# Detection of human herpesvirus 7 infection in young children presenting with exanthema subitum

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In this study, we assessed the prevalence of human herpesvirus-7 (HHV-7) in 141 serum samples from children less than four years of age with exanthematic disease. All samples were negative for measles, rubella, dengue fever and parvovirus B19 infection. Testing for the presence of human herpesvirus-6 (HHV-6)-specific high avidity IgG antibodies by indirect immunofluorescence assay (IFA) revealed two main groups: one composed of 57 patients with recent primary HHV-6 infection and another group of 68 patients showing signs of past HHV-6 infection. Another 16 samples had indeterminate primary HHV-6 infection, by both IgG IFA and IgM IFA. Serum samples were subjected to a nested polymerase chain reaction to detect the presence of HHV-7 DNA. Among patients with a recent primary HHV-6 infection, HHV-7 DNA was present in 1.7% of individuals; however, 5.8% of individuals tested positive for HHV-7 DNA in the group with past primary HHV-6 infection. Among the 16 samples with indeterminate diagnosis, 25% (4/16) had HHV-7 DNA (p < 0.002). We hypothesise that HHV-7 might be the agent that causes exanthema. However, a relationship between clinical manifestations and the detection of virus DNA does not always exist. Therefore, a careful interpretation is necessary to diagnose a primary infection or a virus-associated disease. In conclusion, we detected HHV-7 DNA in young children from the state of Rio de Janeiro, Brazil.

Key words: HHV-7 - children - exanthema subitum - PCR

Human herpesvirus-7 (HHV-7) is a member of the Roseolovirus genus within the Betaherpesvirinae subfamily, which was first isolated from purified, activated CD4<sup>+</sup> T lymphocytes from the peripheral blood of a healthy individual by Frenkel et al. (1990). HHV-7 is closely related to human herpesviruses-6 (HHV-6). Both cause infections that occur in early childhood and cause short febrile diseases and are sometimes associated with cutaneous rash [exanthema subitum (ES)]. Furthermore, HHV-7 and HHV-6 are highly prevalent in the healthy population and are known to establish latency in macrophages and T-lymphocytes. Healthy carriers also frequently shed virus in their saliva. Genetically, their nucleic acid sequence identity ranges from 20-75% in various genes and their virions share several common antigenic epitopes. These similarities have made the development of diagnostic assays challenging (Ward 2005, Caselli & Di Luca 2007). Along with ES, HHV-7 infections have been associated with sporadic cases of pityriasis rosea, hepatitis, neurological manifestations and transplant complications (Black & Pellett 1999).

ES is a classical rash disease of early childhood that is accompanied by the abrupt onset of a high fever that lasts three-four days; a maculopapular rash appears as the child's temperature falls by crisis. As hypothesised by Yamanishi et al. (1988), HHV-6B represents the primary etiological agent of ES and second exanthema episodes are caused by HHV-6 reactivation. However, HHV-7 was isolated from the peripheral blood lymphocytes (PBL) of children with ES that had a previously documented episode of HHV-6-associated ES; furthermore, examination of sera samples revealed IgG seroconversion for HHV-7 (Ueda et al. 1994). In conjunction with HHV-7 seroconversion, many primary cases also showed simultaneous increases in HHV-6 antibody titres. As multiple serological studies indicate that most children acquire HHV-6 prior to HHV-7 (Caserta et al. 1998, Black & Pellett 1999) and Frenkel et al. (1990) showed that HHV-7 infection can reactivate HHV-6 infection, it was hypothesised that reactivated HHV-6 may be the true cause of the clinical symptoms. However, more recent studies have found seroconversion and isolated HHV-7 DNA from the PBL of children with ES symptoms that do not exhibit evidence of prior HHV-6 infection (Torigoe et al. 1995, Caserta et al. 1998). Other explanations for increased HHV-6 antibody titres during primary HHV-7 infection include immune cell stimulation by common antigenic epitopes.

Although exanthematic syndrome is well characterised, it was noted many years ago that the rash is frequently misdiagnosed as measles, rubella or dengue infection (Tait et al. 1996, Oliveira et al. 2003). Thus, primary HHV-6 and HHV-7 infection should be included in the differential diagnosis of rash illnesses in young children. As described by Black et al. (1996), nearly 10% of rash illness patients who were presumptively diagnosed with measles or rubella were seronegative for these viruses

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in laboratory assays; these patients had seroconverted for HHV-7 and were most likely experiencing primary HHV-7 infection (Black et al. 1996). HHV-6 and HHV-7 should also be ruled out during rash presentations attributed to antimicrobial sensitivity to prevent children from incorrectly being diagnosed with allergies to antibiotics. In addition, the accurate diagnosis of HHV-7 and HHV-6 infections would decrease unnecessary antimicrobial prescriptions, reducing the potential for generating antibiotic-resistant microbes (Black & Pellet 1999).

Serological methods can be used for the detection of primary HHV-7 infection; however, immunological cross-reactivity between HHV-6 and HHV-7 is well documented (Ward 2005) and HHV-7 viremia can represent either a primary or a reactivated infection (Hall et al. 2006). Currently, although a specific immunofluorescence technique is accepted as the gold standard for HHV-6 diagnosis, no commercial test is yet available to screen for HHV-7 in the general population.

HHV-7-specific nested and conventional polymerase chain reaction (PCR) primer sets for qualitative, quantitative and multiplex assays have been developed and are useful for detection of viral DNA in human tissue samples and body fluids (Ward 2005).

In this study, we used a nested technique PCR to assess the prevalence of HHV-7 in serum samples from children less than four years of age with exanthematic disease.

The study was conducted between January 1998-December 2006 at the Antônio Pedro University Hospital and a large primary health care unit in Niterói, state of Rio de Janeiro (RJ), Brazil. A total of 141 serum samples were obtained from children younger than four years old who presented with rashes. All samples tested were previously screened and were negative for measles, rubella, dengue fever and parvovirus B19 infections. All samples were also PCR negative for the presence of HHV-6 DNA, as described by Magalhães et al. (2010b). Additionally, samples were tested for the avidity of HHV-6-specific IgG antibodies by indirect immunofluorescence assay (IFA), as described by de Oliveira Vianna et al. (2008). Overall, 57 patients exhibited recent HHV-6 primary infection, defined by low antibody avidity detected by IFA. In contrast, 68 had past HHV-6 primary infection, determined by the presence of high avidity antibodies detected by IFA; thus, the patients in this group did not exhibit any agent associated with rash. The other 16 samples had indeterminate primary HHV-6 infection; in these patients, the only serum available was obtained during the acute phase and was negative HHV-6-specific antibody. In general, these samples were taken less than nine days after rash onset, at a medium of five days after fever onset. In these cases, primary infection could not be excluded by IFA (Oliveira et al. 2003). De Oliveira Vianna et al. (2008) also investigated IgM antibodies by using IFA, but no IgM positivity was detected (Biotrin Human Herpesvirus 6 IgM IFA, Biotrin, Ireland).

