 10.1016/S0503-5565(00)00238-2.

Teets NM, Denlinger DL. 2013. Physiological mechanisms of seasonal and rapid cold-hardening in insects. *Physiological Entomology* 38:105–116 DOI 10.1111/phen.12019.

Teets NM, Gantz JD, Kawarasaki Y. 2020. Rapid cold hardening: ecological relevance, physiological mechanisms and new perspectives. *The Journal of Experimental Biology* 223(Pt 3):jeb203448 DOI 10.1242/jeb.203448.

Ternes P, Franke S, Zähringer U, Sperling P, Heinz E. 2002. Identification and characterization of a sphingolipid Δ4-desaturase family. *Journal of Biological Chemistry* 277:25512–25518 DOI 10.1074/jbc.M202947200.

Terra WR, Espinoza-Fuentes FP, Ribeiro AF, Ferreira C. 1988. The larval midgut of the housefly (Musca domestica): ultrastructure, fluid fluxes and ion secretion in relation to the organization of digestion. *Journal of Insect Physiology* 34:463–472 DOI 10.1016/0022-1910(88)90187-4.

Terra WR, Ferreira C. 2020. Evolutionary trends of digestion and absorption in the major insect orders. *Arthropod Structure and Development* 56:100931 DOI 10.1016/j.asd.2020.100931.

Thompson SN, Barlow JS, Douglas VM. 1975. Preliminary purification and properties of a fatty acid synthetase complex isolated from the blowfly Lucilia sericata. *Insect Biochemistry* 5:571–583 DOI 10.1016/0020-1790(75)90039-6.

Tomáča A, Tollarová M, Overgaard J, Šimek P, Koštál V. 2006. Seasonal acquisition of chill tolerance and restructuring of membrane glycerophospholipids in an overwintering insect: triggering by low temperature, desiccation and diapause progression. *Journal of Experimental Biology* 209:4102–4114 DOI 10.1242/jeb.02484.

Toprak U. 2020. The role of peptide hormones in insect lipid metabolism. *Frontiers in Physiology* 11(434): DOI 10.3389/fphys.2020.00434.
Toprak U, Doğan C, Hegedus D. 2021. A comparative perspective on functionally-related, intracellular calcium channels: the insect Ryanodine and Inositol 1, 4, 5-trisphosphate receptors. Biomolecules 11(7):1031 DOI 10.3390/biom11071031.

Toprak U, Guz N, Gurkan MO, Hegedus DD. 2014. Identification and coordinated expression of perilipin genes in the biological cycle of sunn pest, Eurygaster maura (Hemiptera: Scutelleridae): implications for lipolysis and lipogenesis. Comparative Biochemistry and Physiology - B Biochemistry and Molecular Biology 171:1–11 DOI 10.1016/j.cbpb.2014.02.001.

Toprak U, Hegedus D, Doğan C, Güney G. 2020. A journey into the world of insect lipid metabolism. Archives of Insect Biochemistry and Physiology 104(2):e21682 DOI 10.1002/arch.21682.

Tougeron K. 2019. Diapause research in insects: historical review and recent work perspectives. Entomologia Experimentalis Et Applicata 167:27–36 DOI 10.1111/eea.12753.

Trowell SC, Hines ER, Herlt AJ, Rickards RW. 1994. Characterization of a juvenile hormone binding lipophorin from the blowfly Lucilia cuprina. Comparative Biochemistry and Physiology –Part B: Biochemistry and 109:339–357 DOI 10.1016/0305-0491(94)90018-3.

Troy S, Anderson WA, Spielman A. 1975. Lipid content of maturing ovaries of Aedes aegypti mosquitoes. Comparative Biochemistry and Physiology B 50(3):457–461 DOI 10.1016/0305-0491(75)90258-8.

Truman JW, Riddiford LM. 2019. The evolution of insect metamorphosis: a developmental and endocrine view. Philosophical Transactions of the Royal Society B: Biological Sciences 374(1783):20190070 DOI 10.1098/rstb.2019.0070.

