## **Supplementary Figure Captions**

Fig. S1. **Isothermal titration calorimetry results for the binding of biogenic amine ligands with LJM-11, LJM-17 and LJM-111.** The upper panel of each graph shows the heat changes with each injection as a function of time. The lower panel shows a plot of the calculated enthalpies per injection versus molar ratio of ligand and target (squares). Also shown is the result of fitting the data to a single site binding model using the MicroCal origin software package. Panels 1-6: LJM11; Panels 7-12: LJM111; Panels 13-16: LJM-11 T328A mutant; Panels 17-20: LJM-11 N343A mutant. Below each graph the concentration of the protein in the calorimeter cell (P) and the ligand in the syringe (L) are shown.

Fig. S2. Stereoview of the LJM-11 binding pocket containing serotonin with the ligand covered by a Fo-Fc difference electron density map (colored in blue). The map was calculated using data collected from LJM-11 cocrystallized with serotonin. Protein carbon atoms are colored in white, nitrogen in blue and oxygen in red. Carbon atoms in serotonin are colored in green, with nitrogen colored in blue and oxygen in red. Hydrogen bonds are shown as red dashed lines.

Fig. S3. Alignment of phlebotomine salivary yellow proteins retrieved by a search of the GenBank protein database using the motif shown in Fig. 5A. Residues contained in the motif are shown highlighted in black or yellow. Absolutely conserved motif positions are marked by an asterisk, while motif positions that are not absolutely conserved are marked by a colon. The conserved cysteine positions are highlighted in blue. Abbreviations: PHLARI, *Phlebotomus ariasi*, PHLARA, *P. arabicus*, PHLPER, *P. perniciosus*, PHLARG, *P. argentipes*, PHLDUB, *P. dubosqi*, PHLPAP, *P. papatasi*, LUTLON, *L. longipalpis*.

Fig. S4. Chromatography of T328A and N343A mutants of LJM-11 on Superdex-75 in comparison to the wild-type protein. The retention volumes of the mutants are essentially identical to the wild type, with no indication of high molecular weight aggregates being seen.





(P: 2.5µM, L: 25 µM)



(P: 2.5 µM, L: 25 µM)