Informed consent was obtained from the parents or guardians of the patients. The study protocol was approved by the Hospital's Research Ethics Committee (CEP-CMM/HUAP 85/02). To detect HHV-7 infection, DNA was extracted from 500  $\mu$ L of serum by using QIAmp Kit (QIAgen, Germany) and tested for HHV-7 DNA with the use of a nested PCR assay; reaction conditions and primer sets were as previously described in Magalhães et al. (2010a). Data were analysed using the EPInfo 2004 Statistical Software Package (CDC, Atlanta, EUA, 2004). Prevalence rates were compared through Chi-square tests with a Yates correction. The significance level (p) was set at 0.05.

PCR testing revealed that of the 141 samples, nine were positive for HHV-7 DNA (6.4%). Among the 57 samples that exhibited a recent primary HHV-6 infection, HHV-7 DNA was present in 1.7% (1/57). When we analysed the 68 samples with past primary HHV-6 infection, we observed a frequency of 5.8% (4/68) for the detection of HHV-7 DNA. It is interesting to note that among the 16 acute serum samples with indeterminate diagnosis, 25% (4/16) had HHV-7 DNA (p < 0.002). Although no statistical correlation was observed between female and male patients for cases (1 male) or controls (2 males, 2 females), all four inconclusive samples were from male patients. However, our casuistic was too small to suggest any correlation, as has been described in the literature, associating young girls with a higher sensitivity (Ward 2005).

The frequency rates described here are lower than those previously published (Kidd et al. 1998). Our findings may have resulted from the fact that our study group was very young, mainly comprised of children less than three years of age, making it possible that these children had not been infected yet; this hypothesis was also proposed by Ward (2005). However, these results could also be attributed to the lack of standardisation of *Roseolovirus* diagnosis. As suggested by Black and Pellet (1999), detection of viral DNA in the serum is indicative of an active infection, but less sensitive primer pairs, low viral loads or inhibitors present in the serum could cause false negatives.

Notably, the laboratory diagnosis of HHV-6 and 7 infections is confounded by the limited availability of antibody and DNA tests, problems with antigenic cross-reaction and a lack of understanding of the clinical relevance and epidemiology of these two viruses (Ward 2005).

Regarding *Roseolovirus* primary infection epidemiological data, several authors have proposed that HHV-7 infection usually occurs later than HHV-6 infection (Wyatt et al. 1991, Torigoe et al. 1995, Tanaka-Taya et al. 1996, Ward et al. 2001). However, HHV-7 infection may sometimes occur earlier or as soon as infection by HHV-6 (Oliveira et al. 2003). Consistent with these findings, we examined a one-year old child with a recent HHV-6 infection and HHV-7 DNA, suggesting the occurrence of a coinfection. Such events have been previously described by Hall et al. (2006). Notably, our study population exhibited a low socio-economic status, which has been associated with early disease exposure (Ongrádi et al. 1999).

In this study, we found that 5.8% of individuals had a past primary HHV-6 infection and HHV-7 DNA. In these patients, the observed exanthema could have been caused by either HHV-7 or by HHV-6 reactivation, as previously observed by Tanaka-Taya et al. (2000) in vitro and by Frenkel and Roffman in 1996 in vivo. Although antibody detection tests to confirm HHV-7 seroconversion were not performed in these studies, these children were three years old or younger, suggesting that HHV-7 could be the agent causing the clinical signs (Oliveira et al. 2003). It is important to emphasise that HHV-6specific PCR was performed and that no positive cases were found (Magalhães et al. 2010b). However, although herpesvirus DNA was detected in the serum of these immunocompetent children, there is not always a relationship between clinical manifestations and the detection of virus DNA. Therefore, a careful interpretation is necessary to diagnose a primary infection or a virusassociated disease (Hara et al. 2002). Prevalence rates described here were similar between cases and controls and no statistical differences were found (p = 0.52).

Among our samples, we detected HHV-7 DNA in 25% of the samples with previously undetermined diagnosis. We speculate that these patients, who were negative for prior exposure to other exanthematic agents, such as rubella, measles, parvovirus B19 and dengue fever, could be presenting an exanthematic episode due to primary HHV-7 infection. This group was previously tested for HHV-6 exposure by IFA detection of IgM antibodies, but no positivity was found and they were still undetermined. In fact, IgM tests usually have low accuracy, related to serum inhibitors and cross-reactivity among herpesviruses; these issues can give rise to both false positive and false negative results (de Oliveira Vianna et al. 2008).

Although PCR detection has not been validated for the clinical diagnosis of HHV-7 infection, given the lack of proper antibody detection assays, it might be further studied as a possible tool for the differential diagnosis of exanthematic disease in young children. In conclusion, we describe HHV-7 DNA detection in young children, corroborating previous findings of HHV-7 infection in RJ.

