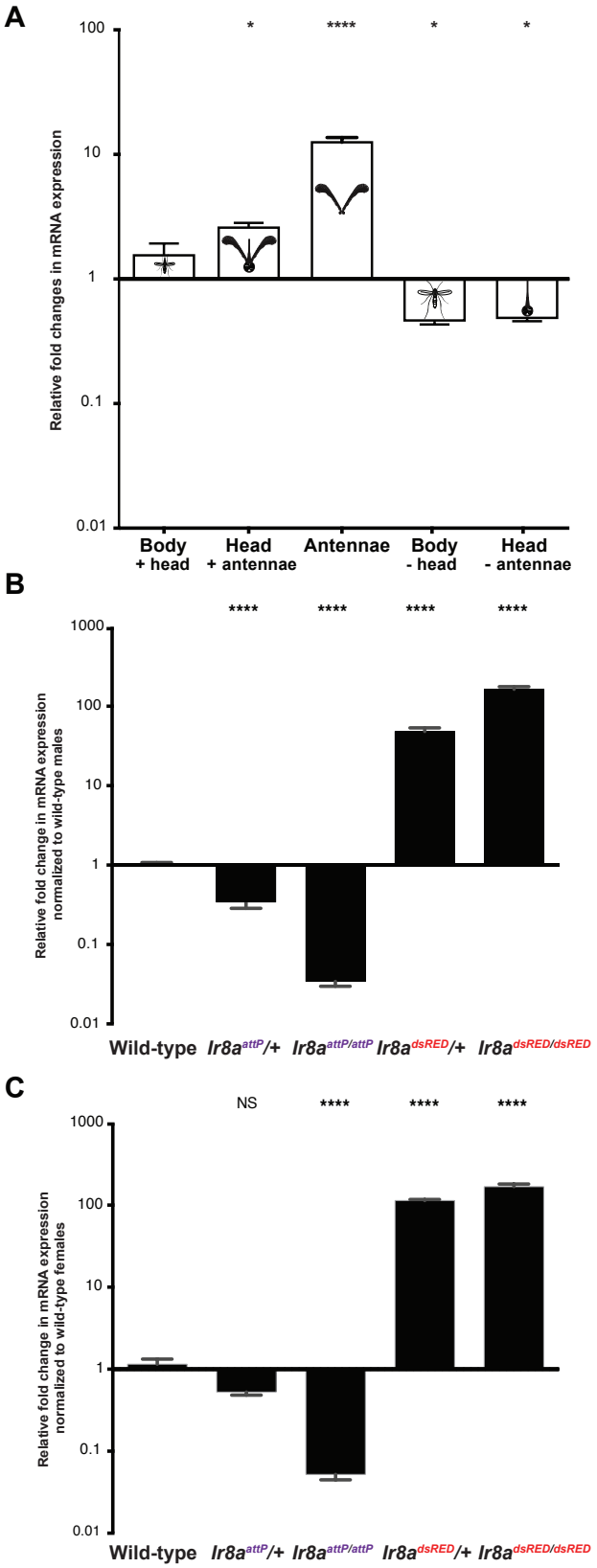

Figure S1: Quantification of *Ir8a* mRNA expression. Related to Figure 1.
(A) Quantitative RT-PCR analysis of *Ir8a* mRNA expression in wild-type female mosquito tissues. Bar plots represent the mean and standard error. Samples marked with asterisks are significantly different from an intact female by Mann-Whitney U test ($p < 0.0001$).(B) Relative fold change in mRNA expression normalized to wild-type males ($p < 0.0001$) and (C) females *Ae. aegypti* mosquitoes ($p < 0.0001$). Bar plots represent the mean and standard error. Data was analyzed by Mann-Whitney U test. Genotypes marked with asterisks are significantly different from wild-type controls.