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Fig. S2



PHLARI_61373243 PHLARA_242564631 PHLPER_76446591 PHLARI_61817273 PHLPER_76446583 PHLDEB_112361963 PHLDEB_112361963 PHLDUB_112497236 PHLDUB_112497236 PHLDUB_112497236 PHLDUB_11249169 PHLPAP_15963517 LUTLON_4887116 LUTLON_77696451	-MKIFMGLIAVVSLQGALAYHVEREYAWKNITFEGIDQASYNIENSIP AFVHDALSKKI -MKIFLCLFAVVSFHGAFAYHVEREYAWKNITYEGIDQASYNIENSIP AFHDAISKKI -MKIFLCLFAVSIQGALASQIEREYAWKNIYEGIDQASYNIENSIP AFHDAISKKI -MKIFLCLFAVSIQGALASQIEREYAWKNISYEGIDPASYSVKNSIWGFAHDAASKKI -MKIFLCLFAVSIQGALASQIEREYAWKNISFEGIDPASYSVKNSIWGFAHDAASKKI -MKFIFLSTIFYQGILGYNVEREYAWRNISFEQNPESSYNVHSIMGFAHDAASKKI -MKFIFLSVLALASFQHVFCDDVERFYAWRNITEDVKEGTYRPEDVIPEGVTHDAKTKKL -MKFILSVLALASFQUVFCDDVERFYAWRNITEDVKEGTYRPEDVIPEGVTHDAKTKKL -MKLILTVLAFLSLQVALSDDVGRLYEWSKIDIVGVSPSVYDSSNIIPGVAYDADSKML -MKLILTVLAFLSLQVALSDDVGRLYEWSKIDIVGVSPSVYDSSNIIPGVAYDADSKKL -MKFIFLSVLALASFQHVFCDVERFYAWRNITEDVKEGTYRPEDVIPGUVDASTAKKL -MKLILTVLAFLSLQVALSDDVGRLYEWSKIDIVGVSPSVYDSSNIIPGVAYDADSKML -MKLILTVLAFLSLQVALSDDVGRLYEWSKIDIVGVSPSVDFSNIIPGVAYDADSKML -MKFFFLSVLALAVSQUASDVGRAYEWSKILDVGVPFNAYDSGNIVPGVAYDADSKML -MKFFFLAVTFGLAVLFGUSLSNITFCDJCDDTDYFKFNIFGLAVDFEGYRL -MKVFFSIFTLVLFQGTLGADT-QGYKWKQLLYNNVTPGSYNPDNMISAFAYDAEGEKL -MKLFFFLYTFGLVQTIFGVEIKQGFKWNKLIVEGDTSENFNPDNNIIAFFYDESQKL
PHLARI_61373243 PHLARA_242564631 PHLPER_76446551 PHLARI_161817273 PHLPER_76446543 PHLDUB_112361963 PHLPAP_15963519 PHLDUB_112497236 PHLDUB_112497236 PHLDUB_112497236 PHLPAP_15963517 LUTLON_41397462 LUTLON_77696451	IIAIPRIYPQVPITLTQLDTTKHPERSPPLEKFPGSDKLTSVYZPMLDEC FTITPRRYPQVPITLTELDTSKHPERSPPLSKFPGSDLINVYGPVIDEC FTAVPRRSPQIPFTLTELDTTKHPERSPPLSKFPGSDNISVYGPVIDEC FTITPRLNQVPITLTEDSIKYPGGSPPLSKFPGSDNISVYGPVIDEC FVAVPRRYPQVPHTLTELETKKHPERSPPLSKFPGGSDKLISVYGPVIDEC