Chapter 9

Odour-mediated host selection and discrimination in mosquitoes

A. Hinze, S.R. Hill and R. Ignell*

Disease Vector Group, Unit of Chemical Ecology, Department of Plant Protection Biology, Swedish University of Agricultural Sciences, Alnarp, Sweden; rickard.ignell@slu.se

Abstract

Haematophagous female mosquitoes differ in their selection of hosts, ranging from generalists to specialists. Specialist mosquitoes, particularly those that prefer to feed on humans, constitute a significant threat to human health, as they can transmit pathogens causing, e.g. malaria, yellow fever, dengue and West Nile fever. To select and discriminate among potential vertebrate host species, mosquitoes rely heavily on their sense of smell. In this chapter, we distinguish between host preference and choice, terms that often are used erroneously in conjunction with host selection and discrimination, and the methods used to define these behaviours. Increasing evidence suggest that mosquitoes rely on odour blends, often composed of shared generic volatile organic compounds, for host discrimination. The identity of these host-related compounds is discussed, along with available information on their cognate chemosensory receptors and neural circuitry. Fundamental knowledge underlying the molecular mechanisms regulating odour-mediated host selection will continue to be key for our improved understanding of the genetic basis and evolution of host discrimination. While there has been significant progress in revealing the mechanisms regulating odour-mediated host discrimination in mosquitoes, we conclude that there are still open questions to address.

Keywords: host preference, host choice, chemosensory receptors, evolution

9.1 Introduction

More than 3,500 mosquito species have been described worldwide, including both blood-feeding and non-blood-feeding taxa (Clements, 1999; Lehane, 2005). Host choice by haematophagous mosquitoes is highly diverse, as are their habitats, with female mosquitoes feeding on humans, non-human primates, other mammals, birds, amphibians and even mudskippers, as well as invertebrates (Clements, 1999; Harris *et al.*, 1969; Reeves *et al.*, 2018; Tempelis, 1975; Verhulst *et al.*, 2018). Mosquitoes locate and discriminate among potential hosts based primarily on the detection of olfactory cues in host emanates (Cardé, 2015; McBride, 2016; Takken and Knols, 1999; Takken and Verhulst, 2013; Tchouassi *et al.*, 2022). The majority of mosquito species does not exhibit a preference for specific hosts, but feeds opportunistically within a host range available in their respective habitat (Clements, 1999; Lyimo and Ferguson, 2009; Takken and Verhulst, 2013). The proportion of mosquito species that bite in a non-random manner have been demonstrated

R. Ignell, C.R. Lazzari, M.G. Lorenzo and S.R. Hill (eds)
Sensory ecology of disease vectors
DOI: 10.3920/978-90-8686-932-9_9, © A. Hinze *et al.* 2022

to select hosts based on unique odour signatures (Costantini *et al.*, 1998; DeGennaro *et al.*, 2013; Lehane, 2005; Rudolfs, 1922; Takken and Verhulst, 2013), although the exact mechanism remains vague. This chapter will focus on odour-mediated inter-specific host discrimination; for a review including other sensory modalities, see Wolff and Riffell (2018).

Host preference and host choice are often used interchangeably, but describe two different, although related, concepts (e.g. Fikrig and Harrington, 2021). Host preference is defined as the intrinsic character underlying selection by a female mosquito for one host type over another (e.g. Boreham and Garrett-Jones, 1973). Host choice, on the other hand, is the feeding pattern of a female mosquito in nature that is the result of host preference and other factors, such as host availability (i.e. abundance and accessibility), host defensive behaviour, past foraging experience and physiological state (Lyimo and Ferguson, 2009; Takken and Verhulst, 2013).

The purpose of this chapter is to present the current knowledge of the role of olfaction in host selection amongst different vertebrate species by mosquitoes, with a focus on those species that are anthropophilic, i.e. prefer human hosts, and are thus potential vectors of transmissible diseases. This chapter will try to answer the following questions: How do mosquitoes recognise complex olfactory cues? What makes a host smell unique? How do specialist mosquitoes exploit this uniqueness? How have mosquitoes potentially evolved to do so? Not only are these questions academically intriguing, but they are also of significance to human health and vector control.

9.2 Methods to assess mosquito host choice and preference

Host choice of a female mosquito can readily be determined by analysing the blood meal in the midgut of engorged mosquitoes, either, historically, by precipitin test (Bruce-Chwatt *et al.*, 1966; Tempelis, 1975), or, more recently, by enzyme-linked immunosorbent assay (ELISA; Beier *et al.*, 1988; Lefèvre *et al.*, 2009b) or DNA-based methods (Molaei *et al.*, 2008; Thiemann *et al.*, 2012). Within a population of mosquitoes, different approximations for anthropophily and host choice can then be calculated. The human blood index (HBI), calculated as the proportion of blood meals obtained from humans, is widely used as a measure for anthropophily and is an important component for calculating vectorial capacity, and thus estimating the risk of, e.g. malaria transmission posed by *Anopheles* mosquitoes (Bruce-Chwatt *et al.*, 1966; Garrett-Jones, 1964). However, the HBI reflects host choice, which is not necessarily congruent with host preference, as the feeding choice of a female mosquito in nature is modulated by other factors, such as host availability (e.g. Boreham and Garrett-Jones, 1973; Zimmerman *et al.*, 2006). Related measures, such as the forage ratio (FR; Hess *et al.*, 1968), take the relative abundance of host species into account, but have been criticised for the difficulty of conducting an accurate host census and equating host abundance with availability (Kay *et al.*, 1979). The proposed alternative, the feeding index (FI; Kay *et al.*, 1979), relies on observed, in relation to expected, feeding proportions. Nonetheless, all of these measures deal with the difficulty of disentangling inherent host preference from a variety of external and internal factors, such as host density, accessibility, past foraging experience and physiological state, which demonstrate a certain degree of behavioural plasticity of mosquitoes to adapt to varying conditions (Lyimo and Ferguson, 2009; Takken and Verhulst, 2013). As an example, the sibling species *Anopheles gambiae* and *Anopheles coluzzii* (formerly *An. gambiae* S and M form, respectively; Coetzee *et al.*, 2013), are generally characterised as highly anthropophilic in both laboratory and field experiments when testing for host preference (e.g. Costantini *et al.*, 1998; Lefèvre *et al.*, 2009b; Pates *et al.*, 2001), but feed readily on cattle when humans are not abundant or not accessible due to the use of bed nets (Lefèvre *et al.*, 2009b). The use of bed nets has, in addition, been suggested as a requirement for effective zooprophylaxis, i.e. the reduced risk of human biting in the presence of non-human hosts, against highly anthropophilic mosquitoes, when humans are in close proximity to livestock (Donnelly *et al.*, 2015, but see Asale *et al.*, 2017). Another example includes *Culex pipiens*, a vector of West Nile virus, which prefers to feed on the American robin, but when birds migrate south in late summer and early fall, they switch to less preferred, but more available, mammalian hosts, including humans (Edman and Taylor, 1968; Kilpatrick *et al.*, 2006; Thiemann *et al.*, 2011). Moreover, host preference may be modulated by learning (for a general review, see Vinauger *et al.*, 2016); *Culex vishnui* females revisit select hosts after a positive feeding experience (Mwandawiro *et al.*, 2000) and *An. coluzzii* females avoid certain host species after a first negative feeding experience during which they initially did not exhibit a preference (Vantaux *et al.*, 2014). Furthermore, *Aedes aegypti* females were shown to aversively learn the odour of humans and rats, but not chickens (Vinauger *et al.*, 2018).

Consequently, experiments testing for inherent host preference in both field and laboratory settings need to be designed carefully (for a review, see Fikrig and Harrington, 2021). Since host odours are the primary cues used by mosquitoes for host discrimination (Costantini *et al.*, 1998; DeGennaro *et al.*, 2013; Lehane, 2005; McBride *et al.*, 2014; Rudolfs, 1922; Takken and Knols, 1999; Takken and Verhulst, 2013), preference should be tested in a setting that presents female mosquitoes simultaneously with two (or more) odour sources from among which to select. For this purpose, live hosts (DeGennaro *et al.*, 2013; Gillies, 1964; Lefèvre *et al.*, 2009a; McBride *et al.*, 2014; Meza *et al.*, 2019; Rose *et al.*, 2020), odour samples such as worn sleeves, animal hair or feathers (Busula *et al.*, 2015; DeGennaro *et al.*, 2013; McBride *et al.*, 2014; Verhulst *et al.*, 2018; Zhao *et al.*, 2022), headspace collections from hosts or host material (De Moraes *et al.*, 2014) or synthetic blends mimicking host odour (Busula *et al.*, 2015; Okumu *et al.*, 2010) can be used. For methods involving the presentation of host material or host-derived odours instead of live hosts, it is crucial to be aware of potential biases due to, e.g. host size, sorbent material and sampling method. In the field or semi-field, host preference assays include experimental huts with chambers containing hosts (Gillies, 1964), odour-baited traps (Busula *et al.*, 2015; Costantini *et al.*, 1999; Lefèvre *et al.*, 2009b; Okumu *et al.*, 2010), or traps using electrocuting grids surrounding host-odour sources (Meza *et al.*, 2019; Torr *et al.*, 2008). Host preference in the laboratory can be assessed using two-port olfactometers (DeGennaro *et al.*, 2013; Gouck, 1972; Knols *et al.*, 1994; McBride *et al.*, 2014; Rose *et al.*, 2020), Y-tubes (Lefèvre *et al.*, 2009a; Omondi *et al.*, 2019) or continuous observation of mosquito behaviour in a wind tunnel (Lacey *et al.*, 2014). Alternatively, well-controlled one-choice assays may be used, in which the level of attractiveness is measured for several samples individually and subsequently compared (e.g. Majeed *et al.*, 2016; Spanoudis *et al.*, 2020). Resulting from these experiments, the odour-mediated host preferences of mosquitoes may be determined, revealing consistent patterns of preference ranging from generalist to specialist.

9.3 Mosquito olfaction, host odorants and blends

Mosquitoes are equipped with a highly sophisticated olfactory system, which detects, identifies and interprets volatile chemical cues in their environment (reviewed by, e.g. Konopka *et al.*, 2021; Ruel and Bohbot, 2022; Wheelwright *et al.*, 2021). Volatile cues are detected by olfactory sensory neurons (OSNs), whose dendrites are housed in specialised sensilla on the antennae, maxillary palps and labella (Pitts *et al.*, 2022; Suh *et al.*, 2014). Odorants diffuse through pores in the cuticle of these sensilla, where they encounter odorant binding proteins that are thought to act as an initial filter and to transport the typically hydrophobic molecules through the aqueous lymph to reach the chemosensory receptors on the OSN dendrites (e.g. Leal, 2013; Pelosi *et al.*, 2018; Wheelwright *et al.*, 2021). With exceptions (Ye *et al.*, 2021; Younger *et al.*, 2022), each OSN expresses a specific set of receptor(s) belonging to either the odorant receptor (OR), ionotropic receptor (IR) or gustatory receptor (*GR*) gene families (Karner *et al.*, 2015; Suh *et al.*, 2014 and references therein). Odorant receptors, as well as IRs, form multimeric ion channels with one (orco; Larsson *et al.*, 2004) or one or more of three (Ir8a, Ir25a, or Ir76b; Abuin *et al.*, 2011; Benton *et al.*, 2009) co-receptors, respectively. Neurons expressing receptors of the OR family recognise a diverse range of volatile organic compounds (VOCs), such as terpenes, aldehydes, esters, alcohols, aromatics and ketones (Carey *et al.*, 2010), whereas the more conserved IRs have currently been shown to respond to carboxylic acids and amines (Pitts *et al.*, 2017; Raji *et al.*, 2019). Several of these chemical classes have been identified in host emanates (Bernier *et al.*, 1999, 2000, 2008; Penn *et al.*, 2007; Zhao *et al.*, 2022). Odour detection by the GR pathway is limited to carbon dioxide and acetone, key chemical cues present in exhaled breath, that are detected by a complex of two to three GRs (Ghaninia *et al.*, 2019; Liu *et al.*, 2020; Lu *et al.*, 2007; McMeniman *et al.*, 2014; Younger *et al.*, 2022). Axons of OSNs from the antennae and maxillary palps converge onto organised neuropils, called glomeruli, in the antennal lobe (AL), whereas neurons from the labella converge onto the suboesophageal zone (Ghaninia *et al.*, 2007a,b; Riabinina *et al.*, 2016). Sensory input is subsequently relayed to higher brain centres, where information is processed, evaluated and translated into a behavioural response (e.g. Galizia and Rössler, 2010; Heisenberg, 2003; Strutz *et al.*, 2014).