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### Supplementary data

Contig	n	vs. Ae. aegypti Liverpool strain transcripts	е	vs. Liverpool strain genomic supercontigs	vs. Anopheles gambiae	vs. Drosophila melanogaster	Function
1	32	AAEL008802-RA conserved hypothetical protein	e-142	-	AGAP012571	-	
2	10	AAEL008802-RA conserved hypothetical protein	e-143	-	AGAP012571	-	
3	16	AAEL006824-RA cytochrome P450	0	-	AGAP000877	CG3972	
4	5	AAEL008802-RA conserved hypothetical protein	4e-69	-	AGAP012571	-	
5	2	AAEL008802-RA conserved hypothetical protein	5e-53	-	AGAP012571	-	
6	14	AAEL004851-RA hypothetical protein	1e-99	-	-	-	
8	12	AAEL004054-RA cytochrome P450	0	-	AGAP001076	CG11715	
9	10	AAEL002204-RA fatty acid synthase	0	-	AGAP008468	CG17374	Esterase/lipase/thioesterase
10	8	AAEL003942-RA 60S ribosomal protein L44 L41, putative	e-174	-	AGAP003538	CG7424	
11	5	AAEL004855-RA ADP, ATP carrier protein	0	-	AGAP006782	-	Mitochondrial carrier protein
12	4	AAEL000010-RB ribosomal protein L36, putative	0	-	AGAP002921	CG7622	
13	7	AAEL002832-RA 40S ribosomal protein S26	0	-	AGAP012100	CG10305	
14	2	AAEL010668-RA quinone oxidoreductase	6e-92	Supercont1.363	AGAP006478	-	Alcohol dehydrogenase
15	2	AAEL004851-RA hypothetical protein	2e-33	-	-	-	
16		AAEL011400-RA conserved hypothetical protein	0	-	-	-	Fibrinogen
17	2	AAEL014562-RA 60S ribosomal protein L12	0	-	AGAP010065	CG3195	-
18	2	No hits found	e-138	Supercont1.495	-	-	
19	6	AAEL015404-RA lysozyme P, putative	0	-	AGAP007347	CG1165	
20	3	AAEL002737-RA cytochrome c oxidase, subunit VIIC, putative	e-113	-	AGAP007621	CG2249	
23	1	AAEL009423-RA cd36 antigen	0	Supercont1.408	AGAP010133	CG31741	Adhesion molecule
24	2	AAEL003559-RA conserved hypothetical protein	e-168	Supercont1.114	AGAP005874	CG2669	
26	1	AAEL004420-RB conserved hypothetical protein	0.003	Supercont1.574	AGAP005036	CG3857	
27	1	AAEL014052-RC endoplasmic reticulum protein erp29	3e-50	Supercont1.377	AGAP000395	CG7225	
28	1	AAEL002094-RA conserved hypothetical protein	0	Supercont1.550	-	CG18265	Zinc finger
30	1	AAEL014039-RB conserved hypothetical protein	e-129	-	AGAP000669	CG30415	C C
31	2	AAEL002534-RA 60S ribosomal protein L10	e-77	-	AGAP000953	CG17521	
33	1	AAEL007868-RA ubiquinol-cytochrome c reductase complex 14 kd pro	e-175	-	AGAP012188	CG17856	
34	3	AAEL008188-RA 60S ribosomal protein L6	2e-32	-	AGAP001911	CG11522	
35	2	AAEL009724-RA hypothetical protein	0.00007				Zinc finger
36	1	AAEL013272-RA 60S ribosomal protein L37a	9e-95	-	AGAP009920	CG5827	-
38	1	AAEL004523-RA SecY protein	0	Supercont1.122			
39	1	AAEL003349-RA NADPH cytochrome P450 reductase	e-116	-	AGAP000500	CG11567	
40	2	AAEL003347-conserved hypothetical protein	0	Supercont1.84	-	-	Cellular retinaldehyde- binding/triple function
41	2	No hits found	0	Supercont1.968	AGAP000952	CG9091	Ribosomal protein 60S

List of 326 contigs identified from the expression library generated from oenocytes of Aedes aegypti pupae

Contig	n	vs. Ae. aegypti Liverpool strain transcripts	e	vs. Liverpool strain genomic supercontigs	vs. Anopheles gambiae	vs. Drosophila melanogaster	Function
42	1	AAEL007011-RA conserved hypothetical protein	7e-65	-	AGAP004256	CG11259	LIM, zinc-binding
43	2	AAEL002325-RA conserved hypothetical protein	2e-34	Supercont1.285	AGAP007143	CG32210	
44	1	AAEL003791-RA conserved hypothetical protein	e-139	Supercont1.77	AGAP000261	CG7556	Myb, DNA-binding Heat shock protein DnaJ, N- terminal
45	1	AAEL002115-RA hypothetical protein	3e-64	Supercont1.86	-	-	Zinc finger, C2H2-type
43	2	AAEL014048-RA hypothetical protein	2e-34	Supercont1.285	AGAP009925	CG11614	Recoverin
44	1	AAEL003791-RA conserved hypothetical protein	e-139	Supercont1.77	AGAP000261	CG7556	Myb, DNA-binding Heat shock protein DnaJ, N- terminal
45	1	AAEL002115-RA hypothetical protein	3e-64	Supercont1.86	-	-	Zinc finger, C2H2-type
47	1	AAEL009770-RA ubiquitin-conjugating enzyme, E2	e-114	Supercont1.428	AGAP000495	CG3018	Ubiquitin (protein processing)
49	2	AAEL009506-RA 40S ribosomal protein S20	2e-59	Supercont1.725	AGAP010591	CG15693	•
50	1	AAEL012039-RA zinc finger protein	4e-63	Supercont1.644	AGAP004637	CG2125	
51	2	AAEL013407-RA catalase	6e-21	-	AGAP004904	CG6871	
52	1	AAEL008629-RA abc transporter	0	-	-	CG9663	ATPase
55	3	AAEL002339-RA conserved hypothetical protein	4e-25	Supercont1.410	AGAP004671	CG4738	
56	1	AAEL013271-RA organic cation transporter	2e-46	Supercont1.47	AGAP008335	CG9317	Major facilitator super- family general substrate transporter
57	3	AAEL012750-RA transcription factor TFIIH-subunit, putative	0	Supercont1.495	AGAP011110	CG8151	1
58	1	AAEL000352-RA hypothetical protein	8e-15	-	-	-	
59	1	AAEL003945-RA transcription initiation factor IIF alpha subunit	6e-59	-	AGAP002779	CG10281	
63	2	AAEL007824-RA ribosomal protein S29, putative	2e-46	Supercont1.47	AGAP001595	CG8495	
64	1	AAEL010243-RA abnormal X segregation, putative	0	Supercont1.1113	AGAP009776	CG9703	Nuclear metabolism
65	1	AAEL013865-RA conserved hypothetical protein	e-157	-	-	CG30380	
66	1	AAEL003799-RA conserved hypothetical protein	0	Supercont1.97	-	-	
67	1	No hits found	e-130	Supercont1.382	-	-	
68	11	AAEL013583-RA 60S ribosomal protein L23	4e-21	-	AGAP010252	CG3661	
70	1	AAEL000582-RA pickpocket	e-159	Supercont1.590	-	CG9703	Na+ channel, amiloride- sensitive
73	2	AAEL006169-RA cathepsin d	0	-	AGAP003277	CG10104	
74	1	AAEL004744-RA ccaat-binding transcription factor subunit a	0	-	AGAP008344	CG10447	
75	1	AAEL011711-RA nascent polypeptide associated complex alpha subun	e-132	-	AGAP006766	CG8759	
76	1	AAEL007633-RA dihydropyrimidinase	0	-	AGAP003124	CG1411	Nuclear metabolism

