Supplemental Tables

Table S1. Sequencing data summary, related to STAR methods

Sequencing data summary for the RNA-seq and DNA-seq results.

Animal	Type	tissue	paired/single	#reads	read length	%GC
Oct.vul.	RNA-seq	OL	paired	127049529	151x2	39
Oct.vul.	RNA-seq	SG	paired	126573775	151x2	39
Sepia	RNA-seq	OL	paired	159933775	151x2	39
Sepia	RNA-seq	SG	paired	131031103	151x2	40
Nautilus	RNA-seq	OL	paired	188232900	151x2	41
Nautilus	RNA-seq	Supra	paired	178490917	151x2	41
Oct.vul.	DNA-seq	Sperm sac	paired	498212805	101x2	35
Sepia	DNA-seq	Sperm sac	paired	500285022	101x2	33
Nautilus	DNA-seq	Sperm sac	paired	503446649	101x2	35

Table S2. Transcriptome assembly and ORF statistics, related to STAR methods

Transcriptome assembly statistics, and ORF statistics (based on the longest isoform found for each Trinity "gene"), for the different species.

	Squid	Sepia	Oct.vul.	Oct.bim.	Nautilus	Aplysia
Total Trinity 'transcripts'	151477	240756	201414	271576	458827	256514
Total Trinity 'genes'	107025	168878	150616	207439	282627	196908
Contig N50	755	687	784	749	992	1802
Median contig length	334	323	334	340	352	387
Mean contig length	573.65	543.02	579.98	574.31	662.03	869.75
Total assembled bases	61395149	91704707	87354553	119133693	187107820	223102930
Number of ORFs	12218	14954	13005	17786	11139	22951
Number of unique proteins	9385	10967	10218	12852	8485	17283
Mean ORF length	1369	1155	1317	1253	1392	1147
Median ORF length	1026	780	969	882	999	663
Total ORF length	16725027	17272626	17129859	22292061	15501153	26321973

Table S3. Extraordinary extent of A-to-I RNA editing in coleoid cephalopods, related to Figure 1.

In all species but Oct.bim., the majority of ORFs found contained recoding events. The higher number of ORFs detected and the somewhat lower fraction of edited ORFs in Octopus bim. is due to the different composition of sub-tissues used for transcriptome assembly (OL, sub, supra and ANC, compared with OL and SG for the other species). Re-assembling a transcriptome using only reads derived from the OL sample of Octopus bim. one finds recoding fraction consistent with the other species. This suggests a considerable variation of editing level across neural sub-tissues.

Animal	***Tissues used***	***# AG sites***	***#recoding sites***	***# ORFs found***	***#ORFs recoded***
Oct.vul.	*OL, SG*	*117842*	*76639 (65%)*	13005	*7953 (61%)*
Oct.bim.	*OL, ANC, sub, supra*	*76862*	*50079 (65%)*	17786	*6964 (39%)*
Oct.bim.	*OL*	*74436*	*48181 (65%)*	10974	*6717 (61%)*
sepia	*OL, SG*	*130636*	*86230 (66%)*	14954	*8537 (57%)*
squid	*OL, GFL*	*82975*	*54287 (65%)*	12218	*6688 (55%)*

Table S8. Multiply recoded proteins, related to Figure 4

List of 24 proteins containing 5 or more highly edited (>=10% editing levels) recoding sites that are shared by all 4 coleoid cephalopod species.

UniProt ID	Protein name	# highly edited, 4-species conserved, recoding sites
O54774	AP-3 complex subunit delta-1	5
O60271	C-Jun-amino-terminal kinase-interacting protein 4	5
O95359	Transforming acidic coiled-coil-containing protein 2	6
P09482	Neuronal acetylcholine receptor subunit alpha-4	5
P13395	Spectrin alpha chain	8
P23468	Receptor-type tyrosine-protein phosphatase delta	8
P41823	Synaptotagmin-1	6
P55162	Membrane-associated protein Hem	6
Q01484	Ankyrin-2	8
Q4KM31	LIM domain-containing protein 2	5
Q5U239	Transmembrane protein 145	5
Q6GLR7	Calcium-dependent secretion activator 1	7
Q6GPD0	Rho GTPase-activating protein 32	5
Q6VNB8	WD repeat and FYVE domain-containing protein 3	8
Q6ZPF3	T-lymphoma invasion and metastasis-inducing protein 2	6
Q7Z3G6	Prickle-like protein 2	5
Q80U22	Iporin	5
Q862Z3	Uromodulin	14
Q8N2Q7	Neuroligin-1	5
Q96RL7	Vacuolar protein sorting-associated protein 13A	12
Q9I8C7	Neuronal acetylcholine receptor subunit alpha-10	7
Q9I8D1	Unconventional myosin-VI	9
Q9NGC3	Centaurin-gamma-1A	9

Table S9. Predicted editing sites in squid, sepia and octopus vulgaris Kv2 channel, related to Figure 6.