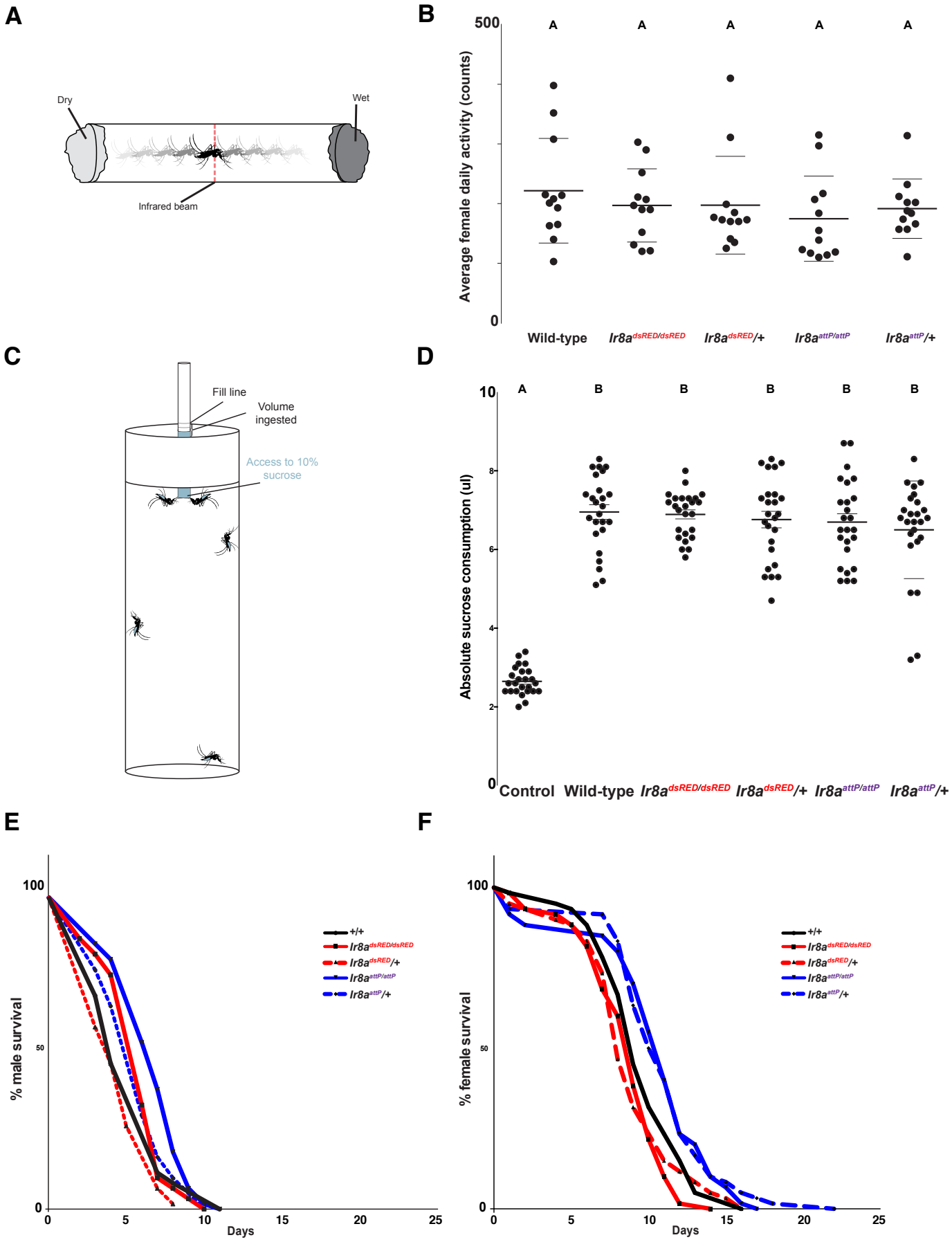
A
Dry
Wet
Infrared beam
B
Average female daily activity (counts)
500
0
A
A
A
A
A
Wild-type
Ir8a dsRED/dsRED
Ir8a dsRED/+
Ir8a attP/attP
Ir8a attP/+
C
Fill line
Volume ingested
Access to 10% sucrose
D
Absolute sucrose consumption (ul)
10
8
6
4
2
0
A
B
B
B
B
B
Control
Wild-type
Ir8a dsRED/dsRED
Ir8a dsRED/+
Ir8a attP/attP
Ir8a attP/+
E
% male survival
100
50
0
0
5
10
15
20
25
Days
+/+
Ir8a dsRED/dsRED
Ir8a dsRED/+
Ir8a attP/attP
Ir8a attP/+
F
% female survival
100
50
0
0
5
10
15
20
25
Days
+/+
Ir8a dsRED/dsRED
Ir8a dsRED/+
Ir8a attP/attP
Ir8a attP/+

Figure S2. Assessing locomotor activity, survival, and sugar-feeding behavior in *Ir8a* mutants. Related to Figure 1.