Tsvetkova NM, Quinn PJ. 1994. Compatible solutes modulate membrane phase behaviour. In: Cossins AR, ed. Temperature adaptation in biological membranes. London: Portland Press, 49–62.

Tufail M, Elmogy M, Ali Fouda MM, Elgendy AM, Bembenek J, Trang LTD, Shao QM, Takeda M. 2009. Molecular cloning, characterization, expression pattern and cellular distribution of an ovarian lipophorin receptor in the cockroach. Leucophaea maderae. Insect Molecular Biology 18:281–294 DOI 10.1111/j.1365-2583.2009.00865.x.

Tupec M, Buček A, Valterová I, Pichová I. 2017. Biotechnological potential of insect fatty acid-modifying enzymes. Zeitschrift Fur Naturforschung - Section C Journal of Biosciences 72(9–10):387–403 DOI 10.1515/znc-2017-0031.

Tvrzicka E, Kremmyda LS, Stankova B, Zak A. 2011. Fatty acids as biocompounds: their role in human metabolism, health and disease - a review. part 1: Classification, dietary sources and biological functions. Biomedical Papers 155:117–130 DOI 10.5507/bp.2011.038.
Urbanek A, Szadziewski R, Stepnowski P, Boros-Majewska J, Gabriel I, Dawgul M, Kamysz W, Sosnowska D, Gołębiowski M. 2012. Composition and antimicrobial activity of fatty acids detected in the hygroscopic secretion collected from the secretory setae of larvae of the biting midge Forcipomyia nigra (Diptera: Ceratopogonidae). Journal of Insect Physiology 58:1265–1276 DOI 10.1016/j.jinsphys.2012.06.014.

Urbanski JM, Benoit JB, Michaud MR, Denlinger DL, Armbruster P. 2010. The molecular physiology of increased egg desiccation resistance during diapause in the invasive mosquito, Aedes albopictus. Proceedings of the Royal Society B: Biological Sciences 2683–2692 DOI 10.1098/rspb.2010.0362.

Valder SM, Hopkins TL, Valder SA. 1969. Diapause induction and changes in lipid composition in diapausing and reproducing faceflies, Musca autumnalis. Journal of Insect Physiology 15:1199–1214 DOI 10.1016/0022-1910(69)90230-3.

Van Anholt RD, Koven WM, Lutzky S, Wendelaar Bonga SE. 2004. Dietary supplementation with arachidonic acid alters the stress response of gilthead seabream (Sparus aurata) larvae. Aquaculture 238:369–383 DOI 10.1016/j.aquaculture.2004.06.001.

Van Den Brink DM, Cubizolle A, Chatelain G, Davoust N, Girard V, Johansen S, Napoletano F, Douren P, Guillou L, Angebault-Prouteau C, Bernoud-Hubac N, Guichardant M, Brabet P, Mollereau B. 2018. Physiological and pathological roles of FATP-mediated lipid droplets in Drosophila and mouse retina. PLoS Genetics 14(9):e1007627 DOI 10.1371/journal.pgen.1007627.

Van Der Horst DJ, Rodenburg KW. 2010. Lipoprotein assembly and function in an evolutionary perspective. Biomolecular Concepts 165–183 DOI 10.1515/bmc.2010.012.

Van Der Horst DJ, Roosendaal SD, Rodenburg KW. 2009. Circulatory lipid transport: Lipoprotein assembly and function from an evolutionary perspective. Molecular and Cellular Biochemistry 326:105–119 DOI 10.1007/s11010-008-0011-3.

Van Der Horst DJ, Ryan RO. 2012. Lipid transport. In: Insect molecular biology and biochemistry. San Diego: Elsevier, 317–345.

Van Der Horst DJ, Van Hoof D, Van Marrewijk WJA, Rodenburg KW. 2002. Alternative lipid mobilization: the insect shuttle system. Molecular and Cellular Biochemistry 239:113–119 DOI 10.1023/A:1020541010547.

