

# Coordinate regulation of RARgamma2, TBP, and TAFII135 by targeted proteolysis during retinoic acid-induced differentiation of F9 embryonal carcinoma cells

## ABSTRACT

The results suggest that normal F9 cell differentiation requires the appropriately timed proteolysis of TBP and TAFII135, which is necessary for the regulation of genes by transactivators and other basal transcription factors.

## INTRODUCTION

In the early 1990s, the first report on the role of RARgamma2 and RARgamma2/3 in the growth of human breast cancer cell lines was published in the journal Cancer Research. The authors demonstrated that RARgamma2 is a potent inhibitor of the PKA pathway and that RARgamma2/3 is activated by retinoic acid-induced differentiation of human breast cancer cell lines [9]. In addition, they showed that RARgamma2/3 is a critical regulator of the TGF- $\beta$  signaling pathway, which plays a role in the tumourigenesis and metastasis of breast cancer cells.

The present study aimed to investigate Recombinant TATA-binding protein (TBP) and a group of TBP-associated factors are the components of the transcription factor enzyme called "TAFIID" [RNA polymerase II (TARIID) [R]. There are at least 12 TAFINIIs that have been identified in TFIIDA, and their presence has been confirmed by evolutionary conservation through cloning of their cDNA samples from yeast to mammals. Temperature-sensitive (TS) mutants have been used to study the TAFII function in living cells, as demonstrated by experiments in yeast where several TFs are required for transcription of most yeast genes [1], whereas FTISA lesions in TTAFI145, TAFICOI150 and TDAFIL90 affect only a small number of genes affecting the cell cycle.] TAFII30 plays a crucial role in regulating cell cycles in mammalian cells, as evidenced by TS mutations in the protein. In addition to these studies, there is a wealth of information about the physiological role of TAFII135 beyond its current understanding. There is increasing evidence that targeted 26S proteasome-mediated proteolysis of transcription factors plays a crucial role in the transactivation process. The stability of activation domains is closely tied to their potency, and mutations in certain regions of the VP16 activator contribute to increased stability. The extent to which the basal transcriptional activator components are subjected to targeted proteolysis is unknown, although it has been investigated. We show that TBP and TAFII135 are selectively depleted in extracts from T-RA differentiated F9 cells and from differentiating C2C12 cells, and that this depletion is due to targeting of these proteins and RAR2 (which are both essential for activating primitive endoderms) during F-9 cell differentiation. This results in stable

## CONCLUSION

Remarkable conclusions We show for the first time that components of the basal transcription machinery are regulated by targeted proteolysis in response to a physiological stimulus, and our results indicate that TAFII135 plays an essential role as part of F9 cell physiology... TAFII (taffetal endothelial interferon immunoglobulin I) is downregulated during F9. Regulation of RADIAL INDEX at high levels promotes cell growth, regulates T-RA signalling and induces invasive mutations.