(A) Diagram of beam break assay to monitor mosquito locomotor activity. (B) Average daily locomotor activity of *Ir8a* mutants after 4 days of fasting measured by the number of infrared beam breaks (counts). On the dot plot, long lines represent the mean and short lines represent standard error. There were no statistical differences among genotypes ($p = 0.6224$, n = 12-13). (C) Diagram of Capillary Feeder (CAFÉ) assay to quantify feeding behavior in mosquitoes. (D) Cumulative sucrose consumption after 18 hours of sugar feeding ($p = 0.9411$, n=25). On the dot plot, long lines represent the mean and short lines represent standard error. Data was analyzed by one-way ANOVA, and genotypes marked with the same letters are not significantly different by post hoc Tukey's HSD test. (E) Percent survival of 300 females under sugar starvation (F) Survival of 300 males under sugar starvation. Data was analyzed using log rank test and Geahand-Wilcoxon test followed by pairwise log rank comparisons with Bonferroni correction (corrected significance threshold; $p < 0.001$). Using this test, $Ir8a^{attP/attP}$ males lived significantly longer than wild-type and $Ir8a^{dsRED/+}$. Whereas, $Ir8a^{attP/attP}$ female mosquitoes lived significantly longer than wild-type, $Ir8a^{dsRED/+}$, and $Ir8a^{dsRED/dsRED}$ mosquitoes. There was no difference for any other pair of curves.

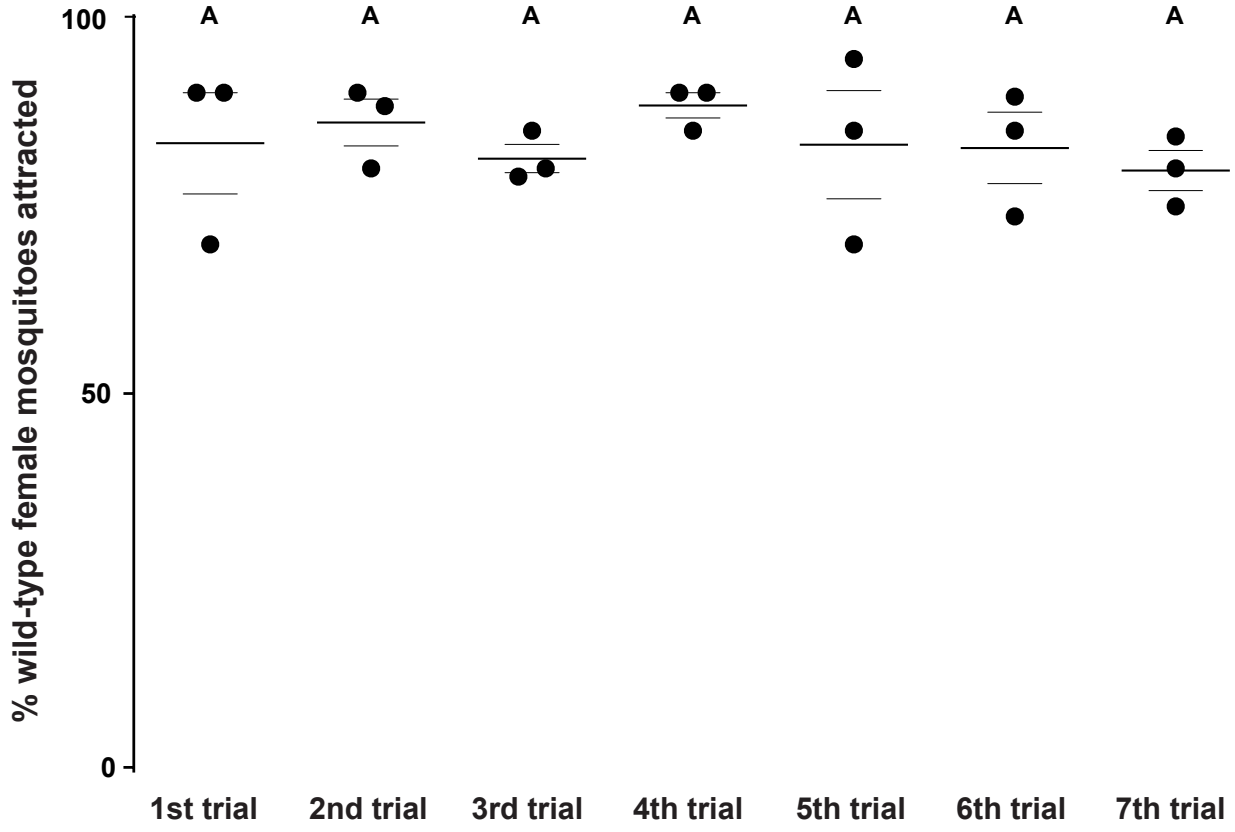

Figure S3: Time course experiment showing mosquito attraction to human-scented nylon sleeves. Related to Figure 4.