FVAVPRRYPQVPHTLTELETKKHPERSPPSKFNSQG-GKEFTSIVGPVIDEC FVAVPRRYPQVPHTLTELETKKHPERSPPLSKFSGKS-SKDLISIVGPVIDEC FVGVPRKSNIPTLAELDTNKYNSSEIRSPPFSKFNSQG-GKEFTSIVGPVIDEC FFGLPRKSKVPITVAQLSTRSYNSAERRDPPLDKFSGKS-KKPLTSVYGPVIDDC FFGLPRKYSKVPITVAQLSTRSYNSAERRDPPLDKFSGKS-KKPLTSVYGPVIDDC FFGIPRIYSRVPITAQLSTRSYNSAERRDPPLDKFSGKS-KKPLTSVYGPVIDDC FFGIPRIYSRVPITAQLSTRSYNSAERRDPPLDKFSGKS-KKPLTSVYGPVIDDC FFAVPRKVPYTLAELDTNKNSLSYSPFEFFKKFKNGG-GKETSIVGPVIDDC FFAVPRKVPYTLAELDTNKNSLSYSPFEFFKKFKNGG-KLTSIVGPVIDDC FFAVPRKVPYTLAELDTNKNSLGVKKHSPLDKFSGKHTGKELTSIVGPVIDDC FLAVPRKLPRVPYTLAEVDTKNSLGVKGKHSPLLKFSGGHTGKELTSIVGPVIDDC
PHLARI 61373243 PHLARA 242564631 PHLPER 76446591 PHLPER 76446593 PHLARG 74486543 PHLDEL 12361963 PHLDUB 112361963 PHLDUB 112497236 PHLDUB 112497236 PHLDUE 112361969 PHLPAP 15963517 LUTLON 4887116 LUTLON 41397462 LUTLON 77696451	RRLWIVDVGQVEYKG-DEQKYPKKNPAIIAYDLTKDNYPEIDRYEIPNIAG-NQIGFGG RRLWIVDAGEVEYKG-DEQKYPKRSAAIIAYDLTKDNYPEIGRYEIPRKIAG-NPLGFGG RRLWIVDAGQVEYKG-DEQKYPKNPAIIAYDLTKENYPEIRRYEIPSKIAGSNTIPFG RRLWIVDAGQVEYKG-DEQKIPKNPAIIAYDLTKDNYPEIDRYEIPNNAG-NPLGFGG RRLWVDVGQVDYKE-GPKYRKQNPAIIAYDLTKDNYPEIDRYEIPNNAG-NPLGFGG RRLWVDVGQVDYKK-NONEYPTNNPEIIAFDLNQEGNPEVHRYKLEGDVAK-TPLGFGG RRLWVLDVGQUDYKK-HGNEYPTNNPEIIAFDLNQEGNPEVHRYKLEGDVAK-TPLGFGG RRLWVLDVGQUDYKK-HGNEYPTNNPEIIAFDLNQEGNPEVHRYKLEGDVAK-TPLGFGG RRLWVLDVGQUDYKK-EKTYPTKNPEIIAFDLTKPNYPEIHRYELTGDAAK-TPLGFGG RRLWVLDVGIVEVEA-ERKTYPTKNPEILAFDLTKENYPEHRYELTGDAAK-TPLGYGG RRLWVLDVGIVENEA-EKTYPTKNPALVAFDLTKENYPEHRYELTGDAAK-TPLGYGG RRLWVLDUGIVENEA-EKKTYPTKNPALVAFDLTKENYPEHRYELTGDAGK-NFLGYGG RRLWVLDUGIVENEA-EKKTYPTNPAINAFDLTKSNYPEIHRYELTGEAGK-NFLGYGG RRLWVDUGVEVENEA-EKKTYPTNPALVAFDLTKENYPEIRKYELTGEAGK-NFLGYGG RRLWVDDGIVENEA-EKKTYPTNPALVAFDLTKENYPEIRKYELTGEAGK-NFLGYGG RRLWVDDGSVEYRSRGAKDYPSHRPAIVAYDLKQENYPEVRYYFPTRLVE-KFYFGG HRLWVVDIGSVEYRSRGAKDYPSHRPAIVAYDLKEANYPEVIRYTFPDNSIE-KPTFLGG
