The ability to integrate experiential information and recall it in the form of memory is observed in a wide range of taxa, and is a hallmark of highly derived nervous systems. Storage of past experiences is critical for adaptive behaviors that anticipate both adverse and positive environmental factors. The process of memory formation and consolidation involve many synchronized biological events including gene transcription, protein modification, and intracellular trafficking: However, many of these molecular mechanisms remain illusive. With Drosophila as a model system we use a nonassociative memory paradigm and a systems level approach to uncover novel transcriptional patterns. RNA sequencing of Drosophila heads during and after memory formation identified a number of novel memory genes. Tracking the dynamic expression of these genes over time revealed complex gene networks involved in long term memory. In particular, this study focuses on two functional gene clusters of signal peptides and proteases. Bioinformatics network analysis and prediction in combination with high-throughput RNA sequencing identified previously unknown memory genes, which when genetically knocked down resulted in behaviorally validated memory defects.