Percent wild-type mosquitoes attracted to human odor trapped on nylon sleeves (one-way ANOVA, n=3). The dot plot represents the mean and standard error. Genotypes marked with the same letters are not significantly different ($p = 0.8576$) by post hoc Tukey's HSD test.

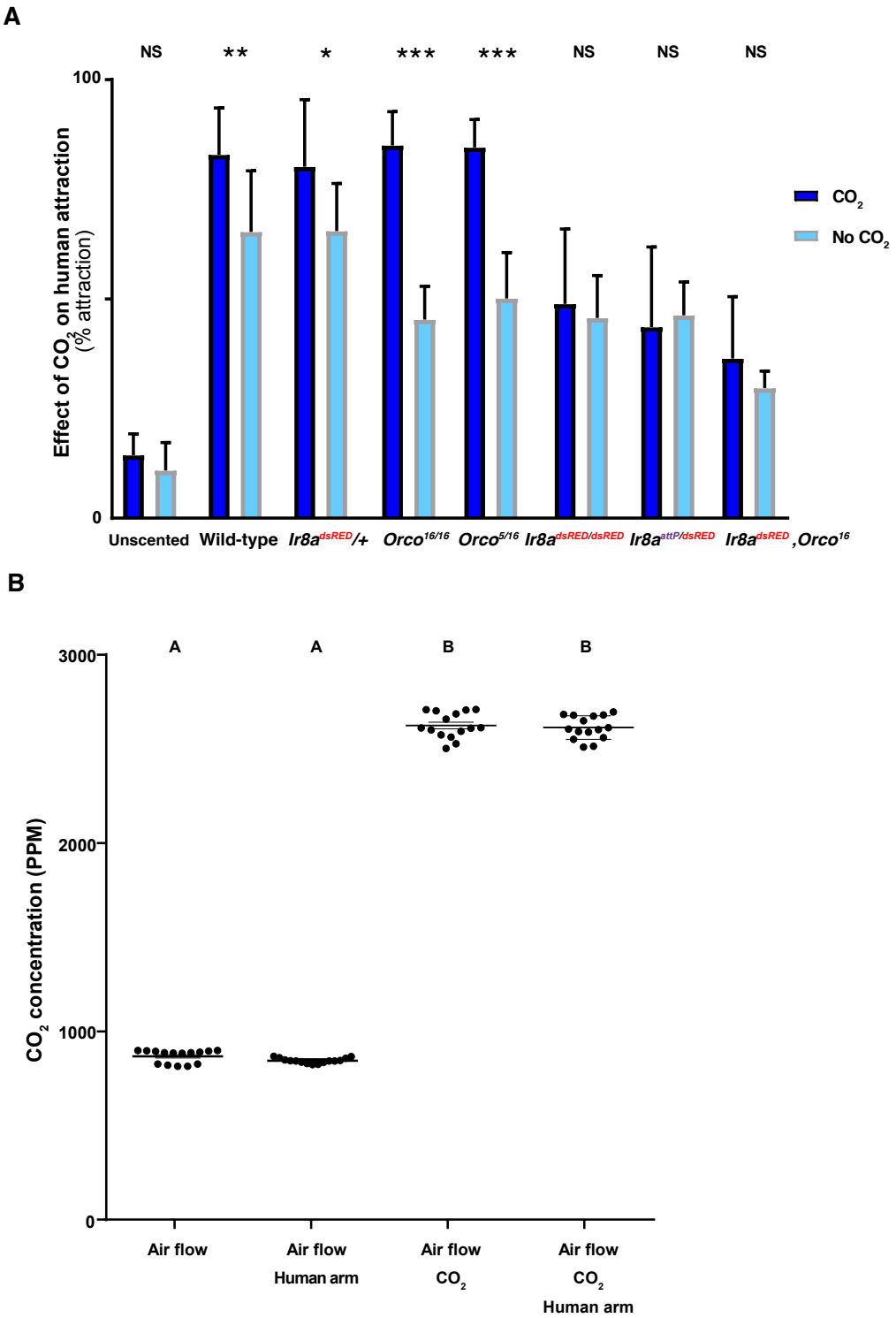

Figure S4: The attraction of *Ir8a* mutants to human odor is not modulated by the presence of CO_2. Related to Figure 4 & 5.

