In the body the brain is the most cholesterol-rich organ. Despite this, remarkably little is known about the mechanisms in the brain that regulate cholesterol homeostasis. Due to the blood-brain barrier, plasma lipoproteins are unable to traverse and instead cholesterol must be synthesized de novo from within the CNS. Thyroid hormone receptors, activated in response to thyroid hormone (T3), are known to modulate the level of serum cholesterol via complex regulatory pathways. By screening for T3-regulated genes we have identified Disp3, a sterol-sensing domain-containing protein that is related to the Dispatched family of proteins. Analysis by RT-PCR and immunohistochemistry demonstrated that DISP3 is predominantly expressed in specific cell types of the brain, retina and testis. DISP3 localizes within the endoplasmic reticulum and was further found to co-localize with cholesterol (Fig. 1). Ectopic expression of DISP3 in fibroblasts resulted in elevated cholesterol levels combined with an altered cholesterol distribution. We propose that DISP3 represents a new molecular link between thyroid hormone and cholesterol metabolism in the brain.

We have also identified, cloned and characterized the first non-mammalian Tpo, chicken thrombopoietin, and its receptor c-Mpl (2). Discovery of chicken Tpo and c-Mpl will greatly facilitate future studies regarding thrombopoietic differentiation (Fig. 2) and haematopoietic stem cell development. Moreover, we have introduced an experimental model of chicken bi-potent thrombo/erythropoietic progenitors that can be used to identify key regulators of cell fate determination (2).

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