A Transgenic Mouse Model that Enables Inducible Knockout of the cAMP Response Element Binding Protein (CREB) in Vascular Smooth Muscle

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Cardiovascular diseases such as hypertension and atherosclerosis induce vascular remodeling that requires changes in gene transcription. The cAMP response element binding protein (CREB) is a transcription factor that is involved in vascular signaling. The Lounsbury lab has found correlations between CREB activity and gene transcription in both cultured vascular smooth muscle cells (VSMCs) and intact arteries; however, a specific role for CREB in vascular function or disease has not been established. The goal of this study was to characterize a transgenic mouse model in which CREB is selectively reduced in smooth muscle at specific time points. The hypothesis is that crossing an αSMA-CRE^{-ERT} mouse with a CREB^{loxp} mouse will result in offspring that exhibit tamoxifen-inducible CREB knockown in both cultured VSMCs and intact arteries. The αSMA-CRE^{-ERT}/CREB^{loxp} animals were injected with tamoxifen to induce knockdown of CREB. Animals injected with vehicle were used as a control. Aorta were dissected and cultured to generate cultured VSMCs. Femoral arteries were dissected and then fixed with formalin and embedded in paraffin. Cultured aortic VSMCs and femoral artery sections were analyzed by immunofluorescence to detect the expression of CREB and α-smooth muscle actin (α-SMA). Cultured VSMCs that were treated with tamoxifen *in vitro* showed significant knockdown of CREB in α-SMA expressing cells, thus the breeding successfully produced a genetically encoded inducible CREB knockdown. Initial *in vivo* experiments using 5 days tamoxifen and sacrifice at 14 days did not show knockdown of CREB in femoral arteries, thus a longer time point is being examined. These results could reinforce the hypothesis that CREB is important for cell signaling in VSMCs. With that knowledge and the established mouse model, future experiments will identify CREB-specific signaling pathways and their effects on the development of cardiovascular diseases.