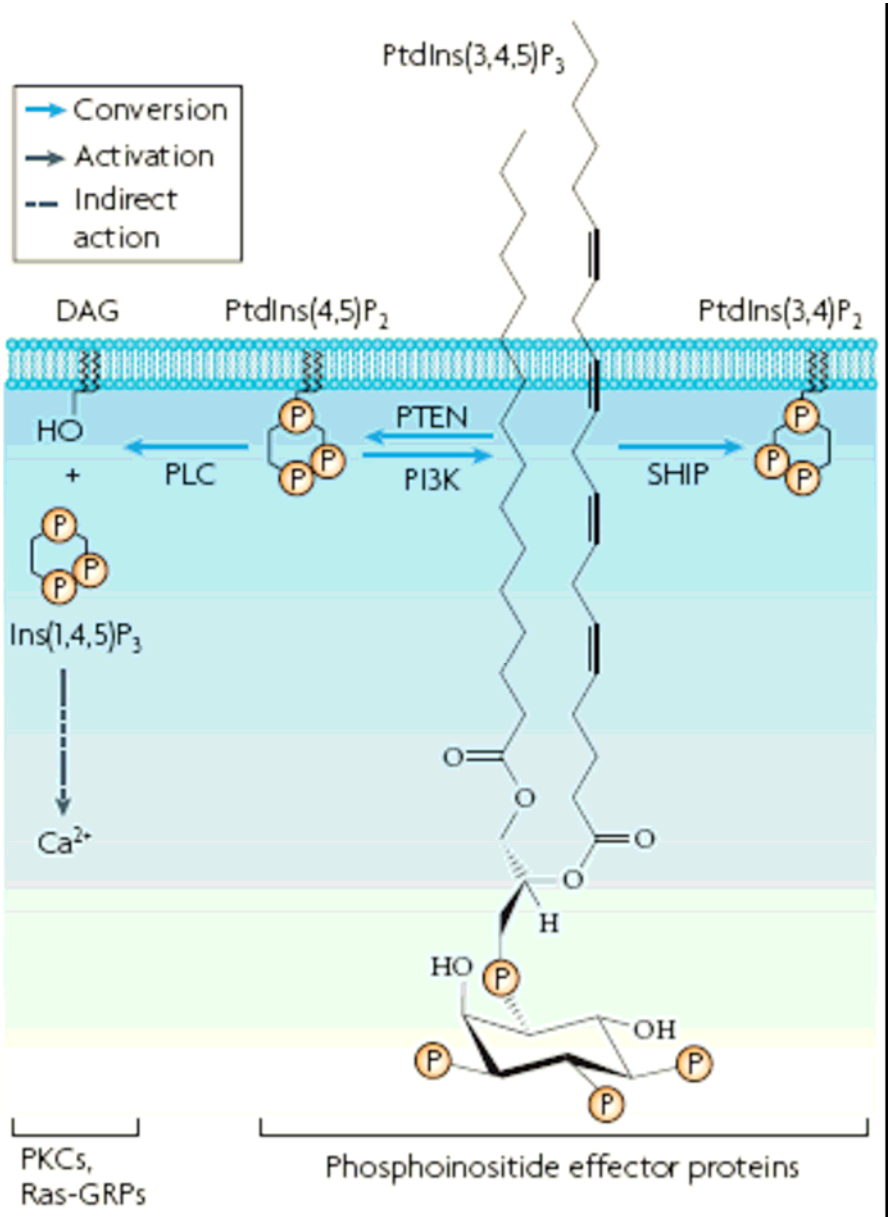
Phosphoinositides as Signal Transducers

- Phospholipase C: different isoforms are activated by different signals that bind either GPCR or RTK