Human, as well as non-human, host odour are complex blends of up to hundreds of individual VOCs (Bernier *et al.*, 1999, 2000, 2008; Birkett *et al.*, 2004; Jaleta *et al.* 2016; Penn *et al.*, 2007). Of the vast spectrum of VOCs present in host odour, mosquitoes detect only a fraction, as the odour space of a species is defined and limited by the selectivity and sensitivity of their chemosensory receptor repertoire (Carey *et al.*, 2010; Omondi *et al.*, 2019; Wang *et al.*, 2010). The tuning of this repertoire, while partly overlapping with that of distantly-related taxa, appears to have evolved to detect specific VOCs present in host emanates, and reflects the ecological adaptation of the mosquito taxa (Carey *et al.*, 2010; Chen *et al.*, 2019; de Fouchier *et al.*, 2017; Pitts *et al.*, 2017; Wang *et al.*, 2010). Available functional data on ORs and IRs, furthermore, suggest that a subset of the OR repertoire, and thus its described odour space, is sufficient to regulate host discrimination in mosquitoes (DeGennaro *et al.*, 2013; McBride *et al.*, 2014; Omondi *et al.*, 2019; Pitts *et al.*, 2017).

Which are the VOCs used by mosquitoes to discriminate between host types? To address this, early studies focussed on individual compounds enriched in human sweat, but less present in the emanations of other animals, such as lactic acid and ammonia (Figure 9.1A; Braks *et al.*, 2001;

Dekker *et al.*, 2002; Smallegange *et al.*, 2005). Lactic acid is approximately 10-times more abundant in human skin emanates than in the emanates of other vertebrates tested, and, while not attractive on its own, attracts female *An. gambiae* and *Ae. aegypti* in combination with carbon dioxide, which is required for activating and gating host-seeking mosquitoes (Acree *et al.*, 1968; Dekker *et al.*, 2002, 2005; McMeniman *et al.*, 2014). Adding lactic acid to cattle odour increases the attraction of *An. gambiae* to a level similar to that to human odour (Dekker *et al.*, 2002), as previously demonstrated for non-attractive animal odours in *Ae. aegypti* (Steib *et al.*, 2001). Such context-dependent behavioural response of *Ae. aegypti* and *An. coluzzii* has also been shown for (*R*)-1-octen-3-ol, a salient mammalian-associated odorant, when added to a background of chicken odour (Majeed *et al.*, 2016). These and other examples, such as ammonia (Braks *et al.*, 2001; Geier *et al.*, 1999; Smallegange *et al.*, 2005), demonstrate that individual compounds do not elicit robust attraction mimicking the behavioural response to more complex host odours. The limitations of using individual or a subset of volatile compounds outside of their ecological context, and neglecting natural release rates, are evident by recent studies demonstrating that blends of salient odour cues, acting additively or synergistically, are consistently more attractive than individual compounds, often eliciting a behavioural response at natural release rates and lower thresholds (Bosch *et al.*, 2000; Mukabana *et al.*, 2012; Okumu *et al.*, 2010; Omondi *et al.*, 2019; Smallegange *et al.*, 2005, 2009; Zhao *et al.*, 2022). This is also true for lactic acid and ammonia when presented in more complex blends (Bosch *et al.*, 2000; Okumu *et al.*, 2010; Smallegange *et al.*, 2005, 2009). Increasing the release rate of individual compounds or of the blend beyond that found naturally in the environment often decreases attraction or elicits avoidance in host-seeking mosquitoes (Logan *et al.*, 2010; Majeed *et al.*, 2016; Menger *et al.*, 2014; Smallegange *et al.*, 2005), likely due to unspecific activation of chemosensory receptors, habituation or sensory adaptation (Andersson *et al.*, 2015; Carey *et al.*, 2010; Hallem and Carlson, 2006; Stengl *et al.*, 1992). Taken together, early studies indicated the differential presence of individual VOCs in host emanates, with more recent studies emphasising the importance of the blend context of these VOCs for robust attraction to potential hosts, and suggesting a role for individual VOCs in host discrimination (Figure 9.1A).

Combined chemical and electrophysiological analyses have enabled the identification of bioactive VOCs in the odour profile of different host species, identifying many compounds that are shared between host species (Figure 9.1B) and other fitness-related resources, such as nectar sources and oviposition sites (e.g. Ignell and Hill, 2020; Takken and Knols, 1999). This concept, termed chemical parsimony, describes that a VOC may occur in multiple contexts and serve different functions, reflecting conserved biosynthetic pathways (Blum, 1996). A ketone highly abundant in human odour, sulcatone, is a candidate odorant mediating host discrimination in *Ae. aegypti* (Figure 9.1A; McBride *et al.*, 2014), but is also common in floral emanates (Knudsen *et al.*, 2006), indicating an additional role outside the context of the animal host (Dekel *et al.*, 2019). Many aldehydes, for example nonanal and decanal, are likewise parsimonious compounds that are differentially abundant within and among host species (Figure 9.1A), nectar sources and oviposition sites (Bernier *et al.*, 2008; Curran *et al.*, 2005; Ignell and Hill, 2020; Omondi *et al.*, 2019; Syed and Leal, 2009; Wondwosen *et al.*, 2016, 2017; Zhao *et al.*, 2022). Increasing evidence suggests that parsimonious compounds make up the core of host odour blends, and that the differential abundance of these VOCs, in concert with other salient host compounds, create the odour signatures that are detected by the olfactory system of mosquitoes and used for host discrimination.

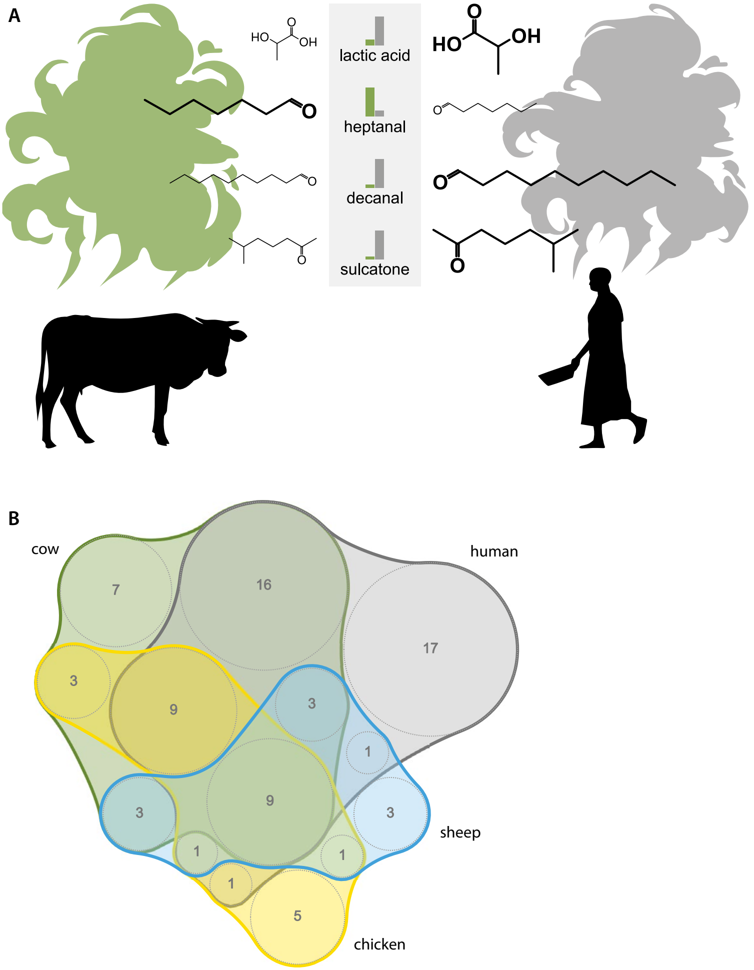

Figure 9.1. Volatile organic compounds are used by mosquitoes for host species discrimination. (A) Select generic volatile organic compounds (VOCs) released at different rates from cattle and human may be exploited by mosquitoes for discriminating among these potential hosts. (B) Quasi-proportional Venn diagram of VOCs emitted by different potential host species that have been shown to elicit a physiological response in female vector mosquitoes. Generic, often parsimonious, VOCs, along with VOCs tentatively identified as species-specific, provide the basis by which female mosquitoes may select and discriminate among potential hosts. Note that the diagram may be biased towards human VOCs and that further analysis will be required to define species-specific and generic VOCs. Data from Allan *et al.* (2006), Bernier *et al.* (2008), Birkett *et al.* (2004), Bosch *et al.* (2000), Bowen (1992), Cooperband *et al.* (2008), Cork and Park (1996), Costantini *et al.* (2001), Curran *et al.* (2005), Ghaninia *et al.* (2019), Gikonyo *et al.* (2002), Harraca *et al.* (2009), Healy *et al.* (2002), Isberg *et al.* (2016), Jaleta *et al.* (2016), Jhumur *et al.* (2007), Knols *et al.* (1997), Majeed *et al.* (2016), Meijerink *et al.* (2000), Mukabana *et al.* (2012), Nyasembe *et al.* (2018), Omondi *et al.* (2019), Owino *et al.* (2015), Peled *et al.* (2012), Penn *et al.* (2007), Qiu *et al.* (2006), Raji *et al.* (2019), Robinson *et al.* (2018), Seenivasagan *et al.* (2014), Smallegange *et al.* (2009), Tchouassi *et al.* (2013), Van den Broek and Den Otter (1999) and Zhao *et al.* (2022), supplemented with unpublished data from RI. Method for quasi-proportional Venn diagram visualisation: Pérez-Silva *et al.* (2018).

Using our current knowledge on the human odour signature detected by mosquitoes, we can start speculating on how female mosquitoes may discriminate among different host types. Sulcatone, geranylacetone and the long-chain aldehydes, decanal and undecanal, are considered human marker compounds, as they are consistently found in higher abundance in human than in non-human emanations (Figure 9.1A; McBride *et al.*, 2014; Zhao *et al.*, 2022). Moreover, these are breakdown products of human sebum (Wisthaler and Weschler, 2010). Human odour, on the other hand, contains a low proportion of short-chain aldehydes, such as hexanal and heptanal, which are more abundant in other animals (Figure 9.1A; Bernier *et al.*, 2008; Zhao *et al.*, 2022), including our closest living relatives, bonobos and chimpanzees (Verhulst *et al.*, 2018). The human odour signature, as defined by both quantitative and qualitative differences in salient and generic VOCs, elicits a unique response in the primary olfactory centre of *Ae. aegypti*, which differs from that elicited by other animal host odours (Zhao *et al.*, 2022). The relative activation of a glomerulus narrowly tuned to long-chain aldehydes and a broadly-receptive glomerulus tuned to generic compounds found in host emanates is sufficient to drive the host-seeking behaviour of this mosquito species. Such combinatorial coding likely allows mosquitoes to recognise and differentiate among different host species.

To further discern the mechanism underlying odour-mediated host discrimination by mosquitoes, it will be critical to expand the analysis to include a larger number of hosts, potential hosts and known non-hosts, as well as to create a platform for high resolution chemical analysis allowing for direct cross-comparison. Once the odour compositions of these species are available, it will be possible to deduce the salient characteristics, which make a host odour, be it human or other, unique and which features are exploited by specialist and generalist mosquitoes. Increasing the complexity of the system, individuals of the same host species show distinct variation within the host odour signature (Qiu *et al.*, 2006; Verhulst *et al.*, 2011, 2018; Zhao *et al.*, 2022). Host odour coding thus needs to be flexible enough to account for intra-specific differences, while being stereotyped enough to discriminate between host and non-host odour.

9.4 Genes, receptors and neurons underlying host preference

The question of how mosquitoes evolved various host preferences by exploiting the uniqueness of host odours can be approached on several levels (Arguello and Benton, 2017; Cande *et al.*, 2013; Zhao and McBride, 2020). First, structural changes, or changes in the expression level of chemosensory and/or regulatory genes, may alter neural specificity and sensitivity to salient host VOCs. Second, changes in the number of neurons or neural connectivity in both the peripheral and central nervous systems may modulate the detection, coding and evaluation of odour stimuli. Fundamental to the exploration of these approaches is undoubtedly the hereditability of host preference, which initially gained attention in the 1960s and 70s, when Gillies (1964) and Mukwaya (1977) performed selection and crossing experiments with mosquito populations of different host preferences. Gillies (1964) demonstrated that it is possible to alter the host preference of *An. gambiae* females, within a few generations of continued selection. A similar selection experiment with anthropophilic *Ae. aegypti* mosquitoes by Mukwaya (1977) was inconclusive, but crosses of anthropophilic and non-anthropophilic strains of *Ae. aegypti* and *Ae. simpsoni*, revealed an intermediate host preference of the offspring, respectively. Subsequent studies on

Anopheles identified specific chromosomal arrangements associated with feeding preference (Lulu *et al.*, 1998; Main *et al.*, 2016; Petrarca and Beier, 1992), although these results may be biased by sampling methodology, host availability and habitat preference (e.g. Main *et al.*, 2016; Meza *et al.*, 2019; Mlacha *et al.*, 2020; Tambwe *et al.*, 2021). Thus, while early studies did not have the means to identify underlying genes, chemosensory receptors or neuronal mechanisms, they clearly demonstrated a genetic component of host preference. With advancing molecular tools, the identification of the first insect odorant receptor genes in *Drosophila melanogaster* (Clyne *et al.*, 1999; Gao and Chess, 1999; Vosshall *et al.*, 1999) and the release of the genome of *An. gambiae* and other mosquito species (Arensburger *et al.*, 2010; Holt *et al.*, 2002; Neafsey *et al.*, 2015; Nene *et al.*, 2007), it is now feasible to correlate differences in gene and microsyntenic structure, as well as expression levels of chemosensory receptors, with anthropophily and host preference in general (DeGennaro *et al.*, 2013; Rinker *et al.*, 2013; McBride *et al.*, 2014; Main *et al.*, 2016). As a result, the molecular and neuronal mechanisms of host choice have received increased attention in the last few years, driven by technological advancements in, e.g. next generation sequencing and gene editing tools for mosquitoes (e.g. reviewed in Chen *et al.*, 2021; Reegan *et al.*, 2016; Riabinina *et al.*, 2016; Zhao *et al.*, 2021).