Contig	n	vs. Ae. aegypti Liverpool strain transcripts	e	vs. Liverpool strain genomic supercontigs	vs. Anopheles gambiae	vs. Drosophila melanogaster	Function
77	1	AAEL007431-RA conserved hypothetical protein	e-105	-	AGAP005149	CG7637	Nucleolar RNA-binding protein Nop10p
78		AAEL006448-RA hypothetical protein	5e-66	Supercont1.537	AGAP010934	-	TonB box, N-terminal
79	1	AAEL013173-RA calcium/calmodulin-dependent protein kinase type 1	0	Supercont1.65	AGAP009034	CG17528	Doublecortin
80	1	AAEL008854-RA conserved hypothetical protein	0	-	AGAP007954	CG12099	Zinc finger
83	1	AAEL004510-RA hypothetical protein	3e-81	-	-	-	
84	1	AAEL004791-RA sorting nexin	2e-94	Supercont1.19	AGAP002081	-	Regulator of G protein signalling
85	1	AAEL001275-RA ef-hand protein nucb1 Flagellar calcium-bindinprotein	0	-	AGAP005608	CG32190	Calflagin
86	1	AAEL009634-RD steroid dehydrogenase	e-106	-	AGAP004532	CG1444	Insect alcohol dehydroge- nase family
88	1	AAEL003594-RA kinectin, putative	0	Supercont1.173	-	-	
89	1	AAEL001930-RA pra1 protein	e-122	-	AGAP005121	CG10373	Prenylated rab acceptor PRA1
90	1	AAEL003105-RA supervillin	4e-76	Supercont1.442	AGAP007181	CG33232	Gelsolin
91	2	No hits found	0	Supercont1.324	-	-	
92	1	AAEL011662-RA plasma glutamate carboxypeptidase	e-134	Supercont1.106	AGAP001262	-	Protease-associated PA
93	1	AAEL008864-RA conserved hypothetical protein	6e-56	Supercont1.85	AGAP010432	CG8531	Heat shock protein DnaJ
94	1	AAEL004829-RA NADH dehydrogenase, putative	0	-	AGAP005621	CG6463	ETC complex I subunit
95	1	AAEL007385-RB ferritin subunit 1	e-113	-	AGAP002465	CG2216	
96	1	AAEL012585-RA 60S ribosomal protein L7	e-150	-	AGAP008916	CG4897	
97	1	AAEL002190-RA conserved hypothetical protein	1e-45	-	AGAP008492	CG4619	
98	2	AAEL010943-RA conserved hypothetical protein	e-170	-	AGAP003734	-	Cellular retinaldehyde- binding/triple function
99	1	AAEL002013-RA hypothetical protein	6e-15	-	-	-	Zinc finger
100	1	AAEL011471-RC 60S ribosomal protein L17	0	-	AGAP001459	CG3203	
101	1	AAEL013273-RA hypothetical protein	0	-	-	-	
102	1	AAEL012241-RA hypothetical protein	e-118	Supercont1.109	AGAP005919	-	
103	1	AAEL000795-RA ubiquitin	4e-94	-	-	-	
104	1	AAEL009737-RA conserved hypothetical protein	e-129	-	AGAP005448	CG9227	
105	1	AAEL014815-RA vacuolar protein sorting-associated protein (vps13)	0	Supercont1.593	AGAP003489	CG15523	Immunoglobulin/major his- tocompatibility complex
106	1	AAEL000572-RA amp dependent ligase	e-109	Supercont1.11	AGAP001763	CG30194	AMP-dependent synthetase and ligase
110		AAEL011870-RA rap55	1e-142	-	AGAP006935	CG10686	Proline-rich region
111	2	AAEL008883-RA conserved hypothetical protein	0	-	AGAP006471	CG18809	
112	1	AAEL014018-RA conserved hypothetical protein	e-129	Supercont1.83	AGAP006045	CG4005	WW/Rsp5/WWP
113	2	No hits found	e-179	Supercont1.89	-	-	

Contig	n	vs. Ae. aegypti Liverpool strain transcripts	e	vs. Liverpool strain genomic supercontigs	vs. Anopheles gambiae	vs. Drosophila melanogaster	Function
114	2	AAEL012698-RA ATP-binding cassette sub-family A member 3, putative	4e-54	Supercont1.2584	AGAP006379	CG1718	ATPase
115	2	AAEL009341-RA ribosomal protein L34, putative	0	-	AGAP009324	CG6090	
116	2	AAEL013536-RA ubiquitin	0	-	-	CG5271	Ribosomal protein L40
117	5	AAEL013542-RA elongase, putative	0	-	AGAP003196	CG16904	GNS1/SUR4 membrane protein
119	1	AAEL001977-RA conserved hypothetical protein	1e-57	Supercont1.306	AGAP008047	CG3173	Phosphotransferase system, HPr serine phosphorylation site
120	1	AAEL009038-RA prolylcarboxypeptidase, putative	0	-	AGAP005914	CG9953	Esterase/lipase/thioesterase
121	1	AAEL012686-RA ribosomal protein S12, putative	8e-51	Supercont1.725	-	CG8415	*
122	2	AAEL004151-RC conserved hypothetical protein	e-120	-	AGAP006612	CG10071	Ribosomal L29e protein
123	1	AAEL010053-RA conserved hypothetical protein	2e-47	Supercont1.42	AGAP002065	CG13848	Cellular retinaldehyde binding/alpha-tocopherol transport
124	1	AAEL010368-RB conserved hypothetical protein	9e-20	Supercont1.148	AGAP006232	CG4289	Peroxisomal membrane anchor protein
125	1	AAEL007898-RA calmin	2e-24	Supercont1.772	AGAP009554	CG33715	Spectrin repeat
126	1	AAEL006406-RC conserved hypothetical protein	0.013	Supercont1.204	-	-	Pheromone/general odorant binding protein
127	1	AAEL008770-RA proteasome subunit beta type	e-119	-	AGAP004991	-	
128	1	No hits found	e-121	Supercont1.136	-	-	
129	1	AAEL010819-RB vacuolar ATP synthase subunit H	e-155	-	AGAP003588	CG11589	Cell signalling
130	1	AAEL012733-RA 60S ribosomal protein L19	1e-59	-	AGAP004422	CG2746	
131		No hits found	0.71	Supercont1.36	-	-	
132	1	AAEL006860-RA ribosomal protein S28, putative	2e-36	-	AGAP003412	CG15527	
133	2	AAEL009214-RA diazepam binding inhibitor, putative	e-120	-	AGAP007460	CG8627	Acyl-coA-binding protein
134	1	AAEL002160-RA gtp-binding protein	0	-	AGAP000672	CG1354	Cell signalling
135	2	AAEL002527-RA conserved hypothetical protein	1e-62	-	AGAP000022	CG2791	Alpha amylase, catalytic subdomain
137	1	AAEL001134-RA methylmalonate-semialdehyde dehydrogenase	e-124	-	AGAP002499	CG17896	
138	1	AAEL015108-RA conserved hypothetical protein	0.020	-	AGAP006965	CG8793	ATPase, F1/V1/A1 com- plex, alpha/beta subunit, nucleotide-binding
139	1	AAEL010308-RA hypothetical protein	e-112	Supercont1.247	AGAP011070	CG18490	
142	1	AAEL007923-RA eukaryotic translation initiation factor 4 gamma	0	-	AGAP004750	CG3845	
143	1	AAEL008136-RA conserved hypothetical protein	0	-	AGAP003975	CG14716	Haem oxygenase
144	1	AAEL004068-RA hypothetical protein	0.004	-	-	-	HMG-I and HMG-Y, DNA- binding