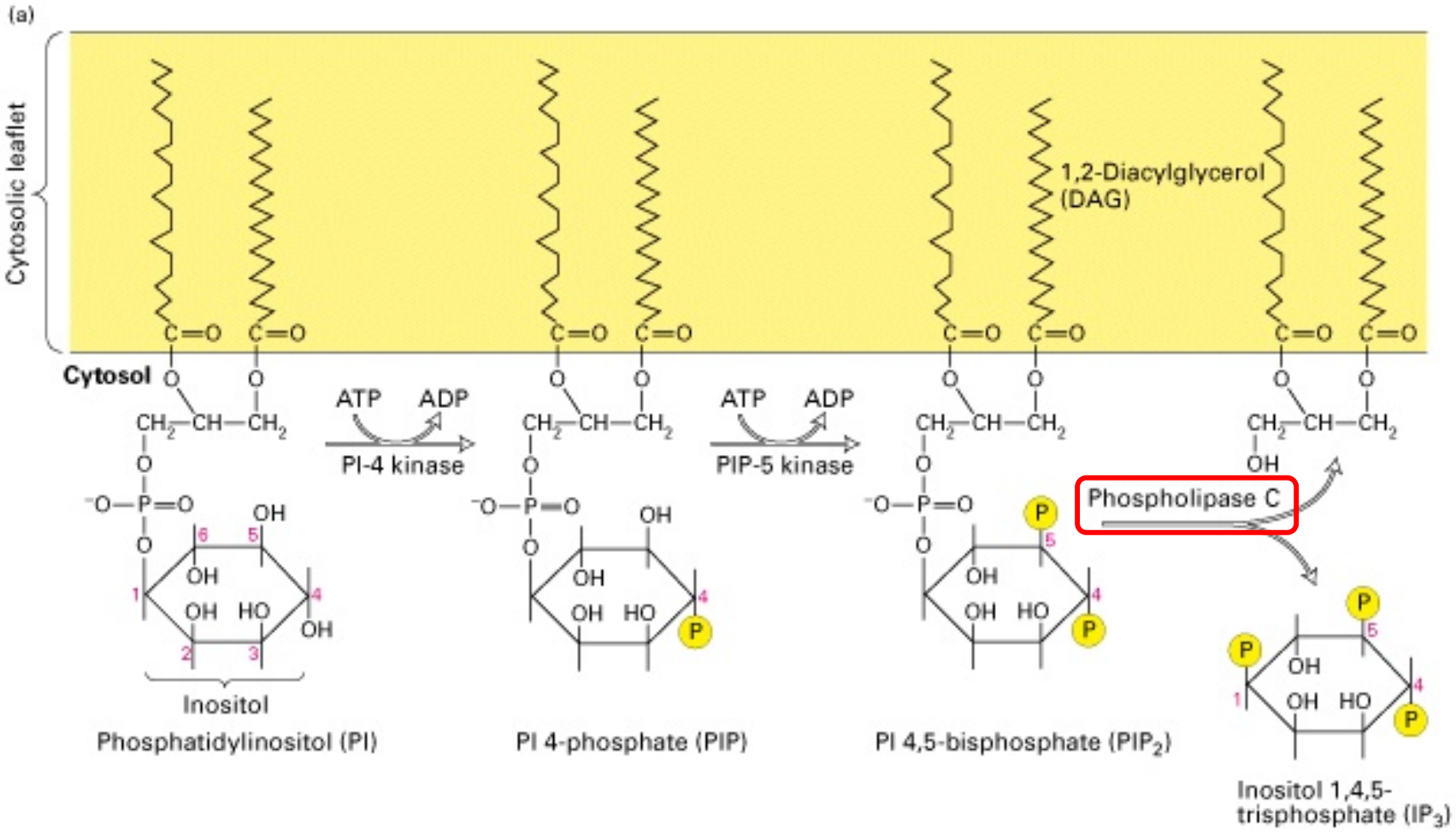
- PI-3 kinase pathway

Intracellular signalling by phosphoinositids



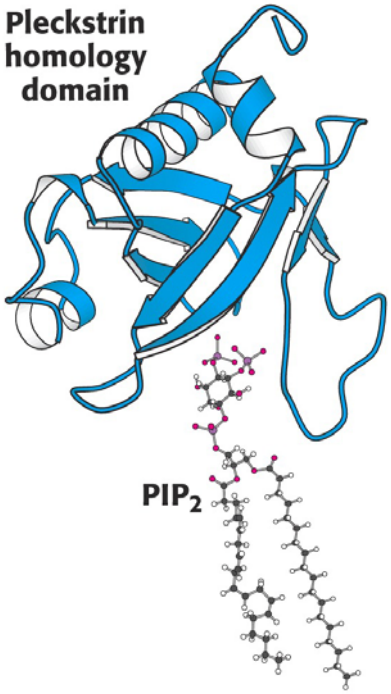