(A) Comparison of female mosquitoes attracted to human odor scented nylon sleeve in the presence and absence of CO_2. The bar plot represents the mean and standard error. Data compared is from figures 4C and 4F and analyzed by Two-way ANOVA, grouped column statistics comparing *Ir8a* and *orco* mutants. Genotypes marked with asterisk are significantly different ($p < 0.001$).

(B) Measurement of Carbon dioxide concentration in the uniport olfactometer at different conditions with amprobe-100. The presence of a human arm in the assay did not significantly increase the concentration of CO_2. The addition of CO_2 to the assay significantly increase the amount of CO_2 concentration detected. Data was analyzed by one-way ANOVA followed by Tukey's multiple comparison test ($p < 0.0001$, n = 15).

Primer name	Sequence
IR8aExon2CRISPRF	GAAATTAATACGACTCACTATA**GGGCGGACAAAATGGCGTAT**GTTTTAGAGCTAGAAATAGC
IR8aExon3CRISPRF	GAAATTAATACGACTCACTATA**GGACATCTGTCGACGATAAC**GTTTTAGAGCTAGAAATAGC
sgRNArev	AAAAGCACCGACTCGGTGCCACTTTTTCAAGTTGATAACGGACTAGCCTTATTTTAACTTGCTATTTCTAGCTCTAAAAC
infusionIR8LA_1	CCATGATTACGAATTCCGGGTGTTTGGTTCTCCAGATTTG
infusionIR8LA_2	ATGGCCATTCGAATTCATAGCATGCGATGTAAGTGCAGGTAC
infusion_IR8RA1	ATGTACAGAGCTCGAGCGGTATTCGACTACTACATTGTCTAC
infusion_IR8RA2	ACTAGTACTTCTCGAGAGTACCGCTTGGTCGGTTTGATCTTC
Ir8a^{dsRED}ForLA3	GTTGTTCATGAACGTGAACAACCGG
Ir8aexon4rev3	CGTTTCCTGTAGGCCCAAGGG
Ir8adsRedForLA1	GAACGTGAACAACCGGAAGTACCT
Ir8a_polyU_For	GCGGCCCAAGTAAGCAGTG
Ir8adsRED_poly_rev2	CAGCAAGTGACGTCAACCCTTC
Ir8a_afterRA_rev	AACCTCGGTAGTTCCAACGCG
SV40For1	CTGCATTCTAGTTGTGGTTTGTCC
Ir8aExon3for1	6-FAM fluorescent modification- CGGATTCTCGGTTCTGGATG
Ir8aExon3rev2	CTCGGTAGTTCCAAGGCGAAAGTA
TaqMan Universal forward primer	ATCAGTCCGATCGCTATGACAAG
TaqMan Universal reverse primer	GGTTGTCAATACCTTTCGGCTTAC

Table S1: Table for oligonucleotides. Related to STAR methods. Table listing the primers and their corresponding oligonucleotide sequences used in the study. Nucleotide sequence in bold letters indicate the CRISPR target sequence.

Individual ID	Age	Race/Ethnicity	Sex
Subject 1	28	Black/African	M
Subject 2	22	Black	M
Subject 3	22	White/Hispanic	F
Subject 4	28	White	M
Subject 5	23	Hispanic	M
Subject 6	22	White/Hispanic	F
Subject 7	26	Hispanic	F
Subject 8	25	White	M
Subject 9	21	Hispanic	F
Subject 10	21	White	F
Subject 11	41	White/Hispanic	M
Subject 12	20	Asian	F
Subject 13	24	Hispanic	M
Subject 14	19	White	F
Subject 15	21	White	F
*Subject 16	24	White/Hispanic	M
*Subject 17	22	White/Hispanic	M
*Subject 18	41	White	M

Table S2: Human subject details for behavioral assays. Related to Figure 3, 4 & 5. Table showing the profile of the subjects used in the uniport olfactometer assay. Attraction to subject number 1 to 15 is shown in figure 4B. Subject number 1 was used exclusively to attract mosquitoes in host-seeking assays besides the uniport experiment represented in figure 4B. Subject 1 was used to control for individual differences that humans subjects present to mosquitoes. Asterisks indicate excluded subject. Subject number 16 to 18 were excluded from the experimental because they withdrew from the experiment or less than 20% of mosquitoes were attracted to them.