Supplemental Figure S1: TransDecoder and BLAST comparisons. (A) TransDecoder-predicted peptides from the *Hermissenda* transcriptome assembly. Predicted proteins are separated to show numbers of predicted complete and incomplete open reading frames. Inlay shows cumulative histogram of TransDecoder predicted proteins. There were 4912 complete sequences, 3515 that were missing the 5’ end and 1851 that were missing the 3’ end. Most of the fragments with just internal sequences are under 200 amino acids in length. (B) BLAST comparisons of the *Hermissenda* transcriptome assembly are shown against published mRNA databases from *Tritonia*, *Aplysia*, and *Lymnaea* with E-values less than 1e-6, using as query *Hermissenda* transcriptome (white bars, tBLASTx) or *Hermissenda* predicted peptides (light grey bars, tBLASTn). (C) BLAST comparisons of the *Hermissenda* transcriptome assembly are shown against published protein databases with E-values less than 1e-6, using as query *Hermissenda* transcriptome cDNA (dark grey bars, BLASTx) or *Hermissenda* predicted peptides (black bars, BLASTp). Protein database abbreviations: Invertebrate RefSeq database (Invert RS), Mammalian RefSeq database (Mamm RS), Non-mammalian vertebrate RefSeq database (Non-mamm vert RS), and SwissProt database (SwissProt). See supplemental methods for database details.

Supplemental Figure S2: GO-terms mapped to the *Hermissenda* transcriptome. (A) Gene ontology (GO) comparisons were done at BLAST2GO level 2 for molecular functions, biological processes, and cellular processes. (B) Selected additional GO-terms are shown from levels 3 to 8. (C) Selected KEGG-pathway predicted enzymes related to learning and memory were calculated using BLAST2GO.

Supplemental Figure S3: Model of *Hermissenda* associative-learning pathways, including gene products predicted from the *Hermissenda* transcriptome. Genes identified in Supplemental Table S1 were used to re-create an associative learning pathway model that has been previously described (Tamse et al., 2003; Blackwell & Farley, 2008). Solid black lines represent known pathways, dashed lines indicate hypothesized pathways. Gene and metabolic product abbreviations: 5-HT (serotonin), GABA (gamma-aminobutyric acid), DAG (diacylglycerol), IP3 (inositol triphosphate), IP3R (inositol triphosphate receptor), AC (adenylyl cyclase), cAMP (cyclic adenosine monophosphate), PLC (phospholipase C), PLA2 (phospholipase 2), AA (arachidonic acid), RyR (ryanodine receptor), PKC (protein kinase C), MAPK (mitogen-activated protein kinase), MEK (ERK-activating kinase), PKA (protein kinase A), Ca (calcium).

Supplemental Figure S4: Comparison of RSEM values and qPCR-derived absolute copy numbers for three *Hermissenda* genes. 5-HT2a, 5-HT transporter, and Pedal peptide 3 precursor gene synthetic RNA standards were used to determine the absolute copy number for each gene in whole brain cDNA. The absolute copy numbers for each gene correlated with their RSEM transcripts per million reads (TPM) values with an $r^2$ value of 0.9999436. Error bars represent standard deviation.

Supplemental Table S1: Select learning-related genes with homologues identified in the *Hermissenda* brain transcriptome. Molluscan genes related to learning or memory were selected from the UniProt/SwissProt database and BLAST searched against the *Hermissenda*
transcriptome. *Hermissenda* gene homologues identified are listed as their contig identification number, and include their transcript length in base pairs (bp), their predicted protein open reading frame (ORF) length in amino acids (aa), and their RSEM-estimated relative abundance in the *Hermissenda* transcriptome as transcripts per million mapped reads (TPM) value. The predicted protein length for each identified gene was compared against published full length genes from other species: if the published gene was 100 or more amino acids longer than the *Hermissenda* predicted gene, then the *Hermissenda* gene was considered a fragment, and was labeled next to the ORF length in the table. If multiple fragments were identified as being part of the same gene, then their contigs are listed in single cells.

**Supplemental Table 2: Gene identification numbers for previously published genes.** The gene identification number and the database location it was retrieved from are listed.

**Supplemental Table 3: Primer sequences for 5-HT receptor verification from whole brain cDNA.**

**References:**