A major breakthrough for identifying the mechanism regulating host discrimination was the study by DeGennaro *et al.* (2013), which demonstrated that the OR pathway is crucial for *Ae. aegypti* to discriminate human from non-human hosts, by knock-out of the OR co-receptor, *orco*. While female *orco* mutants are still attracted to host odours, they no longer prefer human over non-human odour, suggesting that *Ae. aegypti*, and most likely mosquitoes in general, rely on ORs, IRs and GRs to convey signals regulating host attraction, with ORs, in addition, being crucial for host discrimination. In support of this hypothesis, McBride *et al.* (2014) compared the OR repertoire of two subspecies of *Ae. aegypti* with diverging host preferences, the anthropophilic 'domestic' form and the ancestral 'forest' form, which is zoophilic in its host preference. The study found a significant association between mosquito host preference, and both expression and ligand-sensitivity of *AaegOr4*, a receptor responding to sulcatone, a compound enriched in human body odour. In comparison to the zoophilic subspecies, the anthropophilic subspecies demonstrated a higher level of transcript abundance of *AaegOr4*, and expressed several allelic variants that had a higher binding affinity to its ligand sulcatone. Notably, adding sulcatone to the non-preferred guinea pig odour did not elicit a preference in anthropophilic mosquito strains, indicating that although *AaegOr4* expression and sensitivity is tightly associated with host preference, it is likely not the only olfactory pathway involved (McBride *et al.*, 2014). Moreover, while sensitivity to sulcatone may be important in host discrimination, the mechanism by which it is detected is not shared across mosquito species, as there is no orthologue for *AaegOr4* in *Anopheles* mosquitoes (Neafsey *et al.*, 2015), although several *Anopheles* ORs are responsive to sulcatone (Carey *et al.*, 2010; Omondi *et al.*, 2019). Other studies comparing the genome or transcriptome of closely-related species with diverging host preference support the hypothesis that host specialisation is not driven by the evolution of any single host-specific *OR*, but by several changes in *OR* abundance and function that resulted in a receptivity bias towards odours associated with specific hosts (Athrey *et al.*, 2017; Main *et al.*, 2016; Neafsey *et al.*, 2015; Rinker *et al.*, 2013). Differential antennal transcriptome analyses of the closely-related anthropophilic *An. coluzzii* (then named *An. gambiae s.s.*, M form; Coetzee *et al.*, 2013) and the zoophilic *Anopheles quadriannulatus* identified several amino acid changes between orthologous ORs in regions that may affect their function (Rinker *et al.*, 2013). To test this, Rinker *et al.* (2013) used *in silico* modelling, suggesting that the odour receptivity of the specialist *An. coluzzii* is a refinement of the broadly-receptive generalist sibling species *An. quadriannulatus*. Not only are these refinements found to be changes in sensitivity, but they can also reflect regulation of selectivity and pattern of expression, as demonstrated for the *Cx. quinquefasciatus Or8* paralogous receptors, *CquiOr113*, *CquiOr114b* and *CquiOr118b* (Hill *et al.*, 2015; Xu *et al.*, 2015). While all current evidence support ORs as the regulators of host preference, at this point we cannot fully exclude the possibility that other chemosensory genes may play a role in host discrimination. The aforementioned studies identified additional significant and prominent differences in gene sequences and transcription levels of chemosensory genes outside the class of *OR*s (Athrey *et al.*, 2017; McBride *et al.*, 2014; Rinker *et al.*, 2013), specifically *IR*s. Further functional characterisation of ORs and the largely overlooked IRs is thus crucial to identify potential candidate receptors involved in mediating mosquito host preference.

Comparative *in vivo* single sensillum recordings, in which the response of single OSNs to synthetic host VOCs were assessed, further support the hypothesis that differences in host preference is reflected in the sensitivity and proportion of OSNs responding to host or non-host VOCs, and the complete loss or gain of OSN types (Ghaninia *et al.*, 2019; Majeed *et al.*, 2016, 2017; McBride *et al.*, 2014; Van den Broek and Den Otter, 1999; Zhao and McBride, 2020 and references therein). Support for this hypothesis is most evident in studies comparing the OSN repertoire of the closely related species within the *An. gambiae* complex that differ in host preference (Ghaninia and Ignell, unpublished data; Van den Broek and Den Otter, 1999). These studies demonstrate a correlation between host preference and the sensitivity and the number of functional classes of OSNs tuned to host VOCs, such as phenolic derivatives, geranylacetone, 1-octen-3-ol and fatty acids. This suggests that evolutionary adaptation for specific hosts or a host range is regulated by changes at the peripheral olfactory system, determined by the type and expression of endogenous chemosensory receptors on the OSN dendrites (Hallem *et al.*, 2004; McBride *et al.*, 2014; Rinker *et al.*, 2013).

At the level of the central olfactory circuitry, host preference may be regulated by differential weighing of the input from the peripheral olfactory system by second order neurons in the antennal lobe (AL), and further processing in higher brain centres (Zhao and McBride, 2020 and references therein). While there currently is no study targeting the central mechanisms of host preference directly, a recent study in *Ae. aegypti* by Zhao *et al.* (2022) proposed a coding mechanism by which human and non-human odours can be discriminated at the AL level. These authors demonstrated that human and non-human odours elicit activation of distinct combinations of glomeruli, and that human odour in particular elicits activity in a specialised glomerulus tuned to the long-chain aldehydes decanal and undecanal. Furthermore, the authors proposed a model in which human identity is encoded by the relative activation of the 'human-specific' and a broadly tuned glomerulus, and demonstrated that a synthetic binary blend mimicking the human ratio of glomerular activation was sufficient to elicit host-seeking behaviour. Whether the distinct activation of AL glomeruli by human and non-human odours is sufficient to convey odour valence to higher brain centres, as described in *D. melanogaster*, remains to be assessed (Knaden *et al.*, 2012; Mohamed *et al.*, 2019; Strutz *et al.*, 2014).

Future exploration, using state-of-the-art tools, e.g. gene editing, gene drive and inducible gene expression, will facilitate the identification and characterisation of the neural circuitry underlying host discrimination and choice in mosquitoes (Chen *et al.*, 2021; Riabinina *et al.*, 2016; Sorrells *et al.*, 2021; Zhao *et al.*, 2021). For this purpose, the study by Auer *et al.* (2020) in *Drosophila* may serve as a benchmark to demonstrate adaptations in receptor tuning and neuronal connectivity underlying behavioural divergence. Despite correlative links between olfactory gene expression, neural function and host preference, no causal evidence of such links has yet been provided. A compelling experiment would be to genetically knock out a candidate receptor and rescue that knockout with the ectopic expression of its orthologous receptor, mediating species-specific host preference endogenously or in a related mosquito species. While a knockdown study of two ORs in *Ae. albopictus* by Liu *et al.* (2016) did not find an effect on host discrimination, two studies in *Drosophila* were the first to establish a causal connection between genetic differences in OR gene sequence and resource preference (Auer *et al.*, 2020; Matsunaga *et al.*, 2022).

9.5 Evolution of host specialisation in mosquitoes

Based on the principles of natural selection, resource specialisation in any species evolves only if it is associated with benefits for the reproductive success of an animal (MacArthur and Pianka, 1966). Although females of most mosquito species are generalists or poly-specialists (Clements, 1999; Lehane, 2005), i.e. they feed randomly on hosts or a host range present in their habitat, there are intriguing examples of host specialists, such as *Uranotaenia rutherfordi*, which appears to feed exclusively on the Kandian shrub frog (de Silva *et al.*, 2020). Due to their involvement in disease transmission, most research has inevitably focused on the few mosquito species that have evolved a preference for humans, such as *Ae. aegypti*, *An. gambiae* and *An. coluzzii* that vector infection to more than 300 million people, resulting in 700,000 deaths annually (World Health Organization, 2020). However, while our understanding of the evolution of host specialisation is biased towards humans, the principles may be applicable to other species.

Anthropophily likely arose concomitantly with the increase in human population density, starting from circa 10,000 years ago during the course of the Neolithic revolution, in which many human societies transitioned from nomadic hunting and gathering to agriculture and settlements (Ayala and Coluzzi, 2005; Besansky *et al.*, 1994). At this time, humans became more numerous and sedentary, making this host resource increasingly predictable. Intense human land-use, accompanied by deforestation and irrigation, furthermore provided ample breeding sites for mosquitoes (Besansky *et al.*, 2004; Lyimo and Ferguson, 2009; Rose *et al.*, 2020). Genetic studies of both mosquito and human populations confirm that anthropophilic subpopulations of, e.g. *Ae. aegypti* and *Cx. pipiens* evolved within this time frame (Besansky *et al.*, 2004; Crawford *et al.*, 2017; Fonseca *et al.*, 2004), and select *An. gambiae s.l.* evolved a preference for human hosts (White *et al.*, 2011), as indicated by human adaptation to high malaria mortality occurring within the last 6,000 years (Flint *et al.*, 1993; Tishkoff *et al.*, 2001). Anthropophily in mosquitoes likely evolved several times independently, as major speciation events in mosquitoes occurred long before the emergence of hominins about 4.5 million years ago (Krzywinski *et al.*, 2006; Neafsey *et al.*, 2015; Prüfer *et al.*, 2012). The two genera of *Aedes* and *Anopheles* diverged about 145 to 226 million years ago (Krzywinski *et al.*, 2006; Reidenbach *et al.*, 2009), with several species-specific expansions of the chemosensory gene repertoire observed to date (Arensburger *et al.*, 2010; Bohbot *et al.*, 2007; Neafsey *et al.*, 2015). As an example, the number of OR genes range from 77 in *An. gambiae s.s.* (Neafsey *et al.*, 2015) to 117 in *Ae. aegypti* (Matthews *et al.*, 2018) and 180 in *Cx. quinquefasciatus* (Arensburger *et al.*, 2010). From an evolutionary perspective, it is interesting how these anthropophilic mosquito species have resolved the same problem of differentiating human odour from that of other species by using an overlapping, yet divergent, chemosensory repertoire.

Two main hypotheses, while not mutually exclusive, have been proposed to explain the evolution of anthropophily in mosquitoes (Costantini *et al.*, 1999; Lyimo and Ferguson, 2009; Powell *et al.*, 2018; Rose *et al.*, 2020). First, anthropophily may have arisen as a result of direct fitness benefits from feeding on humans. Dietary speciation is predicted to evolve if there is a trade-off between using a limited versus a large variety of food resources (Egas *et al.*, 2004; Futuyma and Moreno, 1988; Jaenike, 1990; MacArthur and Pianka, 1966; Pyke *et al.*, 1997). In mosquito evolution, specialism may be advantageous when one host species is abundant and there are additional fitness advantages, such as high energetic gains of feeding on that host or low host defensive behaviour (Lyimo and Ferguson, 2009). Generalism, however, may be favoured when the chance of encountering a specific host species is low and/or there are limited fitness advantages from feeding on a restricted host range. Mosquito reproduction and survival does indeed vary with the host type on which they feed, but reports on the nutritional benefits of human blood for anthropophilic mosquitoes diverge in their conclusion (Harrington *et al.*, 2001; Lyimo *et al.*, 2012; Nayar and Sauerman Jr, 1977; Woke, 1937). Secondly, anthropophily might be a by-product of mosquitoes seeking and adapting to favourable microhabitats associated with human dwellings, with benefits either for individual survival and/or for breeding (Costantini *et al.*, 1999; Powell *et al.*, 2018; Rose *et al.*, 2020). Recent work by Rose *et al.* (2020) in *Ae. aegypti* found a strong association between human preference and dry season intensity, suggesting seasonal dependence on human-made breeding sites, such as stored water, as a key factor driving the evolution of anthropophily. Thus, human feeding preference may have evolved due to specialisation to the reliantly high abundance of humans in close proximity. In the context of other, non-anthropophilic, specialist mosquito species, the evolution of host specialisation may have been driven by similar mechanisms. Whether the preference for a limited variety of host species is a cause or an outcome of specialisation remains open (Futuyma and Moreno, 1988).

9.6 Conclusion and future perspectives

While there has been significant progress in our understanding of the mechanisms regulating odour-mediated host discrimination in mosquitoes, there are still many open questions to address. The initial step would be to extend the analysis of the odour profiles of potential host species in order to pave the way for extensive comparative studies determining qualitative and quantitative differences in volatile composition. Second, chemosensory receptors mediating host preference require systematic deorphanisation and recharacterisation, using ecologically relevant odours and concentrations, including both ORs and IRs. Third, despite correlative evidence, experimental support is required to describe causative links among receptor expression, function and neural circuits with host discrimination, using the constantly improving and expanding tool set of genetic methods in mosquitoes. Ultimately, understanding the regulation of mosquito host preference may aid in developing new tools and strategies to control mosquito populations and thus reduce disease transmission. Promising approaches are zooprophylaxis, the development of novel lures for odour-baited traps (e.g. Homan *et al.*, 2016; Okumu *et al.*, 2010) and the identification of repellent compounds from non-hosts (e.g. Jaleta *et al.*, 2016). While further analysis is required for identifying and evaluating the active VOCs, the major constraints to overcome are the cost, time and corporate partners required for meeting regulations and subsequent registration of novel odour-based tools.

