Early gene expression changes preceding thyroid hormone-induced involution of a thyrotrope tumor.

Wood WM, Sarapura VD, Dowding JM, Woodmansee WW, Haakinsson DJ, Gordon DF, Ridgway EC. Division of Endocrinology, Metabolism and Diabetes, Department of Medicine, University of Colorado Health Sciences Center, Denver, Colorado 80262, USA. William.Wood@uchsc.edu

Abstract
Treatment with thyroid hormone (TH) results in shrinkage of a thyrotropic tumor grown in a hypothyroid host. We used microarray and Northern analysis to assess the changes in gene expression that preceded tumor involution. Of the 1,176 genes on the microarray, 7 were up-regulated, whereas 40 were decreased by TH. Many of these were neuroendocrine in nature and related to growth or apoptosis. When we examined transcripts for cell cycle regulators only cyclin-dependent kinase 2, cyclin A and p57 were down-regulated, whereas p15 was induced by TH. Retinoblastoma protein, c-myc, and mdm2 were unchanged, but E2F1 was down-regulated. TH also decreased expression of brain-derived neurotrophic factor, its receptor trkB, and the receptor for TRH. These, in addition to two other genes, neuronatin and PB cadherin, which were up- and down-regulated, respectively, showed a more rapid response to TH than the cell cycle regulators and may represent direct targets of TH. Finally, p19ARF was dramatically induced by TH, and although this protein can stabilize p53 by sequestering mdm2, we found no increase in p53 protein up to 48 h of treatment. In summary, we have described early changes in the expression of genes that may play a role in TH-induced growth arrest of a thyrotropic tumor. These include repression of specific growth factor and receptors and cell cycle genes as well as induction of other factors associated with growth arrest and apoptosis.

Comment in
Editorial: New strategy to solve the etiopathogenetic conundrum of pituitary adenomas. [Endocrinology. 2002]