### Supplementary data

Contig	n	vs. Ae. aegypti Liverpool strain transcripts	e	vs. Liverpool strain genomic supercontigs	vs. Anopheles gambiae	vs. Drosophila melanogaster	Function
145	10	AAEL010668-RA quinone oxidoreductase	e-106	Supercont1.363	AGAP006478	-	Alcohol dehydrogenase
146	3	AAEL007023-RA estradiol 17 beta-dehydrogenase	0	-	AGAP008667	CG3415	GroES-like Fatty acid synthase
147	1	AAEL009626-RA ankyrin repeat domain protein	8e-10	-	-	-	Immunoglobulin/ major histocompatibility complex
148	3	AAEL009994-RA 60S ribosomal protein L4	e-131	-	AGAP002306	CG5502	, i
149	2	AAEL003893-RA dna repair protein xp-c/rad4	0	Supercont1.470	AGAP003342	CG8153	
150	1	AAEL013434-RA Spatzle 1A	5e-04	Supercont1.53	-	-	
152	2	AAEL000987-RA 60S ribosomal protein L8	0	-	AGAP005802	CG1263	
153	1	AAEL000765-RA hexamerin 2 beta	0	-	-	CG2559	Arthropod hemocyanin/ insect LSP
154	1	AAEL001764-RA histone-fold protein CHRAC subunit, putative	e-130	-	AGAP005051	CG13399	Histone-like transcription factor/archaeal histone/ DNA topoisomerase
155	1	No hits found	0	Supercont1.658	-	-	-
156	1	AAEL010017-RA cytochrome B5	e-177	-	AGAP007121	CG2140	
158	1	AAEL007833-RA hypothetical protein	e-124	-	-	-	
159	1	AAEL006472-RA rabconnectin	e-116	Supercont1.388	AGAP010490	CG3585	WD-40 repeat
160	1	AAEL001247-RA conserved hypothetical protein	e-121	-	AGAP005602	CG15715	Zinc finger
161		No hits found	e-171	Supercont1.296	-	-	
162	1	AAEL003063-RA semaphorin	5e-69	Supercont1.284	AGAP005742	CG6446	
163	2	AAEL005753-RA serine protease	3e-80	-	-	-	
164	1	AAEL015617-RA conserved hypothetical protein	e-106	-	AGAP007614	CG30173	
165	1	AAEL009925-RA amidase	5e-87	-	AGAP002377	CG7900	
166	1	AAEL012122-RA 26S proteasome regulatory subunit S3	2e-99	Supercont1.125	AGAP009082	CG10484	
167	1	AAEL011010-RA conserved hypothetical protein	6e-97	-	AGAP012515	CG4692	
168	1	AAEL002568-RA conserved hypothetical protein	3e-87	-	-	-	EGF-like region
169	1	AAEL013236-RA proteasome subunit beta type 5,8	e-173	-	AGAP010718	CG12323	
170	1	AAEL009699-RA hypothetical protein	4e-34	Supercont1.998	-	-	Cytochrome P450
171	1	AAEL015592-RA structural maintenance of chromosomes smc1	0	Supercont1.612	AGAP002947	CG6057	ABC transporter related
172	1	AAEL009782-RA brain chitinase and chia	2e-45	-	AGAP000436	CG3044	
173	1	AAEL013221-RC 60S ribosomal protein L10a	0	-	AGAP011298	CG3843	
174	1	AAEL006482-RA sugar transporter	4e-60	Supercont1.127	AGAP001160	CG31100	
175	1	AAEL007679-RA conserved hypothetical protein	0	-	-	CG13994	Protein phosphatase inhibitor
176	1	AAEL008731-RA hypothetical protein	2e-89	-	-	-	

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Contig	n	vs. Ae. aegypti Liverpool strain transcripts	е	vs. Liverpool strain genomic supercontigs	vs. Anopheles gambiae	vs. Drosophila melanogaster	Function
177	1	AAEL006203-RA Juvenile hormone-inducible protein, putative	0	Supercont1.162	-	-	
178	1	AAEL013007-RA cytochrome c oxidase, subunit VB, putative	0	- op	AGAP008724	CG11015	
180	1	AAEL006698-RA 60S ribosomal protein L31	e-107	-	AGAP011896	CG1821	
181	1	AAEL009608-RA 28S ribosomal protein S16, mitochondrial	0	-	AGAP004818	CG8338	
182	1	AAEL003020-RA tailless	0	Supercont1.195	AGAP000819	CG1378	Nuclear hormone receptor, DNA-bindin
184		AAEL001887	e-116	Supercont1.45	AGAP008988	CG2718	Glutamine synthetase 1, mitochondrial precursor
185	4	AAEL008219-RA elongase, putative	7e-07	-	AGAP007264	-	*
186	1	AAEL000640-RB alanine-glyoxylate aminotransferase	3e-10	-	AGAP012404	CG11241	Aminotransferase class-III
187	2	AAEL003324-RA acidic ribosomal protein P1, putative	6e-10	-	AGAP007740	CG4087	Ribosomal protein 60S
189	2	AAEL008481-RB 60S ribosomal protein L18	8e-67	-	AGAP007580	CG8615	1
191	1	AAEL004071-RA nitrogen fixation protein nifu	0		AGAP005813	CG9836	
193	1	AAEL004027-RA glucose dehydrogenase	0	-	-	CG9509	Alcohol oxidase
194	1	AAEL004175-RA 40S ribosomal protein S17	0	-	AGAP004887	CG3922	
195	1	AAEL001164-RA NADH: ubiquinone dehydrogenase, putative	0	-	AGAP008653	CG3214	Proton-pumping
198	1	AAEL003505-RA jun	0	Supercont1.1051	AGAP006386	CG2275	Transcription factor Jun
199	1	AAEL004120-RA Niemann-Pick Type C-2, putative	0	-	AGAP012352	CG11314	protein and Def2/Der2 allergen-immunoglobulin- like
200	1	AAEL011056-RA transcription factor HES-1	1e-53	Supercont1.809	-	CG10446	Basic helix-loop-helix dim- erisation region bHLH
201	1	AAEL005901-RB 40S ribosomal protein S3a	e-136	-	AGAP003532	CG2168	C C
202	1	AAEL011287-RA ubiquitin specific protease	0	Supercont1.793	AGAP000884	CG15817	Involucrin repeat-insoluble envelope beneath the plasma membrane
203	1	AAEL013661-RA actin binding protein, putative (thymosin beta-4-)	8e-81	Supercont1.304	AGAP000235	CG4944	1
204	1	AAEL005725-RA conserved hypothetical protein	3e-51	Supercont1.470	AGAP002839	CG3184	WD-40 repeat signal transduction and transcrip- tion regulation to cell cycle control and apoptosis
205	1	AAEL007283-RA acetyl-coa synthetase	3e-85	-	AGAP001473	CG6432	Long chain fatty acid Co-A ligase
206 207	1 1	AAEL001501-RA anamorsin, putative AAEL009124-RA cytochrome P450	0.44 0	- Supercont1.390	AGAP008883	CG4180 CG10240	C
208	1	AAEL002533-RA conserved hypothetical protein	e-144	-	AGAP001084	CG4020	Male sterility protein-that converts wax fatty acids to fatty alcohols

