

## Regulation of ATF4 Gene Expression by Steroid Hormones in Mouse Uterus

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Activating transcription factor 4 (ATF4) is a ubiquitous basic leucinezipper transcription factor that is a member of the ATF/cyclic adenosine monophosphate responsive element-binding (CREB) protein family. The expression of many eukaryotic genes is strictly regulated by a series of transcription factor that bind to the cis-acting promoter or enhancer elements in a sequence-specific manner. Murine and human complementary DNAs are 85% homologous in nucleotide sequence in the region encompassing the open reading frame. ATF4 is constitutively expressed in a wide variety of organs, including the brain, heart, liver, spleen, kidney, lung, thymus and testis. ATF4 is shown to regulate cell proliferation and differentiation in a broad number of tissues during embryo development. Estrogen and progesterone are the steroids that play important roles in the regulation of mammalian reproduction. One primary action of these hormones is to regulate the proliferation and differentiation in the uterus. So, the object of this study was to investigate the expression of ATF4 in the mouse uterus by RT-PCR and real-time PCR. To obtain each estrous stage uterus from mice, vaginal smears were daily checked and classified according to the stage of the estrous cycle. Uteri were isolated from each mouse and frozen in liquid nitrogen. To determine the effects of steroid hormones,  $17\beta$ -estradiol ( $E_2$ ; 0.3  $\mu$ g/mouse) and progesterone ( $P_4$ ; 1 mg/mouse), the OVX mice were injected with steroids subcutaneously. Experimental group is  $E_2$ ,  $P_4$  treatment group and  $P_4$  in combination with  $E_2$  treatment group. Mice were killed at 6, 12, and 24 h after lastly steroid hormones injection and uteri were collected in each group. RT-PCR and real-time PCR results showed that ATF4 was highly expressed in the estrus-stage during the estrous cycle and ATF4 was up-regulated expression in the OVX uterus by  $17\beta$ -estradiol injection. These results suggest that ATF4 might be regulated by steroid hormones in the mouse uterus and was concerned in uterine development.