Death-associated protein 3 is overexpressed in human thyroid oncocytic tumours

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Background: The human death-associated protein 3 (hDAP3) is a GTP-binding constituent of the small subunit of the mitochondrial ribosome with a pro-apoptotic function.

Methods: A search through publicly available microarray data sets showed 337 genes potentially coregulated with the DAP3 gene. The promoter sequences of these 337 genes and 70 out of 85 mitochondrial ribosome genes were analysed in silico with the DAP3 gene promoter sequence. The mitochondrial role of DAP3 was also investigated in the thyroid tumours presenting various mitochondrial contents.

Results: The study revealed nine transcription factors presenting enriched motifs for these gene promoters, five of which are implicated in cellular growth (ELK1, ELK4, RUNX1, HOX11-CTF1, TAL1-ternary complex factor 3) and four in mitochondrial biogenesis (nuclear respiratory factor-1 (NRF-1), GABPA, PPARG-RXRA and estrogen-related receptor alpha (ESRRA)). An independent microarray data set showed the overexpression of ELK1, RUNX1 and ESRRA in the thyroid oncocytic tumours. Exploring the thyroid tumours, we found that DAP3 mRNA and protein expression is upregulated in tumours presenting a mitochondrial biogenesis compared with the normal tissue. ELK1 and ESRRA were also showed upregulated with DAP3. Conclusion: ELK1 and ESRRA may be considered as potential regulators of the DAP3 gene expression. DAP3 may participate in mitochondrial maintenance and play a role in the balance between mitochondrial homoeostasis and tumourigenesis.

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