Contig	n	vs. Ae. aegypti Liverpool strain transcripts	е	vs. Liverpool strain genomic supercontigs	vs. Anopheles gambiae	vs. Drosophila melanogaster	Function
209	1	AAEL004691-RA ring finger	0	-	AGAP005202	CG16982	Zinc finger bind DNA, RNA, protein and/or lipid substrates
210	2	AAEL010756-RA 40S ribosomal protein S19	1e-71	-	AGAP010933	CG4464	
211	1	AAEL014903-RA 40S ribosomal protein S24	2e-44	-	AGAP005131	CG3751	
212		No hits found	2e-49	Supercont1.222	-	-	
214	2	AAEL008144-RA amp dependent ligase	0	-	AGAP010870	CG3394	AMP synthaselong chain fatty acid Co-A ligase, acetyl-CoA synthetase
215	2	AAEL009257-RA conserved hypothetical protein	e-130	-	AGAP007768	CG14028	Cytochrome c oxidase subunit VIc
216	1	AAEL006096-RA Gelsolin precursor	0	-	AGAP011369	CG1106	
217	1	AAEL011295-RA conserved hypothetical protein	e-120		AGAP008921		
218	1	AAEL011042-RA conserved hypothetical protein	0	-	AGAP006832	-	
220	1	AAEL003921-RA anopheles stephensi ubiquitin, putative	e-133	-	AGAP002389	CG7215	
221	1	AAEL010731-RA conserved hypothetical protein	e-168	-	AGAP009095	CG3077	Phox-like-cell signalling, vesicular trafficking, protein sorting and lipid modifica- tion
222	1	AAEL002565-RA titin	1e-92	Supercont1.113	AGAP001633	CG32019	Immunoglobulin-like domains
224	1	AAEL003320-RA conserved hypothetical protein	3e-38	Supercont1.1024	AGAP004724	-	Salmonella/Shigella invasin protein C
225	2	AAEL002401-RA proteasome subunit beta type	e-176	-	AGAP008837	CG17301	r
226	2	AAEL013574-RB apolipoprotein D, putative	e-168	-	AGAP011478	-	Transport of nutrients
227	1	AAEL005931-RA 6-phosphogluconate dehydrogenase	e-140	-	AGAP004197	CG3724	
228	1	AAEL004180-RA conserved hypothetical protein	3e-70	Supercont1.311	AGAP000106	CG7277	Aerobic ubiquinone biosyn- thesis pathway
229	1	AAEL010405-RA alkyldihydroxyacetonephosphate synthase	6e-74	-	AGAP004358	CG10253	Catalyses the oxidation of a wide variety of substrates
230	1	AAEL010573-RB ribosomal protein S25, putative	8e-89	-	AGAP004462	CG6684	
231	1	AAEL012798-RA lumbrokinase-3(1) precursor, putative	2e-24	Supercont1.566	-	-	Peptidase S1A, chymot- rypsin
232	1	AAEL014555-RA Ump1p protein, putative	0	-	AGAP009647	CG9324	Proteasome maturation fac- tor UMP1
233	1	AAEL013614-RB clathrin heavy chain	0	Supercont1.48	AGAP009647	CG9324	
235	1	AAEL002017-RA protein serine/threonine kinase, putative	4e-98	Supercont1.83	-	CG11390	Insect pheromone-binding protein A10/OS-D
236	1	AAEL002293-RA conserved hypothetical protein	e-113	-	AGAP011825	-	r'ottinitio, oo D

Contig	n	vs. Ae. aegypti Liverpool strain transcripts	e	vs. Liverpool strain genomic supercontigs	vs. Anopheles gambiae	vs. Drosophila melanogaster	Function
237	2	AAEL006389-RA cathepsin 1	9e-63	-	AGAP012577	CG8947	
238	1	AAEL003471-RA hypothetical protein	1e-48	Supercont1.744	AGAP004764	-	Zinc finger
239	1	AAEL005997-RA allergen, putative	0	-	-	CG6783	Cytosolic fatty-acid binding
240	12	AAEL006824-RA cytochrome P450	0	-	AGAP000877	-	
241	1	AAEL012224-RA zinc finger protein	4e-39	-	AGAP009068	-	
242	1	AAEL006050-RA nuclear RNA export factor 2 (NXF2), putative	4e-37	Supercont1.42	AGAP002004	CG4118	Regulates all receptor-me- diated transport between the nucleus and the cytoplasm
243	1	AAEL007869-RA hypothetical protein	2e-92	-	-	-	Zinc finger
244	1	AAEL009080-RA importin 7	6e-33	Supercont1.288	AGAP007299	CG7935	· ·
246	1	AAEL008786-RA caax prenyl protease ste24	4e-37	Supercont1.37	AGAP004470	CG9000	ABC transporter related- which uses the hydrolysis of ATP to energize diverse biological systems
247	1	AAEL011656-RA 40S ribosomal protein S15	1e-27	-	AGAP001274	CG8332	
248	1	AAEL010230-RA NADH: ubiquinone dehydrogenase, putative	1e-92	Supercont1.113	AGAP009865	CG9306	Complex 1 LYR protein- believed to be be required for iron-sulphur custer biogenesis
249	1	AAEL008583-RA conserved hypothetical protein	e-150	Supercont1.96	AGAP011880	CG8833	DNA-damage-repair proteins
250	1	AAEL002933-RA conserved hypothetical protein	0	-	AGAP007147	-	Exosome-associated-DNA double-strand repair
251	1	AAEL007065-RA adp-ribosylation factor, arf	e-113	-	AGAP012014	CG8385	Vesicle biogenesis in intra- cellular traffic
252	1	AAEL000171-RA hypothetical protein	2e-78	Supercont1.55	-	-	Zinc finger
253	1	AAEL001664-RA hypothetical protein	e-106	-	-	-	
254	1	AAEL003160-RA conserved hypothetical protein	e-105	-	-	CG6770	
255	1	AAEL011587-RA ribosomal protein L27, putative	0	-	AGAP011687	CG4759	
256		AAEL006061-RA proteasome subunit alpha type	2e-73	-	AGAP001995	CG5266	
257	1	AAEL011676-RA amp dependent coa ligase	0	Supercont1.178	AGAP008557	CG12512	The family of enzymes includes luciferase, long chain fatty acid Co-A ligase, acetyl-CoA syn- thetase
258	1	AAEL000912-RA conserved hypothetical protein	0	-	AGAP010788	-	Male sterility-involved in male gametogenesis
259	2	AAEL000673-RA conserved hypothetical protein	0	-	AGAP011983	CG10424	Carbohydrate kinase