Acknowledgements

We would like to thank our two reviewers for their valuable comments.

References

Abuin, L., Bargeton, B., Ulbrich, M.H., Isacoff, E.Y., Kellenberger, S. and Benton, R., 2011. Functional architecture of olfactory ionotropic glutamate receptors. Neuron 69: 44-60. http://doi.org/10.1016/j.neuron.2010.11.042

Acree, F., Turner, R.B., Gouck, H.K., Beroza, M. and Smith, N., 1968. L-Lactic acid: a mosquito attractant isolated from humans. Science 161: 1346-1347. http://doi.org/10.1126/science.161.3848.1346

Allan, S.A., Bernier, U.R. and Kline, D.L., 2006. Attraction of mosquitoes to volatiles associated with blood. Journal of Vector Ecology 31: 71-78. https://doi.org/10.3376/1081-1710(2006)31[71:AOMTVA]2.0.CO;2

Andersson, M.N., Löfstedt, C. and Newcomb, R.D., 2015. Insect olfaction and the evolution of receptor tuning. Frontiers in Ecology and Evolution 3: 53. https://doi.org/10.3389/fevo.2015.00053

Arensburger, P., Megy, K., Waterhouse, R.M., Abrudan, J., Amedeo, P., Antelo, B., Bartholomay, L., Bidwell, S., Caler, E., Camara, F., Campbell, C.L., Campbell, K.S., Casola, C., Castro, M.T., Chandramouliswaran, I., Chapman, S.B., Christley, S., Costas, J., Eisenstadt, E., Feschotte, C., Fraser-Liggett, C., Guigo, R., Haas, B., Hammond, M., Hansson, B.S., Hemingway, J., Hill, S.R., Howarth, C., Ignell, R., Kennedy, R.C., Kodira, C.D., Lobo, N.F., Mao, C., Mayhew, G., Michel, K., Mori, A., Liu, N., Naveira, H., Nene, V., Nguyen, N., Pearson, M.D., Pritham, E.J., Puiu, D., Qi, Y., Ranson, H., Ribeiro, J.M.C., Roberston, H.M., Severson, D.W., Shumway, M., Stanke, M., Strausberg, R.L., Sun, C., Sutton, G., Tu, Z., Tubio, J.M.C., Unger, M.F., Vanlandingham, D.L., Vilella, A.J., White, O., White, J.R., Wondji, C.S., Wortman, J., Zdobnov, E.M., Birren, B., Christensen, B.M., Collins, F.H., Cornel, A., Dimopoulos, G., Hannick, L.I., Higgs, S., Lanzaro, G.C., Lawson, D., Lee, N.H., Muskavitch, M.A.T., Raikhel, A.S. and Atkinson, P.W., 2010. Sequencing of *Culex quinquefasciatus* establishes a platform for mosquito comparative genomics. Science 330: 86-88. https://doi.org/10.1126/science.1191864

Arguello, J.R. and Benton, R., 2017. Open questions: Tackling Darwin's 'instincts': the genetic basis of behavioral evolution. BMC Biology 15: 26. https://doi.org/10.1186/s12915-017-0369-3

Asale, A., Duchateau, L., Devleesschauwer, B., Huisman, G. and Yewhalaw, D., 2017. Zooprophylaxis as a control strategy for malaria caused by the vector *Anopheles arabiensis* (Diptera: Culicidae): a systematic review. Infectious Diseases of Poverty 6: 160. https://doi.org/10.1186/s40249-017-0366-3

Athrey, G., Cosme, L.V., Popkin-Hall, Z., Pathikonda, S., Takken, W. and Slotman, M.A., 2017. Chemosensory gene expression in olfactory organs of the anthropophilic *Anopheles coluzzii* and zoophilic *Anopheles quadriannulatus*. BMC Genomics 18: 751. https://doi.org/10.1186/s12864-017-4122-7

Auer, T.O., Khallaf, M.A., Silbering, A.F., Zappia, G., Ellis, K., Álvarez-Ocaña, R., Arguello, J.R., Hansson, B.S., Jefferis, G.S.X.E., Caron, S.J.C., Knaden, M. and Benton, R., 2020. Olfactory receptor and circuit evolution promote host specialization. Nature 579: 402-408. https://doi.org/10.1038/s41586-020-2073-7

Ayala, F.J. and Coluzzi, M., 2005. Chromosome speciation: humans, *Drosophila*, and mosquitoes. Proceedings of the National Academy of Sciences of the USA 102: 6535-6542. https://doi.org/10.1073/pnas.0501847102

Beier, J.C., Perkins, P.V., Wirtz, R.A., Koros, J., Diggs, D., Gargan, T.P. and Koech, G., 1988. Bloodmeal identification by direct enzyme-linked immunosorbent assay (ELISA), tested on *Anopheles* (Diptera: Culicidae) in Kenya. Journal of Medical Entomology 25: 9-16. https://doi.org/10.1093/jmedent/25.1.9

Benton, R., Vannice, K.S., Gomez-Diaz, C. and Vosshall, L.B., 2009. Variant ionotropic glutamate receptors as chemosensory receptors in *Drosophila*. Cell 136: 149-162. https://doi.org/10.1016/j.cell.2008.12.001

Bernier, U.R., Allan, S.A., Quinn, B.P., Kline, D.L., Barnard, D.R. and Clark, G.G., 2008. Volatile compounds from the integument of White Leghorn chickens (*Gallus gallus domesticus* L.): candidate attractants of ornithophilic mosquito species. Journal of Separation Science 31: 1092-1099. https://doi.org/10.1002/jssc.200700434

Bernier, U.R., Booth, M.M. and Yost, R.A., 1999. Analysis of human skin emanations by gas chromatography/mass spectrometry. 1. Thermal desorption of attractants for the yellow fever mosquito (*Aedes aegypti*) from handled glass beads. Analytical Chemistry 71: 1-7. https://doi.org/10.1021/ac980990v

Bernier, U.R., Kline, D.L., Barnard, D.R., Schreck, C.E. and Yost, R.A., 2000. Analysis of human skin emanations by gas chromatography/mass spectrometry. 2. Identification of volatile compounds that are candidate attractants for the yellow fever mosquito (*Aedes aegypti*). Analytical Chemistry 72: 747-756. https://doi.org/10.1021/ac990963k

Besansky, N.J., Hill, C.A. and Costantini, C., 2004. No accounting for taste: host preference in malaria vectors. Trends in Parasitology 20: 249-251. https://doi.org/10.1016/j.pt.2004.03.007

Besansky, N.J., Powello, J.R., Cacconet, A., Hamm, D.M., Scott, J.A. and Collins, F.H., 1994. Molecular phylogeny of the *Anopheles gambiae* complex suggests genetic introgression between principal malaria vectors. Proceedings of the National Academy of Sciences of the USA 91: 6885-6888. https://doi.org/10.1073/pnas.91.15.6885

Birkett, M.A., Agelopoulos, N., Jensen, K.M., Jespersen, J.B., Pickett, J.A., Prijs, H.J., Thomas, G., Trapman, J.J., Wadhams, L.J. and Woodcock, C.M., 2004. The role of volatile semiochemicals in mediating host location and selection by nuisance and disease-transmitting cattle flies. Medical and Veterinary Entomology 18: 313-322. https://doi.org/10.1111/j.0269-283X.2004.00528.x

Blum, M.S., 1996. Semiochemical parsimony in the Arthropoda. Annual Review of Entomology 41: 353-374. https://doi.org/10.1146/annurev.en.41.010196.002033

Bohbot, J., Pitts, R.J., Kwon, H.W., Rützler, M., Robertson, H.M. and Zwiebel, L.J., 2007. Molecular characterization of the *Aedes aegypti* odorant receptor gene family. Insect Molecular Biology 16: 525-537. https://doi.org/10.1111/j.1365-2583.2007.00748.x

Boreham, P.F.L. and Garrett-Jones, C., 1973. Prevalence of mixed blood meals and double feeding in a malaria vector (*Anopheles sacharovi* Favre). Bulletin of the World Health Organization 48: 605-614.

Bosch, O.J., Geier, M. and Boeckh, J., 2000. Contribution of fatty acids to olfactory host finding of female *Aedes aegypti*. Chemical Senses 25: 323-330. https://doi.org/10.1093/oxfordjournals.chemse.a014042

Bowen, M.F., 1992. Terpene-sensitive receptors in female *Culex pipiens* mosquitoes: electrophysiology and behaviour. Journal of Insect Physiology 38: 759-764. https://doi.org/10.1016/0022-1910(92)90028-C

Braks, M.A.H., Meijerink, J. and Takken, W., 2001. The response of the malaria mosquito, *Anopheles gambiae*, to two components of human sweat, ammonia and L-lactic acid, in an olfactometer. Physiological Entomology 26: 142-148. https://doi.org/10.1046/j.1365-3032.2001.00227.x

Bruce-Chwatt, L.J., Garrett-Jones, C. and Weitz, B., 1966. Ten years' study (1955-64) of host selection by anopheline mosquitos. Bulletin of the World Health Organization 35: 405.

Busula, A.O., Takken, W., Loy, D.E., Hahn, B.H., Mukabana, W.R. and Verhulst, N.O., 2015. Mosquito host preferences affect their response to synthetic and natural odour blends. Malaria Journal 14: 133. https://doi.org/10.1186/s12936-015-0635-1

Cande, J., Prud'homme, B. and Gompel, N., 2013. Smells like evolution: the role of chemoreceptor evolution in behavioral change. Current Opinion in Neurobiology 23: 152-158. https://doi.org/10.1016/j.conb.2012.07.008

Cardé, R.T., 2015. Multi-cue integration: how female mosquitoes locate a human host. Current Biology 25: R793-R795. https://doi.org/10.1016/j.cub.2015.07.057

Carey, A.F., Wang, G., Su, C., Zwiebel, L.J. and Carlson, J.R., 2010. Odorant reception in the malaria mosquito *Anopheles gambiae*. Nature 464: 66-71. https://doi.org/10.1038/nature08834

Chen, J., Luo, J., Gurav, A.S., Chen, Z., Wang, Y. and Montell, C., 2021. A DREaMR system to simplify combining mutations with rescue transgenes in *Aedes aegypti*. Genetics 219: iyab147. https://doi.org/10.1093/genetics/iyab146

Chen, Z., Liu, F. and Liu, N., 2019. Human odour coding in the yellow fever mosquito, *Aedes aegypti*. Scientific Reports 9: 13336. https://doi.org/10.1038/s41598-019-49753-2

Clements, A.N., 1999. The biology of mosquitoes. Volume 2: sensory reception and behaviour. CABI publishing, Wallingford, UK, pp. 752.

Clyne, P.J., Warr, C.G., Freeman, M.R., Lessing, D., Kim, J. and Carlson, J.R., 1999. A novel family of divergent seven-transmembrane proteins: candidate odorant receptors in *Drosophila*. Neuron 22: 327-338. https://doi.org/10.1016/S0896-6273(00)81093-4

Coetzee, M., Hunt, R.H., Wilkerson, R., della Torre, A., Coulibaly, M.B. and Besansky, N.J., 2013. *Anopheles coluzzii* and *Anopheles amharicus*, new members of the *Anopheles gambiae* complex. Zootaxa 3619: 246-274. https://doi.org/10.11646/zootaxa.3619.3.2

Cooperband, M.F., McElfresh, J.S., Millar, J.G. and Carde, R.T., 2008. Attraction of female *Culex quinquefasciatus* Say (Diptera: Culicidae) to odors from chicken feces. Journal of Insect Physiology 54: 1184-1192. https://doi.org/10.1016/j.jinsphys.2008.05.003

Cork, A. and Park, K.C., 1996. Identification of electrophysiologically-active compounds for the malaria mosquito, *Anopheles gambiae*, in human sweat extracts. Medical and Veterinary Entomology 10: 269-276. https://doi.org/10.1111/j.1365-2915.1996.tb00742.x

Costantini, C., Sagnon, N., della Torre, A., Diallo, M., Brady, J., Gibson, G. and Coluzzi, M., 1998. Odor-mediated host preferences of West African mosquitoes, with particular reference to malaria vectors. American Journal of Tropical Medicine and Hygiene 58: 56-63.

Costantini, C., Sagnon, N.F., Torre, A.D. and Coluzzi, M., 1999. Mosquito behavioural aspects of vector-human interactions in the *Anopheles gambiae* complex. Parassitologia 41: 209-220.