Van Handel E. 1993. Fuel metabolism of the mosquito (Culex quinquefasciatus) embryo. Journal of Insect Physiology 39:831–833 DOI 10.1016/0022-1910(93)90115-8.

Vande Velde L, Schtickzelle N, Van Dyck H. 2013. Effect of larval food stress on male adult behaviour, morphology and reproductive investment in the butterfly Pararge aegeria. Evolutionary Ecology 27:221–234 DOI 10.1007/s10682-012-9580-4.

Vatanparast M, Lee DH, Kim Y. 2020. Biosynthesis and immunity of epoxyeicosatrienoic acids in a lepidopteran insect, Spodoptera exigua. Developmental and Comparative Immunology 107:103643 DOI 10.1016/j.dci.2020.103643.

Vaz AH, Jurenka RA, Blomquist GJ, Reitz RC. 1988. Tissue and chain length specificity of the fatty acyl-CoA elongation system in the American cockroach. Archives of Biochemistry and Biophysics 267:551–557 DOI 10.1016/0003-9861(88)90062-8.
Visser B, Ellers J. 2008. Lack of lipogenesis in parasitoids: A review of physiological mechanisms and evolutionary implications. *Journal of Insect Physiology* **54**:1315–1322 DOI 10.1016/j.jinsphys.2008.07.014.

Visser B, Le Lann C, Den Blanken FJ, Harvey JA, Van Alphen JJM, Ellers J. 2010. Loss of lipid synthesis as an evolutionary consequence of a parasitic lifestyle. *Proceedings of the National Academy of Sciences of the United States of America* **107**:8677–8682 DOI 10.1073/pnas.1001744107.

Visser B, Roelofs D, Hahn DA, Teal PEA, Mariën J, Ellers J. 2012. Transcriptional changes associated with lack of lipid synthesis in parasitoids. *Genome Biology and Evolution* **4**:752–762 DOI 10.1093/gbe/evs065.

Voss SC, Spafford H, Dadour IR. 2009. Hymenopteran parasitoids of forensic importance: host associations, seasonality, and prevalence of parasitoids of carrion flies in Western Australia. *Journal of Medical Entomology* **46**:1210–1219 DOI 10.1603/033.046.0532.

Wang DL, Dillwith JW, Ryan RO, Blomquist GJ, Reitz RC. 1982. Characterization of the acylCoA desaturase in the housefly, Musca domestica L. *Insect Biochemistry* **12**:545–551 DOI 10.1016/0020-1790(82)90024-5.

Wang X, Hou Y, Saha TT, Pei G, Raikhel AS, Zou Z. 2017. Hormone and receptor interplay in the regulation of mosquito lipid metabolism. *Proceedings of the National Academy of Sciences of the United States of America* **114**:E2709–E2718 DOI 10.1073/pnas.1619326114.

Wang XG, Johnson MW, Daane KM, Opp S. 2009. Combined effects of heat stress and food supply on flight performance of olive fruit fly (Diptera: Tephritidae). *Annals of the Entomological Society of America* **102**:727–734 DOI 10.1603/008.102.0418.

Wang J, Murphy EJ, Nix JC, Jones DNM. 2020. Aedes aegypti Odorant Binding Protein 22 selectively binds fatty acids through a conformational change in its C-terminal tail. *Scientific Reports* **10**(1):3300 DOI 10.1038/s41598-020-60242-9.

Wang Y-S, Shelomi M. 2017. Review of black soldier fly (Hermetia illucens) as animal feed and human food. *Foods* **6**:91 DOI 10.3390/foods6100091.

Wang C, Xing J, Chin CK, Peters JS. 2002. Fatty acids with certain structural characteristics are potent inhibitors of germination and inducers of cell death of powdery mildew spores. *Physiological and Molecular Plant Pathology* **61**:151–161 DOI 10.1006/pmpp.2002.0429.

Ward JP, Candy DJ, Smith SN. 1982. Lipid storage and changes during flight by triatomine bugs (Rhodnius prolixus and Triatoma infestans). *Journal of Insect Physiology* **28**:527–534 DOI 10.1016/0022-1910(82)90033-6.