Contig	n	vs. Ae. aegypti Liverpool strain transcripts	e	vs. Liverpool strain genomic supercontigs	vs. Anopheles gambiae	vs. Drosophila melanogaster	Function
260	2	AAEL013605-RA hypothetical protein	e-104	-	AGAP006738	CG34018	Proteinase inhibitor I1, Kazal
261	1	AAEL011314-RA epoxide hydrolase	0	-	AGAP008684	CG15101	Detoxification of epoxides
262	1	AAEL004341-RA alpha-esterase	0	-	AGAP006723	CG9858	
263	4	AAEL005065-RA ptpla domain protein	0	-	AGAP003814	CG6746	Protein tyrosine phos- phatase-like protein, PTPLA-post-translational
264	1	AAEL008459-RA conserved hypothetical protein	0.018	-	AGAP000660	CG4557	
265	1	AAEL005065-RA ptpla domain protein	0	-	AGAP003814	CG6746	Protein metabolism
266	1	AAEL007771-RA 60S ribosomal protein L22	4e-	-	AGAP005046	CG7434	
267	1	AAEL009810-RA sideroflexin 1,2,3	2e-94	Supercont1.200	AGAP007119	CG6812	Tricarboxylate/iron carrier- tricarboxylate carrier from rat liver mitochondria
268	1	AAEL011663-RA conserved hypothetical	e-149	-	AGAP001271	CG10228	Protein membrane target- ing/cargo recognition role in vesicular trafficking
269	1	AAEL008131-RA cytidylate kinase	0	-	AGAP003968	CG6092	Adenylate kinase
270	1	AAEL013676-RA 26S protease regulatory subunit	0	-	AGAP007243	CG1489	Protein degradation, mem- brane fusion, microtubule severing, peroxisome bio- genesis, signal transduction and the regulation of gene expression
271	1	AAEL010487-RA conserved hypothetical protein	4e-34	-	AGAP003487	CG4666	
272	2	AAEL003006-RA 2-deoxyglucose-6-phosphate phosphatase	0	-	AGAP003372	CG15441	L-2-haloacid dehalogenase, epoxide hydrolases and phosphatases
273	1	AAEL003006-RA 2-deoxyglucose-6-phosphate phosphatase	0	-	AGAP003372	CG15441	Cell signalling
275	1	AAEL002833-RA cathepsin l	2e-04	-	AGAP011828	CG6692	
276	1	AAEL012903-RA sugar transporter	0	Supercont1.151	AGAP007856	-	Membrane proteins re- sponsible for the binding and transport of various carbohydrates
278	1	AAEL008424-RB sodium/shloride dependent amino acid transporter	4e-37	Supercont1.487	-	CG3252	Symporter activity
279	1	AAEL008188-RA 60S ribosomal protein L6	0	-	AGAP001911	CG11522	
280	1	AAEL005652-RA hypothetical protein	0	Supercont1.168	-	-	
282	1	AAEL006511-RA Anopheles stephensi ubiquitin	0	-	AGAP007927	CG2960	Ribosomal protein
283	2	AAEL006169-RA cathepsin d	0	-	AGAP003277	CG10104	
284	1	AAEL003147-RA conserved hypothetical protein	0	Supercont1.468	AGAP003565	-	Zinc finger

Contig	n	vs. Ae. aegypti Liverpool strain transcripts	e	vs. Liverpool strain genomic supercontigs	vs. Anopheles gambiae	vs. Drosophila melanogaster	Function
288	2	AAEL013661-RA actin binding protein, putative	0	-	AGAP000235	-	Thymosin beta-4-inhibit actin polymerization
290	1	AAEL006389-RA cathepsin l	0	-	AGAP012577		1 5
291	2	AAEL011758-RA peptidyl-prolyl cis-trans isomerase f, ppif	0	-	AGAP000462	CG7768	Peptidyl-prolyl cis-trans isomerase, cyclophilin type-protein folding by catalyzing the cis-trans isomerization of proline imidic peptide bonds in oligopeptides
292	2	AAEL003431-RA proteasome subunit beta type 7,10	0	-	AGAP011423	CG12161	
293	2	AAEL006885-RA 14-3-3 protein sigma, gamma, zeta, beta/alpha	0	-	AGAP007643	CG17870	14-3-3 protein-bind proteins
294	2	AAEL010843-RA conserved hypothetical protein	0	-	AGAP006459	CG17737	Translation initiation factor- directing the ribosome to the proper start site of translation
295	2	AAEL013533-RA conserved hypothetical protein	e-128	-	AGAP008001	CG5277	Ribosomal protein S8E
296	2	AAEL010821-RA 60S acidic ribosomal protein P0	e-112	-	AGAP003592	CG7490	
297	1	AAEL010943-RA conserved hypothetical protein	e-108	-	AGAP003734	-	Cellular retinaldehyde-bind- ing/triple function-visual cycle enzymes
298	1	AAEL004322-RA hypothetical protein	1e-52	Supercont1.524	-	CG6448	
299		No hits found	0	Supercont1.240	-	-	
300	1	AAEL000084-RA elongin b ubiquitin	2e-51	-	AGAP003154	CG4204	Protein processing
301	1	AAEL012200-RA protein kinase C inhibitor, putative	2e-38	-	AGAP006353	CG2862	Histidine triad protein-nucleotide-binding proteins
302		AAEL000284-RA conserved hypothetical protein	0	-	AGAP005673	CG9643	SAM (and some other nu- cleotide) binding motif
303	1	AAEL009829-RA ARL3, putative	0	-	AGAP006688	CG33162	ADP-ribosylation factor- vesicle biogenesis in intrac- ellular traffic
304	1	AAEL007173-RC conserved hypothetical protein	6e-08	-	AGAP004868	CG5174	Tumor protein D52-signal transduction and cell prolif- eration
305	1	AAEL004783-RA ornithine decarboxylase antizyme	0	-	AGAP010131	-	Ornithine decarboxylase antizyme-polyamine syn- thesis
306		No hits found	e-156	Supercont1.394	-	-	