Wymann & Schneiter, Nature, 2008

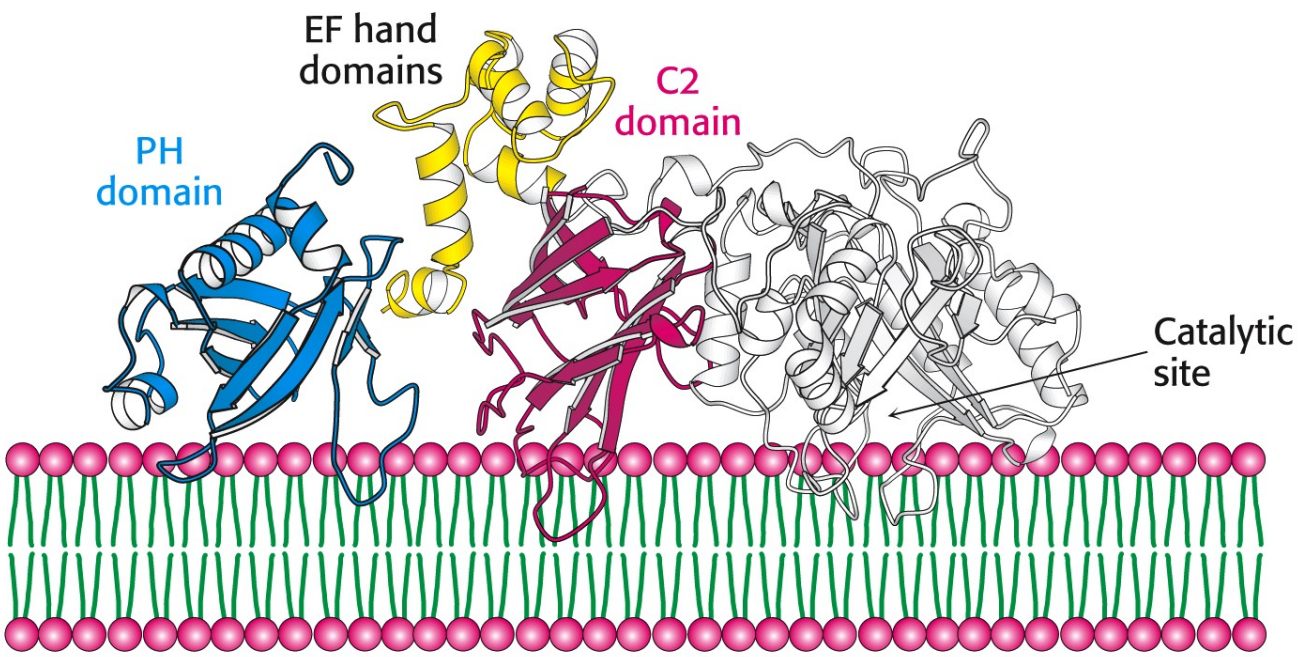
Modification of a common phospholipid precursor generates several second messengers: synthesis of DAG and IP_3

