

Publication

PDZ domain containing protein 1 (PDZK1), a modulator of membrane proteins, is regulated by the nuclear receptor THR β

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Genome wide association studies revealed single nucleotide polymorphisms (SNP) located within the promoter of PDZ domain containing protein 1 (PDZK1) to be associated with serum uric acid levels. Since modulation of transporters and particularly of membrane proteins involved in uric acid handling by PDZK1 has previously been reported, the aim of this study was to analyze the impact of the polymorphisms rs1967017, rs1471633, and rs12129861 on promoter activity and thereby transcription of PDZK1. Cell-based reporter gene assays showed transactivation of the PDZK1-promoter by triiodothyronine mediated by thyroid hormone receptors (THR) α and β . In silico analysis verified localization of the polymorphism rs1967017 within the most likely THR binding site whose deletion reduced THR-mediated transactivation. Furthermore, our study shows regulation of PDZK1 by thyroid hormones, thereby providing a mechanistic basis for the previously reported associations between thyroid hormone status and uric acid homeostasis.

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