Webster MT. 2019. *Apis mellifera*. *Trends in Genetics* **35**:880–881 DOI 10.1016/j.tig.2019.08.003.

Weers PMM, Ryan RO. 2006. Apolipophorin III: role model apolipoprotein. *Insect Biochemistry and Molecular Biology* **36**:231–240 DOI 10.1016/j.ibmb.2006.01.001.

Weers PMM, Van Marrewijk WJA, Beenakkers AMT, Van der Horst DJ. 1993. Biosynthesis of locust lipophorin, Apolipoporphins I and II originate from a common
precursor. *Journal of Biological Chemistry* **268**:4300–4303 DOI 10.1016/s0021-9258(18)53609-7.

Wen X, Wang S, Duman JG, Arifin JFnu, Juwita V, Goddard WA, Rios A, Liu F, Kim SK, Abrol R, De Vries AL, Henling LM. 2016. Antifreeze proteins govern the precipitation of trehalose in a freezing-avoiding insect at low temperature. *Proceedings of the National Academy of Sciences of the United States of America* **113**:6683–6688 DOI 10.1073/pnas.1601519113.

Wicker-Thomas C, Garrido D, Bontonou G, Napal L, Mazuras N, Denis B, Rubin T, Parvy JP, Montagne J. 2015. Flexible origin of hydrocarbon/pheromone precursors in Drosophila melanogaster. *Journal of Lipid Research* **56**:2094–2101 DOI 10.1194/jlr.M060368.

Wiesner A, Losen S, Kopáček P, Weise C, Götz P. 1997. Isolated Apolipophorin III from Galleria mellonella stimulates the immune reactions of this insect. *Journal of Insect Physiology* **43**:383–391 DOI 10.1016/S0022-1910(96)00113-8.

Wigglesworth VB. 1949. The utilization of reserve substances in Drosophila during flight. *The Journal of Experimental Biology* **26**(2):.

Wilfert L, Gadau J, Baer B, Schmid-Hempel P. 2007. Natural variation in the genetic architecture of a host-parasite interaction in the bumblebee Bombus terrestris. *Molecular Ecology* **16**:1327–1339 DOI 10.1111/j.1365-294X.2007.03234.x.

Wille JJ, Kydonieus A. 2003. Palmitoleic acid isomer (C16:1 Δ6) in human skin sebum is effective against gram-positive bacteria. *Skin Pharmacology and Applied Skin Physiology* **16**:176–187 DOI 10.1159/000069757.

Wojciechowska M, Gołębiowski M. 2020. SPME-GC/MS analysis of volatile compounds contained in the insect larvae of Tenebrio molitor and Leptinotarsa decemlineata before and after using insecticides. *Chemistry & Biodiversity* **17**:e1900743 DOI 10.1002/cbdv.201900743.

Wojciechowska M, Stepnowski P, Gołębiowski M. 2019. Identification and quantitative analysis of lipids and other organic compounds contained in eggs of Colorado potato beetle (Leptinotarsa decemlineata). *Journal of Plant Diseases and Protection* **126**:379–384 DOI 10.1007/s41348-019-00216-w.

Wojda I, Staniec B, Sulek M, Kordaczuk J. 2020. The greater wax moth Galleria mellonella: biology and use in immune studies. *Pathogens and Disease* **78**(9):ftaa057 DOI 10.1093/femspd/ftaa057.

Wrońska AK, Boguś MI, Włóka E, Kazek M, Kaczmarek A, Zalewska K. 2018. Cuticular fatty acids of Galleria mellonella (Lepidoptera) inhibit fungal enzymatic activities of pathogenic Conidiobolus coronatus. *PLOS ONE* **13**(3):e0192715 DOI 10.1371/journal.pone.0192715.

Wu Q, Haunerland NH. 2001. A novel fatty acid response element controls the expression of the flight muscle FABP gene of the desert locust, Schistocerca gregaria. *European Journal of Biochemistry* **268**:5894–5900 DOI 10.1046/j.0014-2956.2001.02538.x.

