

Thyroid hormone

Overview: Thyroid hormone receptors (TRs, nomenclature as agreed by NC-IUPHAR Committee on Nuclear Receptors, see Flamant *et al.*, 2006) are nuclear hormone receptors of the NR1A family, with diverse roles regulating macronutrient metabolism, cognition and cardiovascular homeostasis. TRs are activated by thyroxine (T4) and thyroid hormone (T3). Once activated by a ligand, the receptor acts as a transcription factor either as a monomer, homodimer or heterodimer with members of the retinoid X receptor family.

An interaction with integrin $\alpha V\beta 3$ has been suggested to underlie plasma membrane localization of TRs and non-genomic signalling (Bergh *et al.*, 2005).

Nomenclature	TR α	TR β
Systematic nomenclature	NR1A1	NR1A2
Other names	THRA, erbA α , erbA1, EAR7	THRB, erbA β , erbA2
Ensembl ID	ENSG00000126351	ENSG00000151090
Rank order of potency	T3 > T4	T3 > T4
Selective agonists	–	GC1 (Chiellini <i>et al.</i> , 1998)

One splice variant, TR α_2 , lacks a functional DNA-binding domain and appears to act as a transcription suppressor.

Although radioligand-binding assays have been described for these receptors, the radioligands are not commercially available. NH-3 has been described as an antagonist at TRs with modest selectivity for TR β (Nguyen *et al.*, 2002).

Abbreviations: GC1, (3,5-dimethyl-4-[4-hydroxy-3-isopropylbenzyl]phenyloxy)acetate; NH-3, (4-[4-hydroxy-3-isopropyl-5-[4-nitrophenylethynyl]-benzyl]-3,5-dimethylphenoxy)acetate

Further Reading

- Baxter JD, Webb P (2009). Thyroid hormone mimetics: potential applications in atherosclerosis, obesity and type 2 diabetes. *Nat Rev Drug Discov* 8: 308–320.
- Bernal J (2007). Thyroid hormone receptors in brain development and function. *Nat Clin Pract Endocrinol Metab* 3: 249–259.
- Flamant F, Baxter JD, Forrest D, Refetoff S, Samuels H, Scanlan TS *et al.* (2006). International Union of Pharmacology. LIX. The pharmacology and classification of the nuclear receptor superfamily: thyroid hormone receptors. *Pharmacol Rev* 58: 705–711.
- Furuya F, Lu C, Guigon CJ, Cheng SY (2009). Nongenomic activation of phosphatidylinositol 3-kinase signaling by thyroid hormone receptors. *Steroids* 74: 628–634.
- Grover GJ, Mellstrom K, Malm J (2007). Therapeutic potential for thyroid hormone receptor- β selective agonists for treating obesity, hyperlipidemia and diabetes. *Curr Vasc Pharmacol* 5: 141–154.
- Visser WE, Friesema EC, Jansen J, Visser TJ (2008). Thyroid hormone transport in and out of cells. *Trends Endocrinol Metab* 19: 50–56.
- Yen PM, Ando S, Feng X, Liu Y, Maruvada P, Xia X (2006). Thyroid hormone action at the cellular, genomic and target gene levels. *Mol Cell Endocrinol* 246: 121–127.

References

- Bergh JJ *et al.* (2005). *Endocrinology* 146: 2864–2871.
- Chiellini G *et al.* (1998). *Chem Biol* 5: 299–306.
- Nguyen NH *et al.* (2002). *J Med Chem* 45: 3310–3320.