

A Natural variants of p85

	p110 binding	PI3K Activity	JNK Activity	Ins Sens
p85 α	SH3 BH SH2 F	↑	↑	↓
AS53/p55 α	34 aa SH2 F SH2	↑	↔	↑
p50 α	6 aa SH2 F SH2	↑	↔	↑

B Artificial Mutants of p85

	p110 binding	PI3K Activity	JNK Activity	Ins Sens
p85 α	SH3 BH SH2 F	↑	↑	↓
Δ SH3	F BH SH2 F	↓	↔	?
Δ BH	SH3 F SH2 F	↑	↔	?
Δ iSH2	SH3 BH SH2 F F	↓	↑	↓
RARA	SH3 BH SH2 SH2 F	↓	↔	↔
$\Delta\Delta$	F BH SH2 F F	↓	↔	?

Supplemental Figure 2