List of editing sites for cephalopod Kv2.1 orthologs. Numbers in parentheses refer to specific Trinity assembly from our transcriptome. Fractional editing is based on estimates from our pipeline using OL and SG. These are the same channels as those in Fig. 3 and Fig. S10.

Sepia Kv2 (comp267321_c0_seq19)					Octopus Kv2 (comp182915_c0_seq17)					Squid Kv2 (comp141576_c1_seq4)			
nt	unedited codon	edited codon	Fractional Editing		nt	unedited codon	edited codon	Fractional Editing		nt	unedited codon	edited codon	Fractional Editing
1273	S	G	0.064		672	Q	R	0.022		1221	Q	R	0.062
2612	Y	C	0.781		765	H	R	0.517		1225	Q	Q	0.082
2352	Q	Q	0.256		789	H	R	0.869		1227	Q	R	0.116
2909	K	R	0.095		802	P	P	0.277		1231	Q	Q	0.068
2371	I	V	0.081		808	L	L	0.292		1320	H	R	0.525
2786	N	S	0.05		824	T	A	0.031		1332	H	R	0.065
2782	R	G	0.112		845	T	A	0.044		1341	H	R	0.267
2386	K	E	0.068		952	A	A	0.017		1344	Q	R	0.069
1142	H	R	0.063		961	A	A	0.051		1354	P	P	0.114
1329	P	P	0.356		994	A	A	0.035		1357	P	P	0.677
3921	L	L	0.154		1028	R	G	0.914		1376	T	A	0.104
1133	H	R	0.606		1046	S	G	0.142		1444	E	E	0.482
2235	K	K	0.101		1055	S	G	0.11		1460	S	G	0.218
1351	S	G	0.254		1069	V	V	0.103		1513	P	P	0.5
1789	M	V	0.083		1386	Y	C	0.028		1535	S	G	0.321
1040	Q	R	0.075		1418	M	V	0.035		1604	I	V	0.2
1148	H	R	0.104		1477	L	L	0.024		1616	S	G	0.882
1167	P	P	0.026		1479	E	G	0.019		1660	Q	Q	0.121
3179	K	R	0.069		1685	I	V	0.072		1726	R	R	0.182
2500	S	G	0.082		1753	E	E	0.036		1729	E	E	0.603
3705	I	M	0.095		1981	Q	Q	0.132		1737	K	R	0.037
1257	E	E	0.146		1982	I	V	0.382		1767	K	R	0.037
2362	I	V	0.214		2116	I	M	0.046		1773	E	G	0.053
1476	Q	Q	0.061		2241	Y	C	0.374		1799	M	V	0.07
2493	L	L	0.06		2303	I	V	0.704		1816	L	L	0.032
2780	K	R	0.056		2411	R	G	0.031		1827	K	R	0.029
2385	L	L	0.049		2539	K	K	0.065		1973	M	V	0.198
1157	Q	R	0.221		2621	N	D	0.016		1995	E	G	0.12
1542	R	R	0.085		2765	N	D	0.077		2114	R	G	0.463
1189	T	A	0.026		2771	M	V	0.098		2115	E	G	0.302
1237	K	E	0.083		2788	K	K	0.057		2240	I	V	0.921
1096	T	A	0.078		3042	K	R	0.611		2296	E	E	0.047
2056	I	V	0.459		3206	R	G	0.25		2338	V	V	0.041
1545	E	E	0.514		3227	S	G	0.091		2419	K	K	0.078
2644	S	G	0.134							2527	R	R	0.041
1044	Q	Q	0.066							2535	Q	R	0.038
2796	I	M	0.051							2536	Q	Q	0.066
2670	L	L	0.079							2537	I	V	0.831
3928	R	G	0.167							2545	R	R	0.039
1930	K	E	0.23							2648	M	V	0.1
1615	M	V	0.024							2818	K	K	0.033
2674	I	V	0.883							2828	S	G	0.385
1170	P	P	0.117							2854	L	L	0.074
1931	K	R	0.128							2858	I	V	0.979
3004	K	E	0.044							2980	I	M	0.03
1154	H	R	0.164							3093	K	R	0.305
1118	H	R	0.056							3240	E	G	0.038
1192	T	A	0.053							3342	N	S	0.033
2487	I	M	0.054							3971	S	G	0.054
1811	E	G	0.031							4154	S	G	0.062
1432	S	G	0.842										
1038	Q	Q	0.088										
1059	V	V	0.036										
1274	N	S	0.688										
1411	S	G	0.242										