Costantini, C., Birkett, M.A., Gibson, G., Ziesmann, J., Sagnon, N.F. and Mohammed, H.A., 2001. Electroantennogram and behavioural responses of the malaria vector *Anopheles gambiae* to human-specific sweat components. Medical and Veterinary Entomology 15: 259-266. https://doi.org/10.1046/j.0269-283x.2001.00297.x

Crawford, J.E., Alves, J.M., Palmer, W.J., Day, J.P., Sylla, M., Ramasamy, R., Surendran, S.N., Black, W.C., Pain, A. and Jiggins, F.M., 2017. Population genomics reveals that an anthropophilic population of *Aedes aegypti* mosquitoes in West Africa recently gave rise to American and Asian populations of this major disease vector. BMC Biology 15: 1-16. https://doi.org/10.1186/s12915-017-0351-0

Curran, A.M., Rabin, S.I., Prada, P.A. and Furton, K.G., 2005. Comparison of the volatile organic compounds present in human odor using SPME-GC/MS. Journal of Chemical Ecology 31: 1607-1619. https://doi.org/10.1007/s10886-005-5801-4

de Fouchier, A., Walker, W.B., Montagne, N., Steiner, C., Binyameen, M., Schlyter, F., Chertemps, T., Maria, A., François, M-C., Monsempes, C., Anderson, P., Hansson, B.S., Larsson, M.C. and Jacquin-Joly, E., 2017. Functional evolution of Lepidoptera olfactory receptors revealed by deorphanization of a moth repertoire. Nature 8: 15709. https://doi.org/10.1038/ncomms15709 de Silva, W.P.P., Bernal, X.E., Chathuranga, W.G.D., Herath, B.P., Ekanayake, C., Abeysundara, H.T.K. and Karunaratne, S.H.P.P., 2020. Feeding patterns revealed host partitioning in a community of frog-biting mosquitoes. Ecological Entomology 45: 988-996. https://doi.org/10.1111/een.12874.

DeGennaro, M., McBride, C.S., Seeholzer, L., Nakagawa, T., Dennis, E.J., Goldman, C., Jasinskiene, N., James, A.A. and Vosshall, L.B., 2013. Orco mutant mosquitoes lose strong preference for humans and are not repelled by volatile DEET. Nature 498: 487-491. https://doi.org/10.1038/nature12206

Dekel, A., Yakir, E. and Bohbot, J.D., 2019. The sulcatone receptor of the strict nectar-feeding mosquito *Toxorhynchites amboinensis*. Insect Biochemistry and Molecular Biology 111: 103174. https://doi.org/10.1016/j.ibmb.2019.05.009

Dekker, T., Geier, M. and Cardé, R.T., 2005. Carbon dioxide instantly sensitizes female yellow fever mosquitoes to human skin odours. Journal of Experimental Biology 208: 2963-2972. https://doi.org/10.1242/jeb.01736

Dekker, T., Steib, B., Cardé, R.T. and Geier, M., 2002. L-lactic acid: a human signifying host cue for the anthropophilic mosquito *Anopheles gambiae*. Medical and Veterinary Entomology 16: 91. https://doi.org/10.1046/j.0269-283x.2002.00345.x

De Moraes, C.M., Stanczyk, N.M., Betz, H.S., Pulido, H., Sim, D.G., Read, A.F. and Mescher, M.C., 2014. Malaria-induced changes in host odors enhance mosquito attraction. Proceedings of the National Academy of Sciences of the USA 111: 11079-11084. https://doi.org/10.1073/pnas.1405617111

Donnelly, B., Berrang-Ford, L., Ross, N.A. and Michel, P., 2015. A systematic, realist review of zooprophylaxis for malaria control. Malaria Journal 14: 313. https://doi.org/10.1186/s12936-015-0822-0

Edman, J.D. and Taylor, D.J., 1968. *Culex nigripalpus*: seasonal shift in the bird-mammal feeding ratio in a mosquito vector of human encephalitis. Science 161: 67-68. https://doi.org/10.1126/science.161.3836.67

Egas, M., Dieckmann, U. and Sabelis, M.W., 2004. Evolution restricts the coexistence of specialists and generalists: the role of trade-off structure. The American Naturalist 163: 518-531. https://doi.org/10.1086/382599

Fikrig, K. and Harrington, L., 2021. Understanding and interpreting mosquito blood feeding studies: the case of *Aedes albopictus*. Trends in Parasitology 37: 959-975. https://doi.org/10.1016/j.pt.2021.07.013

Flint, J., Harding, R.M., Boyce, A.J. and Clegg, J.B., 1993. 8 the population genetics of the haemoglobinopathies. Baillière's Clinical Haematology 6: 215-262. https://doi.org/10.1016/S0950-3536(05)80071-X

Fonseca, D.M., Keyghobadi, N., Malcolm, C.A., Mehmet, C., Schaffner, F., Mogi, M., Fleischer, R. and Wilkerson, R., 2004. Emerging vectors in the *Culex pipiens* complex. Science 303: 1535-1539. https://doi.org/10.1126/science.1094247

Futuyma, D.J. and Moreno, G., 1988. The evolution of ecological specialization. Annual Review of Ecology and Systematics 19: 207-233.

Galizia, C.G. and Rössler, W., 2010. Parallel olfactory systems in insects: anatomy and function. Annual Review of Entomology 55: 399-420. https://doi.org/10.1146/annurev-ento-112408-085442

Gao, Q. and Chess, A., 1999. Identification of candidate *Drosophila* olfactory receptors from genomic DNA sequence. Genomics 60: 31-39. https://doi.org/10.1006/geno.1999.5894

Garrett-Jones, C., 1964. The human blood index of malaria vectors in relation to epidemiological assessment. Bulletin of the World Health Organization 30: 241.

Geier, M., Bosch, O.J. and Boeckh, J., 1999. Ammonia as an attractive component of host odour for the yellow fever mosquito, *Aedes aegypti*. Chemical Senses 24, 647-653. https://doi.org/10.1093/chemse/24.6.647

Ghaninia, M., Hansson, B.S. and Ignell, R., 2007a. The antennal lobe of the African malaria mosquito, *Anopheles gambiae* – innervation and three-dimensional reconstruction. Arthropod Structure & Development 36: 23-39. https://doi.org/10.1016/j.asd.2006.06.004

Ghaninia, M., Ignell, R. and Hansson, B., 2007b. Functional classification and central nervous projections of olfactory receptor neurons housed in antennal trichoid sensilla of female yellow fever mosquitoes, *Aedes aegypti*. European Journal of Neuroscience 26: 1611-1623. https://doi.org/10.1111/j.1460-9568.2007.05786.x

Ghaninia, M., Majeed, S., Dekker, T., Hill, S.R. and Ignell, R., 2019. Hold your breath – differential behavioral and sensory acuity of mosquitoes to acetone and carbon dioxide. PLoS ONE 14. https://doi.org/10.1371/journal.pone.0226815

Gikonyo, N.K., Hassanali, A., Njagi, P.G., Gitu, P.M. and Midiwo, J.O., 2002. Odor composition of preferred (buffalo and ox) and nonpreferred (waterbuck) hosts of some savanna tsetse flies. Journal of Chemical Ecology 28: 969-981. https://doi.org/10.1023/A:1015205716921

Gillies, M.T., 1964. Selection for host preference in *Anopheles gambiae*. Nature 203: 852.

Gouck, H.K., 1972. Host preferences of various strains of *Aedes aegypti* and *A. simpsoni* as determined by an olfactometer. Bulletin of the World Health Organization 5: 680-683.

Hallem, E.A. and Carlson, J.R., 2006. Coding of odors by a receptor repertoire. Cell 125: 143-160. https://doi.org/10.1016/j.cell.2006.01.050

Hallem, E.A., Ho, M.G. and Carlson, J.R., 2004. The molecular basis of odor coding in the *Drosophila* antenna. Cell 117: 965-979. https://doi.org/10.1016/j.cell.2004.05.012

Harraca, V., Syed, Z. and Guerin, P.M., 2009. Olfactory and behavioural responses of tsetse flies, *Glossina spp*., to rumen metabolites. Journal of Comparative Physiology A 195: 815-824. https://doi.org/10.1007/s00359-009-0459-y

Harrington, L.C., Edman, J.D. and Scott, T.W., 2001. Why do female *Aedes aegypti* (Diptera: Culicidae) feed preferentially and frequently on human blood? Journal of Medical Entomology 38: 411-422. https://doi.org/10.1603/0022-2585-38.3.411

Harris, P., Riordan, D.F. and Cooke, D., 1969. Mosquitoes feeding on insect larvae. Science 164: 184-185. https://doi.org/10.1126/science.164.3876.184

Healy, T.P., Copland, M.J.W., Cork, A., Przyborowska, A. and Halket, J.M., 2002. Landing responses of *Anopheles gambiae* elicited by oxocarboxylic acids. Medical and Veterinary Entomology 16: 126-132. https://doi.org/10.1046/j.1365-2915.2002.00353.x

Heisenberg, M., 2003. Mushroom body memoir: from maps to models. Nature Reviews Neuroscience 4: 266-275. https://doi.org/10.1038/nrn1074

Herre, M., Goldman, O.V., Lu, T.C., Caballero-Vidal, G., Qi, Y., Gilbert, Z.N., Gong, Z., Morita, T., Rahiel, S., Ghaninia, M., Ignell, R., Matthews, B.J., Li, H., Vosshall, L.B. and Younger, M.A., 2022. Non-canonical odor coding in the mosquito. Cell 185: 3104-3123. https://doi.org/10.1016/j.cell.2022.07.024

Hess, A.D., Hayes, R.O. and Tempelis, C.H., 1968. The use of the forage ratio technique in mosquito host preference studies. Mosquito News 28: 386-389.

Hill, S.R., Majeed, S. and Ignell, R., 2015. Molecular basis for odorant receptor tuning: a short C-terminal sequence is necessary and sufficient for selectivity of mosquito Or8. Insect Molecular Biology 24: 491-501. https://doi.org/10.1111/imb.12176

Holt, R.A., Subramanian, G.M., Halpern, A., Sutton, G.G., Charlab, R., Nusskern, D.R., Wincker, P., Clark, A.G., Ribeiro, J.C., Wides, R. and Salzberg, S.L., 2002. The genome sequence of the malaria mosquito *Anopheles gambiae*. Science 298: 129-149. https://doi.org/10.1126/science.1076181

Homan, T., Hiscox, A., Mweresa, C.K., Masiga, D., Mukabana, W.R., Oria, P., Maire, N., Pasquale, A.D., Silkey, M., Alaii, J., Bousema, T., Leeuwis, C., Smith, T.A. and Takken, W., 2016. The effect of mass mosquito trapping on malaria transmission and disease burden (SolarMal): a stepped-wedge cluster-randomised trial. The Lancet 388: 1193-1201. https://doi.org/10.1016/S0140-6736(16)30445-7

Ignell, R. and Hill, S.R., 2020. Malaria mosquito chemical ecology. Current Opinion in Insect Science 40: 6-10. https://doi.org/10.1016/j.cois.2020.03.008

Isberg, E., Bray, D.P., Birgersson, G., Hillbur, Y. and Ignell, R., 2016. Identification of cattle-derived volatiles that modulate the behavioral response of the biting midge *Culicoides nubeculosus*. Journal of Chemical Ecology 42, 24-32. https://doi.org/10.1007/s10886-015-0663-x

Jaenike, J., 1990. Host specialization in phytophagous insects. Annual Review of Ecology and Systematics 21: 243-273.

Jaleta, K.T., Hill, S.R., Birgersson, G., Tekie, H. and Ignell, R., 2016. Chicken volatiles repel host-seeking malaria mosquitoes. Malaria Journal 15: 354. https://doi.org/10.1186/s12936-016-1386-3

Jhumur, U.S., Dötterl, S. and Jürgens, A., 2007. Electrophysiological and behavioural responses of mosquitoes to volatiles of *Silene otites* (Caryophyllaceae). Arthropod-Plant Interactions 1: 245-254. https://doi.org/10.1007/s11829-007-9022-3

Karner, T., Kellner, I., Schultze, A., Breer, H. and Krieger, J., 2015. Co-expression of six tightly clustered odorant receptor genes in the antenna of the malaria mosquito *Anopheles gambiae*. Frontiers in Ecology and Evolution 3: 26. https://doi.org/10.3389/fevo.2015.00026

Kay, B.H., Boreham, P.F.L. and Edman, J.D., 1979. Application of the 'feeding index' concept to studies of mosquito host-feeding patterns. Mosquito News 39: 68-72.

