Introduction: Embryonic transcription factors have been involved in tumourigenesis. The transcription factor TBX1 regulates the embryonic parathyroid cells fate. Indeed, it has never been investigated in human adult parathyroids.

Aim: Expression, function and regulation of the TBX1 gene were analysed in adult normal and tumour parathyroid tissues.

RESULTS: Expression of the embryonic transcription factor TBX1 in human parathyroid tissues: Immunohistochemistry identified 30-70% (mean±SEM, 52.0±7.3%) of cells expressing TBX1 at nuclear levels in normal parathyroid glands (n=5). Parathyroid adenomas (Pads) showed a highly variable proportion of TBX1-expressing cells ranging from 5 to 65% [A,B]. About a half of parathyroid tumours [12 parathyroid carcinomas and 13 adenomas (PAs)] had reduced TBX1+ cells (0-15%), showing deregulated TBX1 mRNA levels [C]. Immunofluorescence on PAs-derived cells identified a subset of cells co-expressing TBX1 and PTH [D]. Western blot analysis on fractionated proteins from PAs (n=11) showed that PAs expressed the 53 kDa isoform C of the TBX1 gene mainly at nuclear level [E].

Effect of TBX1 reduced levels in PAs-derived cells: consistent with the promotion of cell cycle arrest, TBX1 silencing [A] increased CDKN2A/p16 mRNA levels, CDKN1A/p21 mRNA and protein levels and decreased ID1 (inhibitor of DNA binding 1) levels in PAs where any significant change in both GCM2 and PTH levels could be detected by TBX1 silencing[B,C].

Effect of Wnt/β-catenin pathway activation on TBX1 gene expression in HEK293 and PAs-derived cells: During embryonic development, TBX1 is regulated by the activation of the Wnt/β-catenin pathway. Short-term (8 hours) 10-20 mM lithium chloride treatment induced β-catenin nuclear accumulation and inhibited TBX1 mRNA levels in 5 out of 7 PAs cell preparations.

In conclusion, the embryonic transcription factor TBX1 is expressed in a subpopulation of adult parathyroid cells, which is reduced in half of tumours. Reduction of TBX1 expression is associated with cell quiescence, a feature that might be in line with the extremely low cell proliferation rate described in parathyroid tumours.