Xu W, Zhang H, Liao Y, Papanicolaou A. 2020. Characterization of sensory neuron membrane proteins (SNMPs) in cotton bollworm Helicoverpa armigera (Lepidoptera: Noctuidae). *Insect Science* **28**(3):769–779 DOI 10.1111/1744-7917.12816.
Xueke G, Shuai Z, Junyu I, Limin L, Lijuan Z, Jinjie C. 2017. Lipidomics and RNA-Seq study of lipid regulation in Aphis gossypii parasitized by Lysiphlebia japonica. Scientific Reports 7:1364 DOI 10.1038/s41598-017-01546-1.

Yajima M, Takada M, Takahashi N, Kikuchi H, Natori S, Oshima Y, Kurata S. 2003. A newly established in vitro culture using transgenic Drosophila reveals functional coupling between the phospholipase A2-generated fatty acid cascade and lipopolysaccharide-dependent activation of the immune deficiency (IMD) pathway in insect immunity. Biochemical Journal 371:205–210 DOI 10.1042/BJ20021603.

Yoon BK, Jackman JA, Valle-González ER, Cho NJ. 2018. Antibacterial free fatty acids and monoglycerides: biological activities, experimental testing, and therapeutic applications. International Journal of Molecular Sciences 19(4):1114 DOI 10.3390/ijms19041114.

Younes S, Al-Sulaiti A, Nasser EAA, Najjar H, Kamaredinne L. 2020. Drosophila as a model organism in host–pathogen interaction studies. Frontiers in Cellular and Infection Microbiology 10:214 DOI 10.3389/fcimb.2020.00214.

Young HP, Bachmann JAS, Sevala V, Schal C. 1999. Site of synthesis, tissue distribution, and lipophorin transport of hydrocarbons in Blattella germanica (L.) nymphs. Journal of Insect Physiology 45:305–315 DOI 10.1016/S0022-1910(98)00128-0.

Zandawala M, Hamoudi Z, Lange AB, Orchard I. 2015. Adipokinetic hormone signalling system in the Chagas disease vector, Rhodnius prolixus. Insect Molecular Biology 24:264–276 DOI 10.1111/imb.12157.

Zdybicka-Barabas A, Cytryńska M. 2013. Apolipoporphins and insects immune response. Invertebrate Survival Journal 10:58–68.

Zdybicka-Barabas A, Palusińska-Szysz M, Gruszecki WI, Mak P, Cytryńska M. 2014. Galleria mellonella apolipophorin III - An apolipoprotein with anti-Legionella pneumophila activity. Biochimica Et Biophysica Acta - Biomembranes 1838(10):2689–2697 DOI 10.1016/j.bbamem.2014.07.003.

Zdybicka-Barabas A, Stączek S, Mak P, Skrzypiec K, Mendyk E, Cytryńska M. 2013. Synergistic action of Galleria mellonella apolipophorin III and lysozyme against Gram-negative bacteria. Biochimica Et Biophysica Acta - Biomembranes 1828(6):1449–1456 DOI 10.1016/j.bbamem.2013.02.004.

Zhang Y, Chen D, Wang Z. 2009. Analyses of mental dysfunction-related ACSL4 in Drosophila reveal its requirement for Dpp/BMP production and visual wiring in the brain. Human Molecular Genetics 18:3894–3905 DOI 10.1093/hmg/ddp332.

Zhang W, Tettamanti G, Bassal T, Heryanto C, Eleftherianos I, Mohamed A. 2021. Regulators and signalling in insect antimicrobial innate immunity: functional molecules and cellular pathways. Cellular Signalling 83:110003 DOI 10.1016/j.cellsig.2021.110003.

