Bursicon is a neurohormone that regulates the cuticle sclerotization and wing expansion process in insects. Bursicon is a heterodimeric cystine knot protein containing two subunits, burs alpha and burs beta, which are encoded by two genes, *burs alpha* and *burs beta*. In the current study, the *burs alpha* and *burs beta* genes were cloned from the house fly *Musca domestica*. The transcriptional profiles of burs alpha and burs beta genes were analyzed in the central nervous systems of *M. domestica*. Recombinant *M. domestica* bursicon heterodimer (r-bursicon) was expressed in mammalian 293 cells and insect HighfiveTM cells, and was analyzed for bursicon function. Using the r-bursicon with a fly neck-ligation assay and the DNA microarray analysis, a panel of genes that is regulated by bursicon was identified from *M. domestica* and also the fruit fly *Drosophila melanogaster*. Two of these genes, *suppressor of hairless* and *pleckstrin homology*, were cloned and sequenced for further study in *M. domestica* (designated mdSu(H) and mdPH). The mdSu(H) is a transcription factor involved in an important signal transduction pathway, the Notch signaling pathway, and the mdPH is possibly responsible for regulating the G protein coupled receptor 2, which is proposed to be the receptor of bursicon. By studying mdSu(H) and mdPH, we have provided two excellent components that very likely involved in the bursicon regulated signal transduction pathway during the insect cuticle sclerotization and wing expansion process.