Contig	n	vs. Ae. aegypti Liverpool strain transcripts	e	vs. Liverpool strain genomic supercontigs	vs. Anopheles gambiae	vs. Drosophila melanogaster	Function
307	1	AAEL004148-RA heat shock protein 70 (hsp70)-interacting protein	0	-	AGAP010188	CG2720	
308	1	AAEL008425-RA conserved hypothetical protein	0	-	AGAP000832	CG14899	Der1-like-proteolytic sys- tem ER
309	1	AAEL005207-RA neprilysin	2e-77	Supercont1.363	AGAP009791	CG5905	Peptidase M, neutral zinc metallopeptidases, zinc- binding site-peptidases
310	1	AAEL006533-RA Ets domain-containing protein	1e-98	Supercont1.133	AGAP009494	CG2914	Sterile alpha motif/pointed- induction or inhibition of gene transcription
312	1	AAEL001092-RA udp-glucose pyrophosphatase	0	-	AGAP004158	CG31063	Nucleoside diphosphate pyrophosphatase-glycogen biosynthesis
313	1	AAEL003125-RA acyl-coa dehydrogenase	0	-	AGAP006780	CG6638	Beta-oxidation in mitochon- dion
314	1	AAEL011540-RA metalloproteinase, putative	3e-74	Percont1.894	AGAP011475	-	Peptidase
315	1	AAEL003611-RA stearoyl-coa desaturase	1e-26	-	AGAP003050	CG15531	Fatty acid desaturases
316	1	AAEL013407-RA catalase	0	-	AGAP004904	CG6871	
317 318	1	AAEL004716-RB chromodomain helicase dna binding protein No hits found	e-141 e-115	Supercont1.352 Supercont1.293	AGAP008698 -	CG3733	Histone H5
320	1	AAEL004325-RA ribosomal protein L5	0	-	AGAP009031	CG17489	
321	1	AAEL002058-RA hypothetical protein	0	Supercont1.32	AGAP000504	-	
323	1	AAEL009169-RA synaptotagmin, putative	3e-12	Supercont1.51	AGAP003725	CG6643	C2-signal transduction or membrane trafficking
324	1	AAEL011436-RA myosin xv	2e-23	Supercont1.537	AGAP005213	CG2174	-
325	1	AAEL010826-RA histone-lysine n-methyltransferase	e-133	-	-	CG6476	Nuclear protein SET
326	1	AAEL005085-RA 60S ribosomal protein L30	e-159	-	AGAP003816	CG10652	
327	1	AAEL003666-RA leukotriene a-4 hydrolase	0.93	-	AGAP009907	CG10602	Leukotriene A-4 hydrolase/ aminopeptidase
328	1	AAEL012313-RA charged multivesicular body protein 5	0	-	AGAP005100	CG6259	Snf7-
329	1	AAEL012661-RA eukaryotic translation initiation factor	0	-	AGAP007668	CG10881	RNA recognition motif- implicated in regulation of alternative splicing
330	1	AAEL008473-RA cysteine-rich venom protein, putative	0	-	AGAP007583	CG16995	Pathogenesis-related proteins
333	1	AAEL001964-RA protein serine/threonine kinase, putative	0	-	-	-	Cell signalling
334	1	AAEL001513-RA wd-repeat protein	0.97	-	-	-	Cell signalling
335	1	AAEL012925-RA carbon catabolite repressor protein	4e-29	-	-	-	Endonuclease/exonuclease/ phosphatase
336	1	AAEL004278-RA conserved hypothetical protein	3e-09	-	-	-	

Contig	n	vs. Ae. aegypti Liverpool strain transcripts	e	vs. Liverpool strain genomic supercontigs	vs. Anopheles gambiae	vs. Drosophila melanogaster	Function
337	1	AAEL009278-RA conserved hypothetical protein	e-122	-	-	-	
338	1	AAEL007845-RA rab5	0	-	-	-	Regulators of vesicle biogenesis in intracellular traffic
340	1	AAEL002225-RA 5-oxoprolyl-peptidase, putative	2e-72	-	-	-	Peptidase C15, pyroglu- tamyl peptidase I
341	1	AAEL009274-RA conserved hypothetical protein	0	-	-	-	
342	1	AAEL010087-RA proteasome subunit alpha type	0	-	-	-	
343	1	AAEL009507-RA glucose-6-phosphate 1-dehydrogenase	7e-65	-	-	-	
345	1	AAEL009764-RB xaa-pro aminopeptidase	0	-	-	-	Peptidase M24
346	1	AAEL002260-RA conserved hypothetical protein	e-119	-	-	-	
347	1	AAEL006785-RB 60S ribosomal protein L18a	5e-28	-	-	-	
348	1	AAEL010777-RA thioredoxin (TRX), putative	e-180	-	-	-	Protein disulphide oxidore- ductase
349	1	AAEL010132-RA Pray For Elves, putative	2e-76	Supercont1.321	-	-	Leucine-rich repeat-protein- protein interaction/nervous system protein-protein interaction/immunity/neuro- nal connectivity
351	1	AAEL002508-RA 26S protease regulatory subunit 6a	0	-	-	-	
352	1	AAEL007293-RA camp-dependent protein kinase catalytic subunit	e-174	-	-	-	Protein kinase-phosphor- ylation
353	1	AAEL014821-RB hypothetical protein	8e-48	-	-	-	
355	1	AAEL006087-RA conserved hypothetical protein	0	Supercont1.1051	-	-	
356	1	AAEL001747-RA conserved hypothetical protein	0	-	-	-	
358	1	AAEL001037-RA ribosomal rna methyltransferase	0	-	-	-	
361	1	AAEL008789-RA apolipophorin-III, putative	0	-	-	-	
362	1	AAEL009436-RA conserved hypothetical protein	1e-17	-	-	-	
363	1	AAEL005799-RA peptidyl-prolyl cis-trans isomerase g, ppig	0	-	-	-	Peptidyl-prolyl cis-trans isomerase, cyclophilin type-protein folding by catalyzing the cis-trans isomerization of proline imidic peptide bonds in oligopeptides
364	1	AAEL010012-RA gtp-binding protein sar1	0	-	-	-	Protein trafficking. They may modulate vesicle bud- ding and uncoating within the Golgi apparatus

#### Supplementary data

Contig	n	vs. Ae. aegypti Liverpool strain transcripts	e	vs. Liverpool strain genomic supercontigs	vs. Anopheles gambiae	vs. Drosophila melanogaster	Function
365	1	AAEL013756-RA zinc/iron transporter	0	-	-	-	
367	1	AAEL013103-RA conserved hypothetical protein	3e-15	-	-	-	
369		No hits found	6e-37	Supercont1.1330	-	-	
370	1	AAEL000615-RA hypothetical protein	0	-	-	-	
371	1	No hits found	e-136	Supercont1.880	-	-	
373	1	AAEL010801-RB conserved hypothetical protein	e-159	-	-	-	
375	1	AAEL008159-RA short-chain dehydrogenase	0	-	-	-	Insect alcohol dehydroge- nase family
378	1	AAEL009637-RA cathepsin b	0				
380	1	AAEL007291-RA replication factor A, 14kD-subunit, putative	4e-30	-	-	-	

accession numbers listed are those assigned to genes previously identified via the whole genome sequence of *Ae. aegypti* Liverpool strain transcripts, *An. gambiae* and *D. melanogaster*. Expressed sequence tags (ESTs) identified in this study were deposited in dbEST under accessions. n: number of sequences used to make each contig.