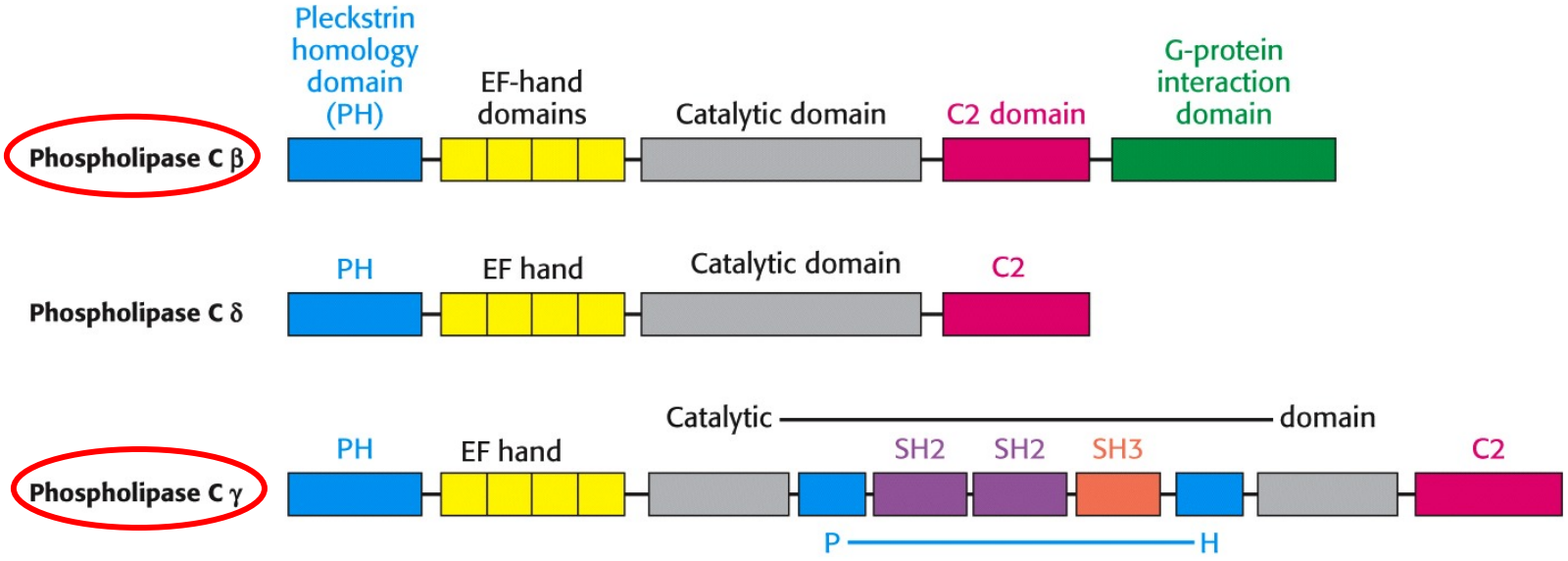


Lodish et al. Molecular Biology of the Cell

Phospholipase C Isoforms

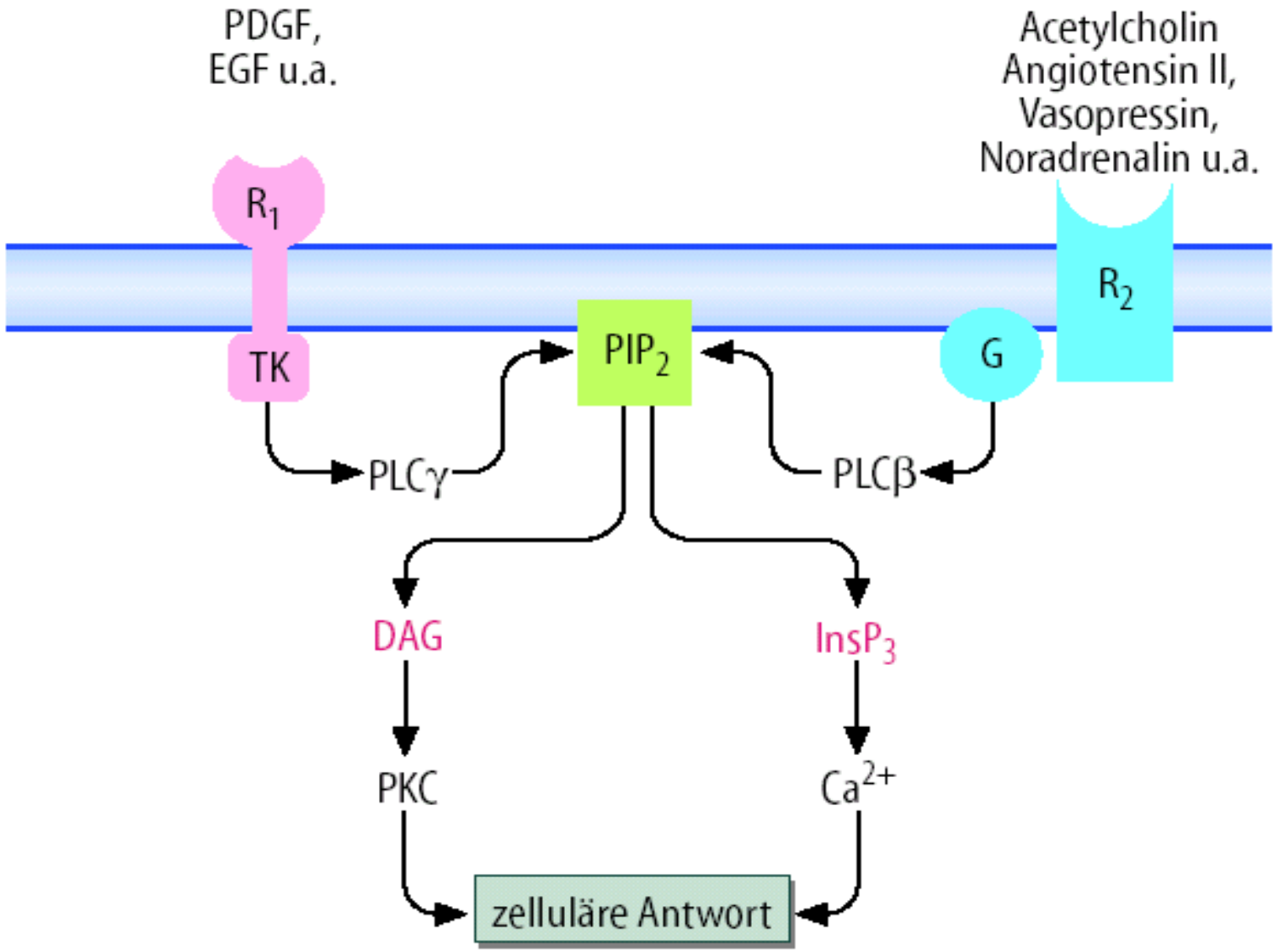






Berg, Tymoczko, Stryer: Biochemistry, 2002