Kilpatrick, A.M., Kramer, L.D., Jones, M.J., Marra, P.P. and Daszak, P., 2006. West Nile virus epidemics in North America are driven by shifts in mosquito feeding behavior. PLoS Biology 4: e28. https://doi.org/10.1371/journal.pbio.0040082

Knaden, M., Strutz, A., Ahsan, J., Sachse, S. and Hansson, B.S., 2012. Spatial representation of odorant valence in an insect brain. Cell Reports 1: 392-399. https://doi.org/10.1016/j.celrep.2012.03.002

Knols, B., De Jong, R. and Takken, W., 1994. Trapping system for testing olfactory responses of the malaria mosquito *Anopheles gambiae* in a wind tunnel. Medical and Veterinary Entomology 8: 386-388. https://doi.org/10.1111/j.1365-2915.1994.tb00104.x

Knols, B.G.J., Van Loon, J.J.A., Cork, A., Robinson, R.D., Adam, W., Meijerink, J., De Jong, R. and Takken, W., 1997. Behavioural and electrophysiological responses of the female malaria mosquito *Anopheles gambiae* (Diptera: Culicidae) to Limburger cheese volatiles. Bulletin of Entomological Research 87: 151-159. https://doi.org/10.1017/S0007485300027292

Knudsen, J.T., Eriksson, R., Gershenzon, J. and Ståhl, B., 2006. Diversity and distribution of floral scent. The Botanical Review 72: 1-120. https://doi.org/10.1663/0006-8101(2006)72[1:DADOFS]2.0.CO;2

Konopka, J.K., Task, D., Afify, A., Raji, J., Deibel, K., Maguire, S., Lawrence, R. and Potter, C.J., 2021. Olfaction in *Anopheles mosquitoes*. Chemical Senses 46: bjab021. https://doi.org/10.1093/chemse/bjab021

Krzywinski, J., Grushko, O.G. and Besansky, N.J., 2006. Analysis of the complete mitochondrial DNA from *Anopheles funestus*: an improved dipteran mitochondrial genome annotation and a temporal dimension of mosquito evolution. Molecular Phylogenetics and Evolution 39: 417-423. https://doi.org/10.1016/j.ympev.2006.01.006

Lacey, E.S., Ray, A. and Carde, R.T., 2014. Close encounter: contributions of carbon dioxide and human skin odour to finding and landing on a host in *Aedes aegypti*. Physiological Entomology 39: 60-68. https://doi.org/10.1111/phen.12048

Larsson, M.C., Domingos, A.I., Jones, W.D., Chiappe, M.E., Amrein, H. and Vosshall, L.B., 2004. Or83b encodes a broadly expressed odorant receptor essential for *Drosophila* olfaction. Neuron 43: 703-714. https://doi.org/10.1016/j.neuron.2004.08.019

Leal, W.S., 2013. Odorant reception in insects: roles of receptors, binding proteins, and degrading enzymes. Annual Review of Entomology 58: 373-391. https://doi.org/10.1146/annurev-ento-120811-153635

Lefèvre, T., Gouagna, L.C., Dabire, K.R., Elguero, E., Fontenille, D., Costantini, C. and Thomas, F., 2009a. Evolutionary lability of odour-mediated host preference by the malaria vector *Anopheles gambiae*. Tropical Medicine & International Health 14: 228-236. https://doi.org/10.1111/j.1365-3156.2009.02206.x

Lefèvre, T., Gouagna, L., Dabiré, K.R., Elguero, E., Fontenille, D., Renaud, F., Costantini, C. and Thomas, F., 2009b. Beyond nature and nurture: phenotypic plasticity in blood-feeding behavior of *Anopheles gambiae s.s.* when humans are not readily accessible. The American Journal of Tropical Medicine and Hygiene 81: 1023-1029. https://doi.org/10.4269/ajtmh.2009.09-0124

Lehane, M.J., 2005. The biology of blood-sucking in insects. Cambridge University Press, Cambridge, UK, pp. 336.

Liu, F., Ye, Z., Baker, A., Sun, H. and Zwiebel, L.J., 2020. Gene editing reveals obligate and modulatory components of the CO_2 receptor complex in the malaria vector mosquito, *Anopheles coluzzii*. Insect Biochemistry and Molecular Biology 127: 103470. https://doi.org/10.1016/j.ibmb.2020.103470

Liu, H., Liu, T., Xie, L., Wang, X., Deng, Y., Chen, C.H., James, A.A. and Chen, X.G., 2016. Functional analysis of Orco and odorant receptors in odor recognition in *Aedes albopictus*. Parasites & Vectors 9: 363. https://doi.org/10.1186/s13071-016-1644-9

Logan, J.G., Stanczyk, N.M., Hassanali, A., Kemei, J., Santana, A.E.G. Ribeiro, K.A.L., Pickett, J.A. and Mordue, A.J., 2010. Arm-in-cage testing of natural human-derived mosquito repellents. Malaria Journal 9: 239. https://doi.org/10.1186/1475-2875-9-239

Lu, T., Qiu, Y.T., Wang, G., Kwon, J.Y., Rutzler, M., Kwon, H., Pitts, R.J., Van Loon, J.J.A., Takken, W., Carlson, J.R. and Zwiebel, L.J., 2007. Odor coding in the maxillary palp of the malaria vector mosquito *Anopheles gambiae*. Current Biology 17: 1533-1544. https://doi.org/10.1016/j.cub.2007.07.062

Lulu, M., Hadis, M., Mekonnen, Y. and Asfaw, T., 1998. Chromosomal inversion polymorphisms of *Anopheles arabiensis* from some localities in Ethiopia in relation to host feeding choice. Ethiopian Journal of Health Development 12: 23-28.

Lyimo, I.N. and Ferguson, H.M., 2009. Ecological and evolutionary determinants of host species choice in mosquito vectors. Trends in Parasitology 25: 189-196. https://doi.org/10.1016/j.pt.2009.01.005

Lyimo, I.N., Keegan, S.P., Ranford-Carthwright, L.C. and Ferguson, H.M., 2012. The impact of uniform and mixed species blood meals on the fitness of the mosquito vector *Anopheles gambiae s.s.*: does a specialist pay for diversifying its host species diet? Journal of Evolutionary Biology 25: 452-460. https://doi.org/10.1111/j.1420-9101.2011.02442.x

MacArthur, R.H. and Pianka, E.R., 1966. On optimal use of a patchy environment. The American Naturalist 100: 603-609. https://doi.org/10.1086/282454

Main, B.J., Lee, Y., Ferguson, H.M., Kreppel, K.S., Kihonda, A., Govella, N.J., Collier, T.C., Cornel, A.J., Eskin, E., Kang, E.Y., Nieman, C.C., Weakley, A.M. and Lanzaro, G.C., 2016. The genetic basis of host preference and resting behavior in the major African malaria vector, *Anopheles arabiensis*. PLoS Genetics 12: e1006303. https://doi.org/10.1371/journal.pgen.1006303

Majeed, S., Hill, S.R., Birgersson, G. and Ignell, R., 2016. Detection and perception of generic host volatiles by mosquitoes modulate host preference: context dependence of (*R*)-1-octen-3-ol. Royal Society Open Science 3: 160467. https://doi.org/10.1098/rsos.160467

Majeed, S., Hill, S.R., Dekker, T. and Ignell, R., 2017. Detection and perception of generic host volatiles by mosquitoes: responses to CO_2 constrains host-seeking behaviour. Royal Society Open Science 4: 170189. https://doi.org/10.1098/rsos.170189

Matsunaga, T., Reisenman, C.E., Goldman-Huertas, B., Brand, P., Miao, K., Suzuki, H.C., Verster, K.I., Ramírez, S.R. and Whiteman, N.K, 2022. Evolution of olfactory receptors tuned to mustard oils in herbivorous Drosophilidae. Molecular Biology and Evolution 39: msab362. https://doi.org/10.1093/molbev/msab362

Matthews, B.J., Dudchenko, O., Kingan, S.B., Koren, S., Antoshechkin, I., Crawford, J.E., Glassford, W.J., Herre, M., Redmond, S.N., Rose, N.H., Weedall, G.D., Wu, Y., Batra, S.S., Brito-Sierra, C.A., Buckingham, S.D., Campbell, C.L., Chan, S., Cox, E., Evans, B.R., Fansiri, T., Filipović, I., Fontaine, A., Gloria-Soria, A., Hall, R., Joardar, V.S., Jones, A.K., Kay, R.G.G., Kodali, V.K., Lee, J., Lycett, G.J., Mitchell, S.N., Muehling, J., Murphy, M.R., Omer, A.D., Partridge, F.A., Peluso, P., Aiden, A.P., Ramasamy, V., Rašić, G., Roy, S., Saavedra-Rodriguez, K., Sharan, S., Sharma, A., Smith, M.L., Turner, J., Weakley, A.M., Zhao, Z., Akbari, O.S., Black, W.C., Cao, H., Darby, A.C., Hill, C.A., Johnston, J.S., Murphy, T.D., Raikhel, A.S., Sattelle, D.B., Sharakhov, I.V., White, B.J., Zhao, L., Aiden, E.L., Mann, R.S., Lambrechts, L., Powell, J.R., Sharakhova, M.V., Tu, Z., Robertson, H.M., McBride, C.S., Hastie, A.R., Korlach, J., Neafsey, D.E., Phillippy, A.M. and Vosshall, L.B, 2018. Improved reference genome of *Aedes aegypti* informs arbovirus vector control. Nature 563: 501-507. https://doi.org/10.1038/s41586-018-0692-z

McBride, C.S., 2016. Genes and odors underlying the recent evolution of mosquito preference for humans. Current Biology 26: R41-R46. https://doi.org/10.1016/j.cub.2015.11.032

McBride, C.S., Baier, F., Omondi, A.B., Spitzer, S.A., Lutomiah, J., Sang, R., Ignell, R. and Vosshall, L.B., 2014. Evolution of mosquito preference for humans linked to an odorant receptor. Nature 515: 222-227. https://doi.org/10.1038/nature13964

McMeniman, C.J., Corfas, R.A., Matthews, B.J., Ritchie, S.A. and Vosshall, L.B., 2014. Multimodal integration of carbon dioxide and other sensory cues drives mosquito attraction to humans. Cell 156: 1060-1071. https://doi.org/10.1016/j.cell.2013.12.044

Meijerink, J., Braks, M.A.H., Brack, A.A., Adam, W., Dekker, T., Posthumus, M.A., Van Beek, T.A. and Van Loon, J.J.A., 2000. Identification of olfactory stimulants for *Anopheles gambiae* from human sweat samples. Journal of Chemical Ecology 26: 1367-1382. https://doi.org/10.1023/A:1005475422978

Menger, D.J., Van Loon, J.J. and Takken, W., 2014. Assessing the efficacy of candidate mosquito repellents against the background of an attractive source that mimics a human host. Medical and Veterinary Entomology 28: 407-413. https://doi.org/10.1111/mve.12061

Meza, F.C., Kreppel, K.S., Maliti, D.F., Mlwale, A.T., Mirzai, N., Killeen, G.F., Ferguson, H.M. and Govella, N.J., 2019. Mosquito electrocuting traps for directly measuring biting rates and host-preferences of *Anopheles arabiensis* and *Anopheles funestus* outdoors. Malaria Journal 18: 83. https://doi.org/10.1186/s12936-019-2726-x

Mlacha, Y.P., Chaki, P.P., Muhili, A., Massue, D.J., Tanner, M., Majambere, S., Killen, G.F. and Govella, N.J., 2020. Reduced human-biting preferences of the African malaria vectors *Anopheles arabiensis* and *Anopheles gambiae* in an urban context: controlled, competitive host-preference experiments in Tanzania. Malaria Journal 19: 418. https://doi.org/10.1186/s12936-020-03495-z

Mohamed, A.A.M., Retzke, T., Chakraborty, S.D., Fabian, B., Hansson, B.S., Knaden, M. and Sachse, S., 2019. Odor mixtures of opposing valence unveil inter-glomerular crosstalk in the *Drosophila* antennal lobe. Nature Communications 10: 1201. https://doi.org/10.1038/s41467-019-09069-1

Molaei, G., Andreadis, T.G., Armstrong, P.M. and Diuk-Wasser, M., 2008. Host-feeding patterns of potential mosquito vectors in Connecticut, USA: molecular analysis of bloodmeals from 23 species of *Aedes*, *Anopheles*, *Culex*, *Coquillettidia*, *Psorophora*, and *Uranotaenia*. Journal of Medical Entomology 45: 1143-1151. https://doi.org/10.1093/jmedent/45.6.1143

Mukabana, W.R., Mweresa, C.K., Otieno, B., Omusula, P., Smallegange, R.C., Van Loon, J.J. and Takken, W., 2012. A novel synthetic odorant blend for trapping of malaria and other African mosquito species. Journal of Chemical Ecology 38: 235-244. https://doi.org/10.1007/s10886-012-0088-8

Mukwaya, L.G., 1977. Genetic control of feeding preferences in the mosquitoes *Aedes* (*Stegomyia*) *simpsoni* and *aegypti*. Physiological Entomology 2: 133-145. https://doi.org/10.1111/j.1365-3032.1977.tb00091.x

Mwandawiro, C., Boots, M., Tuno, N., Suwonkerd, W., Tsuda, Y. and Takagi, M., 2000. Heterogeneity in the host preference of Japanese encephalitis vectors in Chiang Mai, northern Thailand. Transactions of the Royal Society of Tropical Medicine and Hygiene 94: 238-242. https://doi.org/10.1016/S0035-9203(00)90303-1

Nayar, J.K. and Sauerman Jr, D.M., 1977. The effects of nutrition on survival and fecundity in Florida mosquitoes. Journal of Medical Entomology 14: 167-174. https://doi.org/10.1093/jmedent/14.2.167

