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Transcriptional Regulation of the *Drosophila raf* Proto-oncogene

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Raf-1, a protein serine/threonine kinase located primarily in the cytosol, serves as central intermediate in many signaling pathways, ultimately regulating cell proliferation, differentiation, and development by connecting upstream tyrosine kinases with downstream serine/threonine kinases such as MAPK and MAPKK. *D-raf*, a *Drosophila* homolog of the human *c-raf-1*, is also required for the regulation of cell proliferation and differentiation.

We confirmed that expression of the *D-raf* gene is regulated by the DNA replication-related element (DRE)/DRE-binding factor (DREF) system which have been known to regulate transcription of the genes encoding DNA polymerase α , PCNA, Cyc A and dE2F. In addition to DRE, we found E2F recognition site and STAT binding site in the 5'-flanking region of *D-raf* and demonstrated the fact that the E2F recognition site sequences and STAT binding site are also important for *D-raf* gene expression by using cultured cell system and transgenic flies.

Further, we demonstrated that the *D-raf* gene is another target of the homeodomain protein Zen, Ftz and Engrailed.