## **Supporting Information**

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Mutant designation	Mutated residues	Description
G 376R	<sup>376</sup> <sup>376</sup> <u>G</u> GA → <u>A</u> GA G R	Mutation of amino acid 376
K376E	<sup>379</sup> <sup>379</sup> <u>A</u> AA → <u>G</u> AA K E	Mutation of amino acid 379
E439del	439 440 GA <u>A GA</u> T E D	Deletion of amino acid 439
KS459delN	459 460 ΑΑ <u>Α ΑG</u> Τ <b>κ s</b>	Deletion of amino acid 459, mutation of amino acid 460 to N .
D560Y	<u>G</u> AC → <u>I</u> AC <b>D</b> Y	Mutation of amino acid 560
DKRMNS560del	559 560 561 562 563 564 565 AT <u>I GAC AAA CGT ATG AAC AG</u> C I D K R M N S	Deletion of amino acids 560-565
N564K	$AA\underline{C} \xrightarrow{564} AA\underline{G}$ N K	Mutation of amino acid 564
R574fs	574 575 A <u>GA</u> AAG <b>R K</b>	Frame shift at position 574, premature stop codon at position 600
T 576 del	576 577 A <u>CG</u> AGA TR	Deletion of amino acid 576
W 583 del	583 584 T <u>GG T</u> TG W L	Deletion of amino acid 583

Underlined nucleotides are deleted in the mutants.

Fig. S1. List of the mutants and their effects on the amino acid sequence of p85.



**Fig. S2.** Controls documenting the p110 isoform specificity of the inhibitors used in Figs. 6 and 7. The following inhibitors were used in this experiment:  $p110\alpha$  inhibitor A66 (700 nM), p110 $\beta$  inhibitor TGX-221 (250 nM), p110 $\gamma$  inhibitor AS-604850 (5  $\mu$ M), and p110 $\delta$  inhibitor IC87114 (5  $\mu$ M). Chicken embryo fibroblasts were transfected with RCAS vector constructs expressing p110 $\alpha$  H1047R, p110 $\beta$ , p110 $\gamma$ , or p110 $\delta$ . The cultures were overlaid with nutrient agar either containing or not containing inhibitor. Overlays were replenished every second day, and foci of transformed cells were counted on posttransfection day 10. The plot shows relative efficiencies of transformation (ratio of focus count in the presence of inhibitor to the focus count in the absence of inhibitor).



Fig. S3. Inhibitors specific for  $p110\beta$  and  $p110\delta$  do not affect signaling that is induced by the p85 mutants.



**Fig. S4.** Dose–response of oncogenic transformation induced by the  $p110\alpha$  mutant H1047R or the p85 mutant KS459delN to rapamycin. Focus formation by the p85 mutant is significantly more sensitive to rapamycin than focus formation induced by the  $p110\alpha$  mutant.