Neafsey, D.E., Waterhouse, R.M., Abai, M.R., Aganezov, S.S., Alekseyev, M.A., Allen, J.E., Amon, J., Arcà, B., Arensburger, P., Artemov, G., Assour, L.A., Basseri, H., Berlin, A., Birren, B.W., Blandin, S.A., Brockman, A.I., Burkot, T.R., Burt, A., Chan, C.S., Chauve, C., Chiu, J.C., Christensen, M., Costantini, C., Davidson, V.L.M., Deligianni, E., Dottorini, T., Dritsou, V., Gabriel, S.B., Guelbeogo, W.M., Hall, A.B., Han, M.V., Hlaing, T., Hughes, D.S.T., Jenkins, A.M., Jiang, X., Jungreis, I., Kakani, E.G. Kamali, M., Kemppainen, P., Kennedy, R.C., Kirmitzoglou, I.K., Koekemoer, L.L., Laban, N., Langridge, N., Lawniczak, M.K.N., Lirakis, M., Lobo, N.F., Lowy, E., MacCallum, R.M., Mao, C., Maslen, G., Mbogo, C., McCarthy, J., Michel, K., Mitchell, S.N., Moore, W., Murphy, K.A., Naumenko, A.N., Nolan, T., Novoa, E.M., O'Loughlin, S., Oringanje, C., Oshaghi, M.A., Pakpour, N., Papathanos, P.A., Peery, A.N., Povelones, M., Prakash, A., Price, D.P., Rajaraman, A., Reimer, L.J., Rinker, D.C., Rokas, A., Russell, T.L., Sagnon, N., Sharakhova, M.V., Shea, T., Simão, F.A., Simard, F., Slotman, M.A., Somboon, P., Stegniy, V., Struchiner, C.J., Thomas, G.W.C., Tojo, M., Topalis, P., Tubio, J.M.C., Unger, M.F., Vontas, J., Walton, C., Wilding, C.S., Willis, J.H., Wu, Y., Yan, G., Zdobnov, E.M., Zhou, X., Catteruccia, F., Christophides, G.K., Collins, F.H., Cornman, R.S., Crisanti, A., Donnelly, M.J., Emrich, S.J., Fontaine, M.C., Gelbart, W., Hahn, M.W., Hansen, I.A., Howell, P.I., Kafatos, F.C., Kellis, M., Lawson, D., Louis, C., Luckhart, S., Muskavitch, M.A.T., Ribeiro, J.M., Riehle, M.A., Sharakhov, I.V., Tu, Z., Zwiebel, L.J. and Besansky, N.J., 2015. Highly evolvable malaria vectors: the genomes of 16 *Anopheles* mosquitoes. Science 347: 6217. https://doi.org/10.1126/science.1258522

Nene, V., Wortman, J.R., Lawson, D., Haas, B., Kodira, C., Tu, Z., Loftus, B., Xi, Z., Megy, K., Grabherr, M., Ren, Q., Zdobnov, E.M., Lobo, N.F., Campbell, K.S., Brown, S.E., Bonaldo, M.F., Zhu, J., Sinkins, S.P., Hogenkamp, D.G., Amedeo, P., Arensburger, P., Atkinson, P.W., Bidwell, S., Biedler, J., Birney, E., Bruggner, R.V., Costas, J., Coy, M.R., Crabtree, J., Crawford, M., deBruyn, B., DeCaprio, D., Eiglmeier, K., Eisenstadt, E., El-Dorry, H., Gelbart, W.M., Gomes, S.L., Hammond, M., Hannick, L.I., Hogan, J.R., Holmes, M.H., Jaffe, D., Johnston, J.S., Kennedy, R.C., Koo, H., Kravitz, S., Kriventseva, E.V., Kulp, D., LaButti, K., Lee, E., Li, S., Lovin, D.D., Mao, C., Mauceli, E., Menck, C.F.M., Miller, J.R., Montgomery, P., Mori, A., Nascimento, A.L., Naveira, H.F., Nusbaum, C., O'Leary, S., Orvis, J., Pertea, M., Quesneville, H., Reidenbach, K.R., Rogers, Y., Roth, C.W., Schneider, J.R., Schatz, M., Shumway, M., Stanke, M., Stinson, E.O., Tubio, J.M.C., VanZee, J.P., Verjovski-Almeida, S., Werner, D., White, O., Wyder, S., Zeng, Q., Zhao, Q., Zhao, Y., Hill, C.A., Raikhel, A.S., Soares, M.B., Knudson, D.L., Lee, N.H., Galagan, J., Salzberg, S.L., Paulsen, I.T., Dimopoulos, G., Collins, F.H., Birren, B., Fraser-Liggett, C.M. and Severson, D.W., 2007. Genome sequence of *Aedes aegypti*, a major arbovirus vector. Science 316: 1718-1723. https://doi.org/10.1126/science.1138878

Nyasembe, V.O., Tchouassi, D.P., Pirk, C.W.W., Sole, C.L. and Torto, B., 2018. Host plant forensics and olfactory-based detection in Afro-tropical mosquito disease vectors. PLoS Neglected Tropical Diseases 12: e0006185. https://doi.org/10.1371/journal.pntd.0006185

Okumu, F.O., Killeen, G.F., Ogoma, S., Biswaro, L., Renate, C., Mbeyela, E., Titus, E., Munk, C., Ngonyani, H., Takken, W., Mshinda, H., Mukabana, W.R. and Moore, S.J., 2010. Development and field evaluation of a synthetic mosquito lure that is more attractive than humans. PLoS ONE 5: e8951. https://doi.org/10.1371/journal.pone.0008951

Omondi, A.B., Ghaninia, M., Dawit, M., Svensson, T. and Ignell, R., 2019. Age-dependent regulation of host seeking in *Anopheles coluzzii*. Scientific Reports 9: 9699. https://doi.org/10.1038/s41598-019-46220-w

Owino, E.A., Sang, R., Sole, C.L., Pirk, C., Mbogo, C. and Torto, B., 2015. An improved odor bait for monitoring populations of *Aedes aegypti* – vectors of dengue and chikungunya viruses in Kenya. Parasites & Vectors 8: 253. https://doi.org/10.1186/s13071-015-0866-6

Pates, H.V., Takken, W., Stuke, K. and Curtis, C.F., 2001. Differential behaviour of *Anopheles gambiae sensu stricto* (Diptera: Culicidae) to human and cow odours in the laboratory. Bulletin of Entomological Research 91: 289-296. https://doi.org/10.1079/BER200198

Peled, N., Ionescu, R., Nol, P., Barash, O., McCollum, M., VerCauteren, K., Koslow, M., Stahl, R., Rhyan, J. and Haick, H., 2012. Detection of volatile organic compounds in cattle naturally infected with *Mycobacterium bovis*. Sensors and Actuators B: Chemical 171: 588-594. https://doi.org/10.1016/j.snb.2012.05.038

Pelosi, P., Iovinella, I., Zhu, J., Wang, G. and Dani, F.R., 2018. Beyond chemoreception: diverse tasks of soluble olfactory proteins in insects. Biological Reviews 93: 184-200. https://doi.org/10.1111/brv.12339

Penn, D.J., Oberzaucher, E., Grammer, K., Fischer, G., Soini, H.A., Wiesler, D., Novotny, M.V., Dixon, S.J., Xu, Y. and Brereton, R.G., 2007. Individual and gender fingerprints in human body odour. Journal of the Royal Society Interface 4: 331-340. https://doi.org/10.1098/rsif.2006.0182

Pérez-Silva, J.G., Araujo-Voces, M. and Quesada, V., 2018. nVenn: generalized, quasi-proportional Venn and Euler diagrams. Bioinformatics 34: 2322-2324. https://doi.org/10.1093/bioinformatics/bty109

Petrarca, V. and Beier, J.C., 1992. Intraspecific chromosomal polymorphism in the *Anopheles gambiae* complex as a factor affecting malaria transmission in the Kisumu area of Kenya. The American Journal of Tropical Medicine and Hygiene 46: 229-237. https://doi.org/10.4269/ajtmh.1992.46.229

Pitts, R.J., Derryberry, S.L., Zhang, Z. and Zwiebel, L.J., 2017. Variant ionotropic receptors in the malaria vector mosquito *Anopheles gambiae* tuned to amines and carboxylic acids. Scientific Reports 7: 40297. https://doi.org/10.1038/srep40297

Pitts, R.J., Ibarra Bouzada, L.M.E. and Guerenstein, P.G., 2022. Comparative morphology of the peripheral olfactory system of disease vector arthropods. Chapter 2. In: Ignell, R., Lazzari, C.R., Lorenzo, M.G. and Hill, S.R. (eds.) Sensory ecology of disease vectors. Wageningen Academic Publishers, Wageningen, the Netherlands, pp. 29-70. https://doi.org/10.3920/978-90-8686-932-9_2

Powell, J.R., Gloria-Soria, A. and Kotsakiozi, P., 2018. Recent history of *Aedes aegypti*: vector genomics and epidemiology records. BioScience 68: 854-860. https://doi.org/10.1093/biosci/biy119

Prüfer, K., Munch, K., Hellmann, I., Akagi, K., Miller, J.R., Walenz, B., Koren, S., Sutton, G., Kodira, C., Winer, R., Knight, J.R., Mullikin, J.C., Meader, S.J., Ponting, C.P., Gerton Lunter, G., Higashino, S., Hobolth, A., Dutheil, J., Karakoç, E., Alkan, C., Sajjadian, S., Catacchio, C.R., Ventura, M., Marques-Bonet, T., Eichler, E.E., André, C., Atencia, R., Mugisha, L., Junhold, J., Patterson, N., Siebauer, M., Good, J.M., Fischer, A., Ptak, S.E., Lachmann, M., Symer, D.E., Mailund, T., Schierup, M.H., Andrés, A.M., Kelso, J. and Pääbo, S., 2012. The bonobo genome compared with the chimpanzee and human genomes. Nature 486: 527-531. https://doi.org/10.1038/nature11128

Pyke, G.H., Pulliam, H.R. and Charnov, E.L., 1997. Optimal foraging: a selective review of theory and tests. The Quarterly Review of Biology 52: 2. https://doi.org/10.1086/409852

Qiu, Y.T., Smallegange, R.C., Van Loon, J.J.A., Ter Braak, C.J.F. and Takken, W., 2006. Interindividual variation in the attractiveness of human odours to the malaria mosquito *Anopheles gambiae s. s.* Medical and Veterinary Entomology 20: 280-287. https://doi.org/10.1111/j.1365-2915.2006.00627.x

Raji, J.I., Melo, N., Castillo, J.S., Gonzalez, S., Saldana, V., Stensmyr, M.C. and DeGenarro, M., 2019. *Aedes aegypti* mosquitoes detect acidic volatiles found in human odor using the IR8a pathway. Current Biology 29: 1253-1262. https://doi.org/10.1016/j.cub.2019.02.045

Reegan, A.D., Ceasar, S.A., Paulraj, M.G., Ignacimuthu, S. and Al-Dhabi, N.A., 2016. Current status of genome editing in vector mosquitoes: a review. BioScience Trends 10: 424-432. https://doi.org/10.5582/bst.2016.01180

Reeves, L.E., Holderman, C.J., Blosser, E.M., Gillett-Kaufman, J.L., Kawahara, A.Y., Kaufman, P.E. and Burkett-Cadena, N.D., 2018. Identification of *Uranotaenia sapphirina* as a specialist of annelids broadens known mosquito host use patterns. Communications Biology 1: 92. https://doi.org/10.1038/s42003-018-0096-5

Reidenbach, K.R., Cook, S., Bertone, M.A., Harbach, R.E., Wiegmann, B.M. and Besansky, N.J., 2009. Phylogenetic analysis and temporal diversification of mosquitoes (Diptera: Culicidae) based on nuclear genes and morphology. BMC Evolutionary Biology 9: 298. https://doi.org/10.1186/1471-2148-9-298

Riabinina, O., Task, D., Marr, E., Lin, C.C., Alford, R., O'Brochta, D.A. and Potter, C.J., 2016. Organization of olfactory centres in the malaria mosquito *Anopheles gambiae*. Nature Communications 7: 13010. https://doi.org/10.1038/ncomms13010

Rinker, D.C., Zhou, X., Pitts, R.J., Consortium, A., Rokas, A. and Zwiebel, L.J., 2013. Antennal transcriptome profiles of anopheline mosquitoes reveal human host olfactory specialization in *Anopheles gambiae*. BMC Genomics 14: 749. https://doi.org/10.1186/1471-2164-14-749

Robinson, A., Busula, A.O., Voets, M.A., Beshir, K.B., Caulfield, J.C., Powers, S.J., Verhulst, N.O., Winskill, P., Muwanguzi, J., Birkett, M.A. and Smallegange, R.C., 2018. Plasmodium-associated changes in human odor attract mosquitoes. Proceedings of the National Academy of Sciences of the USA 115: E4209-E4218. https://doi.org/10.1073/pnas.1721610115

Rose, N.H., Sylla, M., Badolo, A., Lutomiah, J., Ayala, D., Aribodor, O.B., Ibe, N., Akorli, J., Otoo, S., Mutebi, J., Kriete, A.L., Ewing, E.G. Sang, R., Gloria-Soria, A., Powell, J.R., Baker, R.E., White, B.J., Crawford, J.E. and McBride, C.S., 2020. Climate and urbanization drive mosquito preference for humans. Current Biology 30: 3570-3579. https://doi.org/10.1016/j.cub.2020.06.092

Rudolfs, W., 1922. Chemotropism of mosquitoes. New Jersey Agricultural Experiment Stations 367: 1-23.

