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COUP-TF1, (Chicken ovalbumin upstream promoter-transcription factor 1), as a positive transcription factor of BDNF gene expression

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Brain-derived neurotrophic factor (BDNF) is an important neuronal survival factor in the central nervous system (CNS), promotes neuron differentiation and survival, and mediates learning and memory. BDNF expression is activated through calcium ion signal and phosphorylation of CREB (cAMP-response element binding protein). COUP-TF1, a member of nuclear receptor superfamily, plays a critical role in CNS development. COUP-TF1 KO mice die within 1-2 days after birth and show improper brain regionalization. We have found that luciferase fused to a part of rat BDNF promoter III was activated by COUP-TF1 in human neuroblastoma SK-N-BE2 and SK-N-MC cell lines in similar folds to CREB activation. Using RT-PCR, we show that both COUP-TF1 and CREB activate BDNF gene expression. These data suggest that COUP-TF1 plays an important regulatory role in BDNF transcription in the brain. We are currently trying to determine a detail mechanism of BDNF regulation by COUP-TF1. [This work was supported by the IBST Grant 2006 and the New Faculty Supporting Grant from Inje University.]

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Daxx is involved in the transcriptional regulation of hTERT

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Daxx functions as a transcriptional modulator in the nucleus. Recently, it has been reported that Daxx specifically represses the transcription of nuclear factor kappa B (NF- κ B) and E2F1 target genes. NF- κ B and E2F1 have been known to regulate TERT, a catalytic subunit of telomerase. In the present study, we report that Daxx is also involved in the transcriptional regulation of TERT. Overexpression of Daxx suppressed transcriptional activation of TERT in U937 and 293 cells in a dose-dependent manner. We found that the repressive effect of Daxx on TERT transcription is mediated by recruiting HDAC to TERT promoter. This inhibitory effect was enhanced by extracellular signals such as IFN- α and γ -irradiation which increase the expression level of Daxx. Taken together, these findings suggest that TERT is a novel target for Daxx-mediated transcriptional repression.

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DDX3 interacts with p68 and p72 DEAD RNA helicase genes and makes a homodimer and/or heterodimer in cells

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DDX3 is a highly conserved member of the DEAD box RNA helicase family and known to be involved in translation and RNA transport. We previously showed that DDX3 interacted with p68, which is also a member of DEAD box RNA helicase family. p68 can make a heterodimer with p72 (Ogilvie V et al., 2003) and both genes are involved in transcription and mRNA processing. Interestingly, DDX3 also interacted with p72 by yeast two-hybrid system. Over the central core, which contains the motifs conserved in the DEAD box family, the homology between p68 and p72 is 90% and the homology between DDX3 and p68 or DDX3 and p72 is approximately 60%, respectively. Here, we will discuss the interactions between DDX3/p68 and DDX3/p72 and biological functions of these proteins. [Supported by grant from the Basic Research Program of the KOSEF]

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Edible immunization against myostatin enhances muscle mass and body weight

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Myostatin, a member of the TGF- β superfamily, is a potent negative regulator of skeletal muscle growth. So, Mice and cattle with mutation in myostatin gene show a marked increase in muscle mass and body weight. Inhibition of the myostatin is predicted to increase muscle mass and improve muscle-related disorders. The objective of this study was to examine the effect of immunization against myostatin on the growth and skeletal muscle mass in mice and chicken. For this study, we create *L. casei* expressing mature domain of chicken myostatin (CMyom) on its cell surface. The surface expression of CMyom protein on *L. casei* was verified by immunoblot and FACS analysis. Oral inoculation of B6SJL mice with *L. casei* expressing CMyom led to antibody responses specific for CMyom and the body weight was significantly heavier than those of the control group. We also investigated the effect of *L. casei* expressing CMyom inoculated through the feed in chicken. Inoculation resulted in significantly level of serum IgG antibodies was induced and also the body weight of chick was significantly heavier than that of the control group at 5 weeks post feed. The results of this study indicate that immunization against myostatin is a potential means to improve skeletal muscle growth and body weight of chick by myostatin blockade.