PHLARI_61373243 PHLARA_242564631 PHLPER_76446591 PHLARI_61817273 PHLPER_76446543 PHLDUB_112361963 PHLDUB_112361963 PHLDUB_112497236 PHLDUB_112497236 PHLDUB_112497236 PHLPAP_15963517 LUTLON_4887116 LUTLON_41397462 LUTLON_77696451	FTVDUTNPKEG CKTFIYITNEDNTLIVYDQEKKDSWKISHGSFKPE-HESNFSHN FTIDTNPTEG GKTFIYITNEDNTLIVYDQEKKDSWKISHGSFKPE-HDSVLTHN FAVDUTNPKEG CKTFIYITNEDNTLIVYDQEKKDSWKISHGSFKPE-HDSTLSHD FTVDUTNPKEG CKTFIYITNEDNTLIVYDQEKKDSWKISHGSFKPE-HESILJHN FAVDUTNPKEG CKTFIYITNEDNTLIVYDQEKKDSWKISHGSFKPE-HESILJHN FAVDUTNPKGG CKTFIYITNEDNTLIVYDQEKKDSWKISHGSFKPE-HESILJHN FAVDUNPKEG CKTFIYITNEDNTLIVYDQEKKDSWKISHGSFKPE-HESILJHN FAVDUNPKEG CKTFIYITNEDNTLIVYDQEKKDSWKISHGSFKPE-HESILJHN FAVDUNPKEG CKTFIYITNEDNTLIVYDQEKKDSWKISHGSFKPE-GSSVTNHK FAVDUNPKEG CSTFIYITNEDNALIVYDKNKNAWKFNDDSFKPEGKSVTNHK FAVDUNPKEG CNDEFTYLITNEIDNALIVYDKKKSDAWLKDDSFKPE-GSSTTHN FAVDUNPKEG CNDEKTYVIANDVENSLIVYDKKKSDAWLKDDSFKPE-GSTTHN FAVDUNPKEG CNDEKTYVIANDENSLIVDKKKSDAWLKDDSFKPE-GVSTTFIN FAVDUNPKEG SETFIYITNELRGALFIYDHKKQDSWVTHFTFKAE-RFTKPDG FAVDVNPKEG SETFIYITNELRGALFIYDHKKQDSWVTHFTFKAE-RFTKPDG
PHLARI_61373243 PHLARA_242564631 PHLPER_76446591 PHLARI_61817273 PHLPER_76446589 PHLARG_74486543 PHLDUB_112361963	G-AQYKYKAGIEGITLGDRDPEGNRPAYYLGGSSTKLFEVSTEALKKKGAKFDPVRLGDR G-KEHKYKVGIEGITLGDRDPEGNRPAYYLGGSSTKLFEISTEYLKKKGAKFDPVRLGDR G-KQYKYRVGLEGITLGDRDPEGNRPAYYLGGSSTKLFEISTKILKEKGAKFDPVNLGNR G-VDHILKLGIEGITLGDRDEEGNRPAYYLGGSSTKLFEVNTKALKKKBGEIEPITLGDR G-AOHILKLGIEGITLGDLDEEGNROAYYLGGSSTKLFRVNTKALKKKAGOIEFTPLGDR GGKKYSYKVGIEGITLGDRDEATGNRMAYYLAGSSTKLYKVNTKALKKKKBDFDIFICJGDR G-EEYTYSVGIEGITLGDRDKDGHRLAYYLAGSSTKVYNVNTANLKKKVKSLKPTLLGER