Ruel, D.M. and Bohbot, J.D., 2022. The molecular and neural determinants of olfactory behaviour in mosquitoes. Chapter 3. In: Ignell, R., Lazzari, C.R., Lorenzo, M.G. and Hill, S.R. (eds.) Sensory ecology of disease vectors. Wageningen Academic Publishers, Wageningen, the Netherlands, pp. 71-115. https://doi.org/10.3920/978-90-8686-932-9_3

Seenivasagan, T., Guha, L. and Parashar, B.D., 2014. Olfaction in Asian tiger mosquito *Aedes albopictus*: flight orientation response to certain saturated carboxylic acids in human skin emanations. Parasitology Research 113: 1927-1932. https://doi.org/10.1007/s00436-014-3840-x

Smallegange, R.C., Qiu, Y.T., Bukovinszkiné-Kiss, G., Van Loon, J.J. and 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. https://doi.org/10.1007/s10886-009-9668-7

Smallegange, R.C., Qiu, Y.T., Van Loon, J.J.A. and Takken, W., 2005. Synergism between ammonia, lactic acid and carboxylic acids as kairomones in the host-seeking behaviour of the malaria mosquito *Anopheles gambiae sensu stricto* (Diptera: Culicidae). Chemical Senses 30: 145-152. https://doi.org/10.1093/chemse/bji010

Sorrells, T.R., Pandey, A., Rosas-Villegas, A. and Vosshall, L.B., 2022. A persistent behavioral state enables sustained predation of humans by mosquitoes. eLife 11: e76663. https://doi.org/10.7554/eLife.76663

Spanoudis, C.G., Andreadis, S.S., Bray, D.P., Savopoulou-Soultani, M. and Ignell, R. 2020. Behavioural response of the house mosquitoes *Culex quinquefasciatus* and *Culex pipiens molestus* to avian odours and its reliance on carbon dioxide. Medical and Veterinary Entomology 34: 129-137. https://doi.org/10.1111/mve.12429

Steib, B.M., Geier, M. and Boeckh, J., 2001. The effect of lactic acid on odour-related host preference of yellow fever mosquitoes. Chemical Senses 26: 523-528. https://doi.org/10.1093/chemse/26.5.523

Stengl, M., Hatt, H. and Breer, H., 1992. Peripheral processes in insect olfaction. Annual Review of Physiology 54: 665-681.

Strutz, A., Soelter, J., Baschwitz, A., Farhan, A., Grabe, V., Rybak, J., Knaden, M., Schmuker, M., Hansson, B.S. and Sachse, S., 2014. Decoding odor quality and intensity in the *Drosophila* brain. eLife 3: e04147. https://doi.org/10.7554/eLife.04147.001

Suh, E., Bohbot, J.D. and Zwiebel, L.J., 2014. Peripheral olfactory signaling in insects. Current Opinion in Insect Science 6: 86-92. https://doi.org/10.1016/j.cois.2014.10.006

Syed, Z. and Leal, W.S., 2009. Acute olfactory response of *Culex* mosquitoes to a human- and bird-derived attractant. Proceedings of the National Academy of Sciences of the USA 106: 18803-18808. https://doi.org/10.1073/pnas.0906932106

Takken, W. and Knols, B.G.J., 1999. Odor-mediated behavior of Afrotropical malaria mosquitoes. Annual Review of Entomology 44: 131-157. https://doi.org/10.1146/annurev.ento.44.1.131

Takken, W. and Verhulst, N.O., 2013. Host preferences of blood-feeding mosquitoes. Annual Review of Entomology 58: 433-453. https://doi.org/10.1146/annurev-ento-120811-153618

Tambwe, M.M., Saddler, A., Kibondo, U.A., Mashauri, R., Kreppel, K.S., Govella, N.J. and Moore, S.J., 2021. Comparison between the human landing catch (HLC), an exposure-free mosquito-electrocuting trap (MET) and a BG-Sentinel trap (BGS) for evaluation of transfluthrin emanator against *Aedes aegypti* using choice and no-choice tests in a semi-field system. Parasites & Vectors in press. https://doi.org/10.21203/rs.3.rs-332021/v1

Tchouassi, D.P., Sang, R., Sole, C.L., Bastos, A.D.S., Teal, P.E.A., Borgemeister, C. and Torto, B., 2013. Common host-derived chemicals increase catches of disease-transmitting mosquitoes and can improve early warning systems for Rift Valley fever virus. PLoS Neglected Tropical Diseases 7: e2007. https://doi.org/10.1371/journal.pntd.0002007

Tchouassi, D.P., Wanjiku, C. and Torto, B., 2022. Host-derived attractants for surveillance and control of mosquitoes. Chapter 33. In: Ignell, R., Lazzari, C.R., Lorenzo, M.G. and Hill, S.R. (eds.) Sensory ecology of disease vectors. Wageningen Academic Publishers, Wageningen, the Netherlands, pp. 851-877. https://doi.org/10.3920/978-90-8686-932-9_33

Tempelis, C.H., 1975. Host-feeding patterns of mosquitoes, with a review of advances in analysis of blood meals by serology. Journal of Medical Entomology 11: 635-653. https://doi.org/10.1093/jmedent/11.6.635

Thiemann, T.C., Brault, A.C., Ernest, H.B. and Reisen, W.K., 2012. Development of a high-throughput microsphere-based molecular assay to identify 15 common bloodmeal hosts of *Culex mosquitoes*. Molecular Ecology Resources 12: 238-246. https://doi.org/10.1111/j.1755-0998.2011.03093.x

Thiemann, T.C., Wheeler, S.S., Barker, C.M. and Reisen, W.K., 2011. Mosquito host selection varies seasonally with host availability and mosquito density. PLoS Neglected Tropical Diseases 5: e1452. https://doi.org/10.1371/journal.pntd.0001452

Tishkoff, S.A., Varkonyi, R., Cahinhinan, N., Abbes, S., Argyropoulos, G., Destro-Bisol, G., Drousiotou, A., Dangerfield, B., Lefranc, G., Loiselet, J., Piro, A., Stoneking, M., Tagarelli, A., Tagarelli, G., Touma, E.H., Williams, S.M. and Clark, A.G., 2001. Haplotype diversity and linkage disequilibrium at human G6PD: recent origin of alleles that confer malarial resistance. Science 293: 455-462. https://doi.org/10.1126/science.1061573

Torr, S.J., della Torre, A., Calzetta, M., Costantini, C. and Vale, G.A., 2008. Towards a fuller understanding of mosquito behaviour: use of electrocuting grids to compare the odour-orientated responses of *Anopheles arabiensis* and *An. quadriannulatus* in the field. Medical and Veterinary Entomology 22: 93-108. https://doi.org/10.1111/j.1365-2915.2008.00723.x

Van den Broek, I.V.F. and Den Otter, C.J., 1999. Olfactory sensitivities of mosquitoes with different host preferences (*Anopheles gambiae s.s.*, *An. arabiensis*, *An. quadriannulatus*, *An. m. atroparvus*) to synthetic host odours. Journal of Insect Physiology 45: 1001-1010. https://doi.org/10.1016/S0022-1910(99)00081-5

Vantaux, A., Lefèvre, T., Dabiré, K.R. and Cohuet, A., 2014. Individual experience affects host choice in malaria vector mosquitoes. Parasites & Vectors 7: 249. https://doi.org/10.1186/1756-3305-7-249

Verhulst, N.O., Qiu, Y.T., Beijleveld, H., Maliepaard, C., Knights, D., Schulz, S., Berg-Lyons, D., Lauber, C.L., Verduijn, W., Haasnoot, G.W., Mumm, R., Bouwmeester, H.J., Claas, F.H.J., Dicke, M., Van Loon, J.J.A., Takken, W., Knight, R. and Smallegange, R.C., 2011. Composition of human skin microbiota affects attractiveness to malaria mosquitoes. PLoS ONE 6. https://doi.org/10.1371/journal.pone.0028991

Verhulst, N.O., Umanets, A., Weldegergis, B.T., Maas, J.P.A., Visser, T.M., Dicke, M., Smidt, H. and Takken, W., 2018. Do apes smell like humans? The role of skin bacteria and volatiles of primates in mosquito host selection. Journal of Experimental Biology 221: jeb185959. https://doi.org/10.1242/jeb.185959

Vinauger, C., Lahondère, C., Cohuet, A., Lazzari, C.R. and Riffell, J.A., 2016. Learning and memory in disease vector insects. Trends in Parasitology 32: 761-771. https://doi.org/10.1016/j.pt.2016.06.003

Vinauger, C., Lahondère, C., Wolff, G.H., Locke, L.T., Liaw, J.E., Parrish, J.Z., Akbari, O.S., Dickinson, M.H. and Riffell, J.A., 2018. Modulation of host learning in *Aedes aegypti* mosquitoes. Current Biology 28: 333-344. https://doi.org/10.1016/j.cub.2017.12.015

Vosshall, L.B., Amrein, H., Morozov, P.S., Rzhetsky, A. and Axel, R., 1999. A spatial map of olfactory receptor expression in the *Drosophila* antenna. Cell 96: 725-736. https://doi.org/10.1016/S0092-8674(00)80582-6

Wang, G., Carey, A.F., Carlson, J.R. and Zwiebel, L.J., 2010. Molecular basis of odor coding in the malaria vector mosquito *Anopheles gambiae*. Proceedings of the National Academy of Sciences of the USA 107: 4418-4423. https://doi.org/10.1073/pnas.0913392107

Wheelwright, M., Whittle, C.R. and Riabinina, O., 2021. Olfactory systems across mosquito species. Cell and Tissue Research 383: 75-90. https://doi.org/10.1007/s00441-020-03407-2

White, B.J., Collins, F.H. and Besansky, N.J., 2011. Evolution of *Anopheles gambiae* in relation to humans and malaria. Annual Review of Ecology, Evolution, and Systematics 42: 111-132. https://doi.org/10.1146/annurev-ecolsys-102710-145028

Wisthaler, A. and Weschler, C.J., 2010. Reactions of ozone with human skin lipids: sources of carbonyls, dicarbonyls, and hydroxycarbonyls in indoor air. Proceedings of the National Academy of Sciences of the USA 107: 6568-6575. https://doi.org/10.1073/pnas.0904498106

Woke, P.A., 1937. Comparative effects of the blood of different species of vertebrates on egg-production of *Aedes aegypti* Linn. American Journal of Tropical Medicine 17: 729-745.

Wolff, G.H. and Riffell, J.A., 2018. Olfaction, experience and neural mechanisms underlying mosquito host preference. Journal of Experimental Biology 221: jeb157131. https://doi.org/10.1242/jeb.157131

Wondwosen, B., Birgersson, G., Seyoum, E., Tekie, H., Torto, B., Fillinger, U., Hill, S.R. and Ignell, R., 2016. Rice volatiles lure gravid malaria mosquitoes, *Anopheles arabiensis*. Scientific Reports 6: 37930. https://doi.org/10.1038/srep37930

Wondwosen, B., Hill, S.R., Birgersson, G., Seyoum, E., Tekie, H. and Ignell, R., 2017. A(maize)ing attraction: gravid *Anopheles arabiensis* are attracted and oviposit in response to maize pollen odours. Malaria Journal 16: 39. https://doi.org/10.1186/s12936-016-1656-0

World Health Organization (WHO), 2020. Fact sheet on vector-borne diseases. Available at: https://www.who.int/en/news-room/fact-sheets/detail/vector-borne-diseases

Xu, P., Zhu, F., Buss, G.K. and Leal, W.S., 2015. 1-Octen-3-ol – the attractant that repels. F1000Research 4: 156. https://doi.org/10.12688/f1000research.6646.1

Ye, Z., Liu, F., Sun, H., Ferguson, S.T., Baker, A., Ochieng, S.A. and Zwiebel, L.J., 2022. Discrete roles of Ir76b ionotropic coreceptor impact olfaction, blood feeding, and mating in the malaria vector mosquito *Anopheles coluzzii*. Proceedings of the National Academy of Sciences 119: e2112385119. https://doi.org/10.1073/pnas.2112385119

Zhao, Z. and McBride, C.S., 2020. Evolution of olfactory circuits in insects. Journal of Comparative Physiology A 206: 353-367. https://doi.org/10.1007/s00359-020-01399-6

Zhao, Z., Tian, D. and McBride, C.S., 2021. Development of a pan-neuronal genetic driver in *Aedes aegypti* mosquitoes. Cell Reports Methods 1: 100042. https://doi.org/10.1016/j.crmeth.2021.100042

Zhao, Z., Zung, J.L., Hinze, A., Kriete, A.L., Iqbal, A., Younger, M.A., Matthews, B.J., Merhof, D., Thiberge, S., Ignell, R., Strauch, M. and McBride, C.S., 2022. Mosquito brains encode unique features of human odour to drive host seeking and preference. Nature 605: 706-712. https://doi.org/10.1038/s41586-022-04675-4

Zimmerman, R.H., Galardo, A.K.R., Lounibos, L.P., Arruda, M. and Wirtz, R., 2006. Bloodmeal hosts of *Anopheles species* (Diptera: Culicidae) in a malaria-endemic area of the Brazilian Amazon. Journal of Medical Entomology 43: 947-956. https://doi.org/10.1093/jmedent/43.5.947