



**Supplementary Figure 4: Cluster analysis of neuropeptide GPCRs.** a) Analysis of rhodopsin type neuropeptide GPCRs. b) Analysis of secretin type neuropeptide GPCRs. Connections are based on blast similarities  $< 1e-50$  (in a) and  $< 1e-70$  (in b). Colour and symbol coding: magenta star = xenacoelomorph, blue filled circle = chordate, light blue square = ambulacrarian, olive upward triangle = ecdysozoan, yellow downwards triangle = spiralian, black diamond = cnidian. A black dot inside a white circle indicates a receptor for which ligand-receptor activation has been shown before. Abbreviations are listed in Supplementary Figure 3.