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Protein phosphorylation is one of the most common and important post-translational modifications, and it regulates a variety of cellular signaling pathways. Protein kinases regulate protein phosphorylation by catalyzing the transfer of the terminal phosphate group (PO_4) of ATP to the hydroxyl group of an amino acid residue[1]. In eukaryotes, protein kinases phosphorylate mainly Ser or Thr residue (protein Ser/Thr kinases, PSKs) or Tyr residue (protein Tyr kinases, PTKs)[2]. There are many subfamilies of protein kinases, as shown in Table 1.

Famliy	Members
Protein Ser/Thr kinases	
AGC famliy	PKA, PKC, PKG
CaMK	CaMK I, CaMK II, CaMK III, CaMK IV, CaMK V
Casein kinase	CK1, CK2
CMGC famliy	CDK, MAPK (ERK, JNK, p38), GSK3, CLK
STE famliy	STE7 (MEK), STE11, STE20 (MAP4K)

TKL famliy	IRAK, LRRK, LIMK, MLK, RIPK, RSTK (TGFBR, BMPR)
Protein Tyr kinases	
Non-receptor famliy	ABL, ACK, FAK, JAK, SRC, SYK
Receptor famliy	ALK, EGFR, FGFR, MET, PDGFR, RET, ROR, ROS, TIE, TRK, VEGFR

Table 1. Subfamilies and members of protein kinases

Take the serine-threonine kinase AKT (also known as protein kinase B or PKB) as an example. AKT is activated downstream of PI3K activation, which is mediated by receptor tyrosine kinase (RTK), cytokine receptors, integrins, or G protein-coupled receptors (GPCRs)[3]. PI3K phosphorylates PIP2 to produce PIP3, which recruits AKT to the plasma membrane. Then AKT is phosphorylated by PDK1 and rapamycin (mTOR) complex 2 (mTORC2). Activated AKT further activates a few key downstream effectors, including mTOR complex 1 (mTORC1), GSK3, and members of the forkhead box O (FOXO) family[4]. The PI3K/AKT/mTOR signaling network plays a major role in promoting cell survival, growth, and proliferation, by inducing various changes to cellular metabolism.

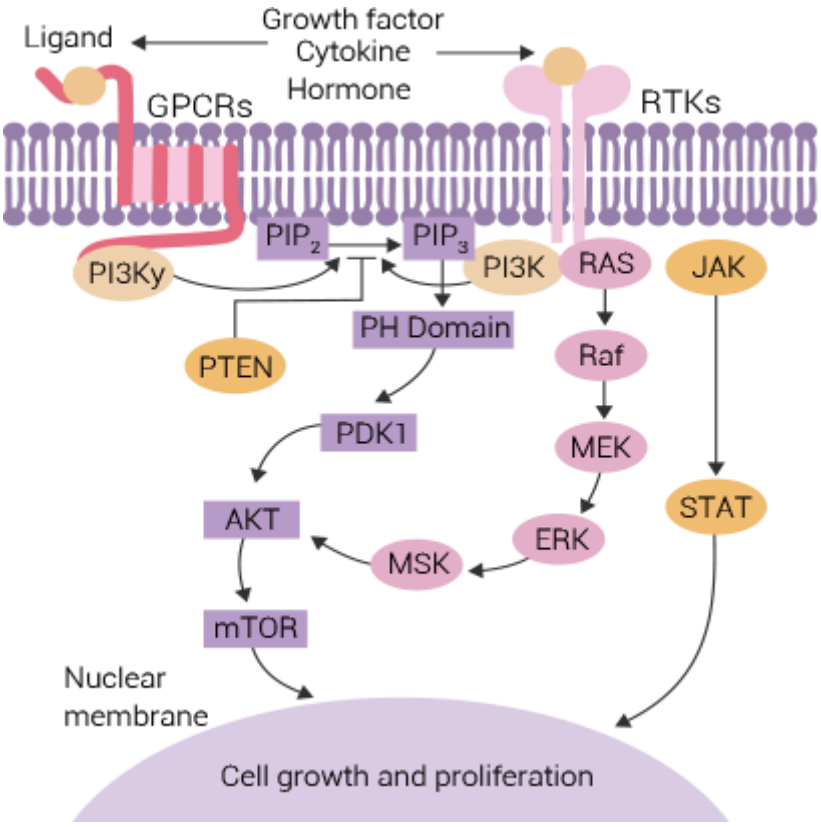

Figure. 1 The overview of PI3K/AKT/mTOR signaling pathway[4]

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