Public Abstract
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GABP Regulation of the Murine GABPα/ATP Synthase Coupling Factor six and human Glutathione Redcutase Promoters
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Understanding of the cellular response to oxidative stress is critical in understanding how homeostasis is maintained. Oxidative stress is brought on by the incomplete reduction of oxygen in the electron transport chain. Several cellular mechanisms are known to be present to remove these oxidizing species. One of the enzymes involved in the antioxidant response is glutathione reductase, which recycles glutathione in both the mitochondria and cytoplasm of the cell. The cytoplasmic and mitochondrial isoforms of glutathione reductase are expressed from a single gene differing only by a mitochondrial leader sequence. In most cells mitochondrial glutathione reductase makes up only three percent of the total glutathione reductase. Understanding how the expression of mitochondrial glutathione reductase is regulated will give insight into potential mechanisms for how mitochondrial glutathione reductase expression maybe increased under oxidative stress. The expression of glutathione reductase is at least in part regulated by GABP. GABP is a transcription factor that is sensitive to the oxidation/reduction level in the cell. GABP has been shown to be essential for cell growth and survival. The expression of GABPα is autoregulated by GABP for a bi-directional promoter that expresses ATP synthatse coupling factor 6 in the opposite direction. This dissertation investigates the regulation of the mGABPα/ATp synthase coupling factor 6 bi-directional promoter and the human glutathione reductase promoter.