

## TR $\alpha$ $\Delta$ 1 is not an inhibitor of nuclear TR $\alpha$ signaling

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**Introduction:** The thyroid hormone receptor (TR)  $\alpha$  is important for physiology and homeostasis, especially for heart rate, body temperature and development of intestinal mucosa. TR $\alpha$  canonically acts as a ligand-dependent transcription factor. Twenty years ago, a truncated transcription variant of TR $\alpha$ , TR $\alpha$  $\Delta$ 1, was identified. This variant lacks the nuclear localization sequence (NLS) and the DNA-binding domain (DBD) and the ligand binding domain is incomplete. At that time, it was reported that TR $\alpha$  $\Delta$ 1 is localized in the cytosol as well as in the nucleus and inhibits the effect of regular TR $\alpha$  on gene expression. Since TR $\alpha$  $\Delta$ 1 lacks the NLS and the DBD we questioned the inhibitory role attributed to TR $\alpha$  $\Delta$ 1.

**Material and Methods:** Transcriptional activity of TR $\alpha$  and TR $\alpha$  $\Delta$ 1 was determined with luciferase reporter assays. A dominant negative mutant with impaired T3 binding was used as control (TR $\alpha$ G291R). FLAG-tagged TR $\alpha$  and TR $\alpha$  $\Delta$ 1 were transfected into HeLa cells. Subcellular localization was studied with confocal microscopy.

**Results:** In HeLa cells, TR $\alpha$  $\Delta$ 1 did not inhibit the transcriptional activity of TR $\alpha$  (Fig. 1A). This was confirmed in several other cell lines. Furthermore, confocal microscopy showed that TR $\alpha$  $\Delta$ 1 is only located in the cytoplasm and not in the nucleus (Fig. 1B).

**Conclusion:** These results are discrepant from early reports on TR $\alpha$  $\Delta$ 1 but in agreement with the absence of an NLS and DBS in TR $\alpha$  $\Delta$ 1. Therefore, TR $\alpha$  $\Delta$ 1 is not an inhibitor of canonical TR $\alpha$  signaling and its physiological role needs to be rethought.

Fig.  
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