

P046 PTEN is destabilised by regulated phosphorylation of Thr-366

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Although PTEN is one of the most commonly mutated tumour suppressors in human cancers, recent evidence from tumour samples shows that loss of PTEN expression in the absence of mutation may also be of great importance in common tumour types such as breast, prostate and colon. Here we show that cellular PTEN is phosphorylated on Thr366 and Ser370 by GSK3 and CK2 respectively and that phosphorylation of both sites is stimulated by hyperosmotic or oxidative stress. Blocking phosphorylation of Thr366 by either mutation or GSK3 inhibition led to a stabilisation of the PTEN protein and treatment of cells with hyperosmotic sorbitol reduced PTEN expression. Our data support a model in which the regulated phosphorylation of Thr366 targets PTEN for degradation.