## Fig. S3 (page 2)

PHLPAP_15963519 PHLDUB_112497236 PHLDUB_112361969 PHLPAP_15963517 LUTLON_4887116 LUTLON_41397462 LUTLON_77696451	G-EQYSYIAGIEGITLGDRNKDGHRPAYYIAGSSTKUYSVNTASLKEKGASLKPRLLGER G-KEHKLETGIEGIALGDRNKEGNRPAYYLAGSSTKLYRLDTKLLKKKGSKLVPKLIGDR G-KEHELKTGIEGIALGDRNKEGNRPAYYLAGSSTKLYRLDTKLLKKKGSKLVPKLIGDR G-KEHKFKAGIEGIALGDRNKEGNRPAYYLAGSSTKLYRLDTKLLKKKGSKLEPKLIGDR GEEQMKYKVGLEGIALGDRNKEGNRPAYYLAGSSTKUYSVNTKELKTENGQLNPQLHGDR G-KEYEFKAGIEGITLGDRDSEGNRPAYYLAGSAIKVYSVNTKELKTENGQLNPQLHGDR G-QQYEYEAGIEGITLGDRDSEGNRPAYYLAGSAIKVYSVNTKELKQKGGKLNPELLGNK x
PHLARI_61373243 PHLARA_242564631 PHLPRR_76446591 PHLARI_61817273 PHLPRR_76446543 PHLDUB_112361963 PHLDUB_112361963 PHLDUB_112361969 PHLDUB_112361969 PHLPAP_15963517 LUTLON_4897116 LUTLON_41397462 LUTLON_77696451	GRHTEATALVYDPKTKVIFFAESDSRQISCWNTQKP-LNHKNTDVIYASSKFIESTDIQI GPKTEATALAYDPKTKVIFFAESDSRQISCWNTQKP-LNHKNTDVIYASAKFIIGOTISI GPHTEAVALYYDPKTKVIFFAESDSRQVSCWNTQKP-LNHKNTDVIFASAKFIIGOTISI GPHTEAVALYYDPKTKVIFFIEYNSKRISCWNTQKS-LNPDNIDVIYHSPDFIEGTISW GSHSEAVALAYDPKTKVIFFEYNSKRISCWNTQKS-LNPDNIDVIYHSPDFIEGTISW GYKTEATALAYDPKTKVIFFAESJSRQVSCWNICKD-LKPENVGVIYTNAYFVEGTIMV GYKTEATALAYDPKTKVIFFAESDSRQVSCWNICKD-LKPENVGVIYTNAYFVEGTIMV GYKTEATALAYDPKTKVIFFAESDSRQVSCWNIKKE-LKPENVGVIYTNAYFVEGTIMV GYKTEATALAYDPKTKVIFFAEDSRQVSCWNIKKE-LKPENVGVIYTNAYFVEGTIMV GYKTEATALAYDPETKVLFFAEDSRQVSCWNIKKE-LKPENVGVIYSAKLNAATMMV GYKTEATALAYDPETKVLFFAEDSRQVSCWNIKKE-LKPENVGVIYSAKLNAATMMV GYKTEATALAYDPETKVLFFAEDSRQVSCWNIKKE-LKPENVGVIYSSKINAATMMV GYKTEATALAYDPETKVLFFAEDSRQVSCWNIKKE-LKPENVGVIYSSKINAATMMV GYKTEATALAYDPETKVLFFAEDSRQVSCWNIKKE-LKPENVGVIYSSKFNAATMMV GKYTDATALAYDPETKVLFFAEDSRQVSCWNIKKE-LKPENVGVIYSSKFNAATMMV GKYTDATALAYDPETKVLFFAEDSRQVSCWNIKKE-LKPENVGVIYSSKFNAATM
PHLARI_61373243 PHLARA_242564631 PHLPER_76446591 PHLARI_61817273 PHLPER_76446589 PHLARG_74406543 PHLDUB_112361963 PHLDUB_112497236 PHLDUB_112497236 PHLDUB_112497236 PHLDUB_112497236 PHLDUB_112963517 LUTLON_4887116 LUTLON_41397462 LUTLON_77696451	DSDSQLWFLSNGOPPIDNLKLTFDKPHIRLMRVD-TKNSIRRTR-CEVKPIKKP DSESQLWFLSNGIPPIENLKLSFDKPHIRLMRVD-TKKSIRRTR-CEVKPIKKP DSESQLWFLSNGIPPIENLQLSFDKPHIRLMRVD-TKKAIRGTK-CEVKPAKP DSESKLWFFSNGIPPIENLQLSFDKPHIRLISVD-TKKSINGTK-CEVKP DSNSTLWVMNGIPPUDPDIUNNE-FYKPQIRLLYVD-TKKSIRGTK-CEVKP DADSTLWFMSNAPPTKIPKIEFDKRPIRLISVD-TKKSIRGTK-CEVKP DADSTLWFMSNAPPTKIPKIPKIEFDKRQIRLMYVP-THRAIRNLP-CEMRKA DSKGFLWFMSNGOPPTD-EKMKYEDPHIRLMKVK-TKKAIKGEKC-QG DSKGFLWFMSNGOPPTD-EKMKYEDPHIRLMKVK-TKKAIKGEKC-QG DSKGFLWFMSNGOPPTD-EKMKYEDPHIRLMKVK-TKKAIKGEKC-QG DSKGFLWFMSNGOPPTD-EKMKYDDPHIRLMKVK-TKKAIKGEKC-QG DSKGFLWFMSNGOPPTD-EKMKYDDPHIRLMKVK-TKKAIKGEKC-QG DSKGFLWFMSNGOPPTD-EKMKYDDPPIRLMKVK-TKKAIKGEKC-QG DSKGGLWFMSNGOPPTD-EKMKYDDPPIRLMKVK-TKKAIKGEKC-QG

Fig S4



Sequence	Accession Number	Mature MW	pl	Annotation
LJM17	AF132518	45.2	5.71	yellow related-protein
LJM11	AY445935	43.2	9.32	yellow related-protein
LJM111	DQ192488	43.0	4.85	yellow related-protein
LJL23	AF131933	35.0	9.14	Apyrase
LJL143	AY445936	32.4	8.45	Unknown
LJL34	AF132511	28.8	9.09	Antigen-5
LJL13	AF420274	26.4	4.93	D7-related protein
LJM10	DQ192486.1	16.6	8.61	C-type lectin
LJS142	DQ192487.1	16.6	7.07	C-type lectin
LJL18	DQ190947.1	16.3	6.49	C-type lectin
LJM04	AAD32197.1	13.8	9.09	SL1 protein
LJL17	AY452695	10.1	4.31	Unknown
LJS192	AY438270.1	9.6	4.21	Unknown
LJL08	M77090	6.9	8.91	Maxadilan
LJL201	AY455919	8.6	4.86	Unknown
LJL38	AY438269.1	2.5	3.34	Unknown

Table S1 – Characteristics of *Lutzomyia longipalpis* salivary proteins