Petr Bartůněk

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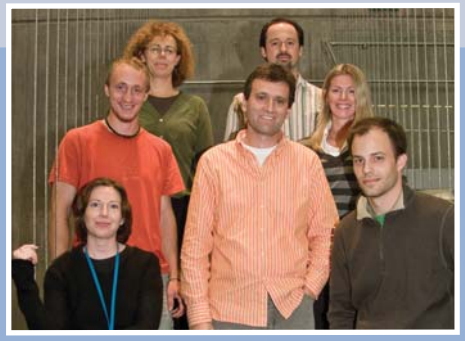
Laboratory of Cell Differentiation

Haematopoietic differentiation, nuclear hormone receptors



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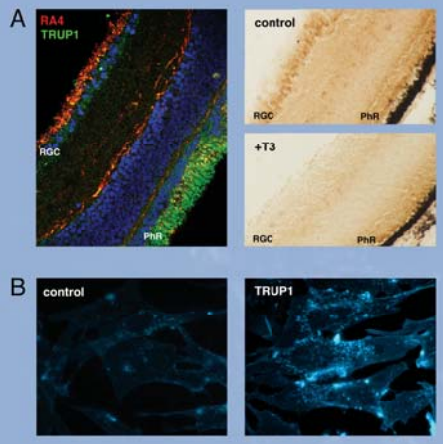

(A) Expression of TRUP1 in chicken retina (left panel). TRUP1 is downregulated by T3 in vivo (right panels) RGC retinal ganglion cells, PhR photoreceptors. Immunohistochemical staining of chicken retina at embryonic day 15. (B) Ectopic expression of TRUP1 in fibroblasts leads to accumulation of cholesterol (stained with filipin) within the cell

Research topics

To date, we have concentrated on characterizing a novel sterol sensing domain-containing protein, TRUP1, that we cloned as a gene directly regulated by thyroid hormone. Evolutionary analysis demonstrates that TRUP1 is closely related to the *dispatched* family of proteins. Its expression predominates in the brain, retina and testis and corresponds with the tissues most profoundly affected by the inactivation of thyroid hormone receptor α and/or β. Over-expression of TRUP1 results in altered cholesterol distribution and accumulation, suggesting that it may regulate cholesterol trafficking/localization in the cell and as such may represent a new molecular link between thyroid hormone action and cholesterol metabolism (Fig. 1).

We have also identified, cloned and characterized the first non-mammalian Tpo, chicken thrombopoietin, and its receptor c-Mpl. Discovery of chicken Tpo and c-Mpl will greatly facilitate future studies regarding thrombocytic differentiation 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 (see Fig. below).

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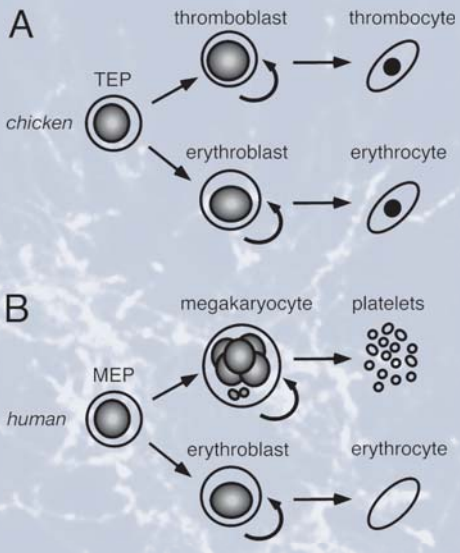
Selected recent papers

1. Bartunek P, Pajer P, Karafiat V, Blendinger G, Dvorak M, Zenke M. bFGF signaling and v-Myb cooperate in sustained growth of primitive erythroid progenitors. **Oncogene.** 2002;21:400-10.
2. Bartunek P, Kralova J, Blendinger G, Dvorak M, Zenke M. GATA-1 and c-myb crosstalk during red blood cell differentiation through GATA-1 binding sites in the c-myb promoter. **Oncogene.** 2003;22:1927-35.
3. Karafiat V, Dvorakova M, Krejci E, Kralova J, Pajer P, Snajdr P, Mandikova S, Bartunek P, Grim M, Dvorak M. Transcription factor c-Myb is involved in the regulation of the epithelial-mesenchymal transition in the avian neural crest. **Cell Mol Life Sci.** 2005;62:2516-25.



Schematic model of (A) thrombocytic (chicken) and (B) megakaryocyte (human) differentiation. Bi-potent thrombo/erythroid progenitor (TEP) and megakaryo/erythroid progenitor (MEP) cells represent a binary switch model to study cell fate determination.