Zhang C, Wei D, Shi G, Huang X, Cheng P, Liu G, Guo X, Liu L, Wang H, Miao F, Gong M. 2019. Understanding the regulation of overwintering diapause molecular mechanisms in Culex pipiens pallens through comparative proteomics. Scientific Reports 9(1):6485 DOI 10.1038/s41598-019-42961-w.
Zhang HJ, Xu W, meng ChenQ, Sun LN, Anderson A, Xia QY, Papanicolaou A. 2020. A phylogenomics approach to characterizing sensory neuron membrane proteins (SNMPs) in Lepidoptera. *Insect Biochemistry and Molecular Biology* 118:103313 DOI 10.1016/j.ibmb.2020.103313.

Zhang Y, Zhang Y, Gao Y, Zhao X, Wang Z. 2011. Drosophila long-chain acyl-CoA synthetase acts like a gap gene in embryonic segmentation. *Developmental Biology* 353:259–265 DOI 10.1016/j.ydbio.2011.02.030.

Zheng Y, Blair D, Bradley JE. 2013. Phylectic Distribution of Fatty Acid-Binding Protein Genes. *PLoS ONE* 8(10):e77636 DOI 10.1371/journal.pone.0077636.

Zheng T, Li H, Han N, Wang S, Hackney Price J, Wang M, Zhang D. 2017a. Functional Characterization of Two Elongases of Very Long-Chain Fatty Acid from Tenebrio molitor L. (Coleoptera: Tenebrionidae). *Scientific Reports* 7: DOI 10.1038/s41598-017-11134-y.

Zheng H, Powell JE, Steele MI, Dietrich C, Moran NA. 2017b. Honeybee gut microbiota promotes host weight gain via bacterial metabolism and hormonal signaling. *Proceedings of the National Academy of Sciences of the United States of America* 114:4775–4780 DOI 10.1073/pnas.1701819114.

Zheng Cj, Yoo JS, Lee TG, Cho HY, Kim YH, Kim WG. 2005. Fatty acid synthesis is a target for antibacterial activity of unsaturated fatty acids. *FEBS Letters* 579:5157–5162 DOI 10.1016/j.febslet.2005.08.028.

Zhou G, Flowers M, Friedrich K, Horton J, Pennington J, Wells MA. 2004. Metabolic fate of [14C]-labeled meal protein amino acids in Aedes aegypti mosquitoes. *Journal of Insect Physiology* 50:337–349 DOI 10.1016/j.jinsphys.2004.02.003.

Zhou G, Gong Z, Su Y, Lin J, Tang K. 2009. Cordyceps fungi: natural products, pharmacological functions and developmental products. *Journal of Pharmacy and Pharmacology* 61:279–291 DOI 10.1211/jpp/61.03.0002.

Zhou G, Miesfeld RL. 2009. Energy metabolism during diapause in Culex pipiens mosquitoes. *Journal of Insect Physiology* 55:40–46 DOI 10.1016/j.jinsphys.2008.10.002.

Zhou G, Pennington JE, Wells MA. 2004. Utilization of pre-existing energy stores of female Aedes aegypti mosquitoes during the first gonotrophic cycle. *Insect Biochemistry and Molecular Biology* 34:919–925 DOI 10.1016/j.ibmb.2004.05.009.

Zhu W, Zhang H, Li X, Meng Q, Shu R, Wang M, Zhou G, Wang H, Miao L, Zhang J, Qin Q. 2016. Cold adaptation mechanisms in the ghost moth Hepialus xiaojinensis: metabolic regulation and thermal compensation. *Journal of Insect Physiology* 85:76–85 DOI 10.1016/j.jinsphys.2015.11.008.

Ziegler R, Ibrahim MM. 2001. Formation of lipid reserves in fat body and eggs of the yellow fever mosquito, Aedes aegypti. *Journal of Insect Physiology* 47:623–627 DOI 10.1016/S0022-1910(00)00158-X.

Ziegler R, Van Antwerpen R. 2006. Lipid uptake by insect oocytes. *Insect Biochemistry and Molecular Biology* 36:264–272 DOI 10.1016/j.ibmb.2006.01.014.

Zubir MZM, Holloway S, Noor NM. 2020. Maggot therapy in wound healing: a systematic review. *International Journal of Environmental Research and Public Health* 17:1–12 DOI 10.3390/ijerph17176103.