

**P005** Three human sec14-like proteins; involvement in transport and cellular signalling

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Three human genes encoding the sec14-like proteins (TAP1/2/3 or supernatant protein factor, SPF) were cloned. These proteins are related to the *Saccharomyces cerevisiae* SEC14p, the alpha-tocopherol-transfer protein (TTP) and the cellular retinaldehyde binding protein (CRALBP). This protein family contains a sec14-like domain responsible for the binding of hydrophobic ligands. The hTAP proteins contain an additional GOLD domain in the carboxy-terminus, which in other proteins (GCP60, PAP7) is known to serve as an adaptor for binding to Golgi giantin or to the mitochondrial peripheral benzodiazepine receptor. Isoelectric point mobility shift assay (IPMS-assay) was used to assess the binding of ligands to recombinant hTAP. The three proteins bind *in vitro* specific phospholipids, squalene as well as different tocopherol species. The ability of hTAPs to influence the activity of phospholipid utilizing enzymes was assessed. The hTAPs are able to modulate *in vitro* the activity of recombinant phosphatidylinositol-3-kinase and tocopherol modulates kinase activity in an hTAP-dependent manner, possibly by competition with phosphatidylinositol. The results suggest that the hTAP proteins may regulate the amounts and distribution of cellular tocopherols, phospholipids or squalene. By modulating the intracellular targeting of these ligands to enzymes and organelles, the hTAPs may influence the activity of lipid dependent enzymes. In this manner, binding of tocopherols (or other hydrophobic ligands) to hTAPs may modulate signal transduction as well as biosynthetic processes.