PLC-induced release of Ca^{2+} from the ER is mediated by IP_3



Löffler, Petrides, Biochemie und Pathobiochemie

PLCβ is an effector targeted by GPCRs

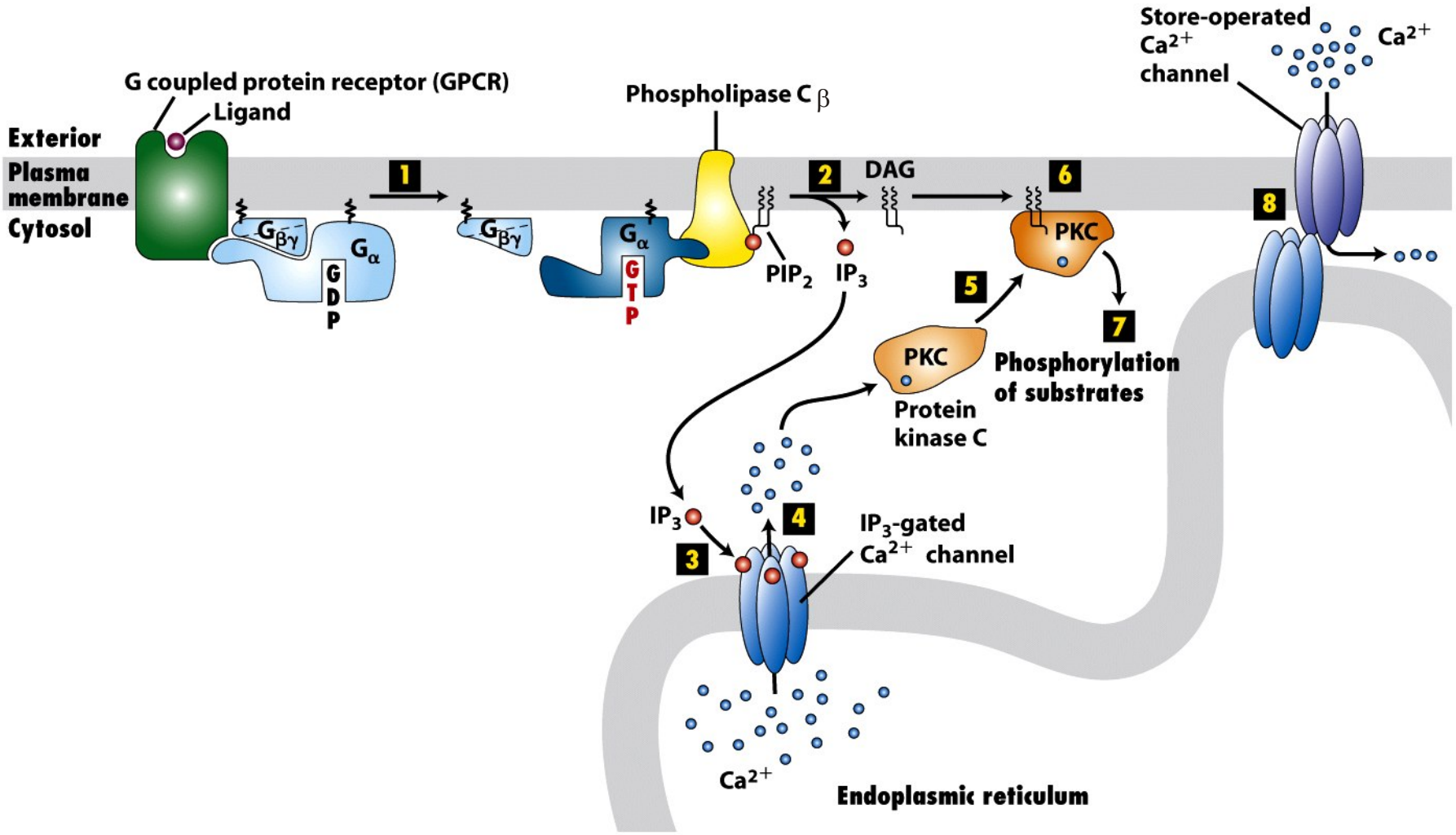
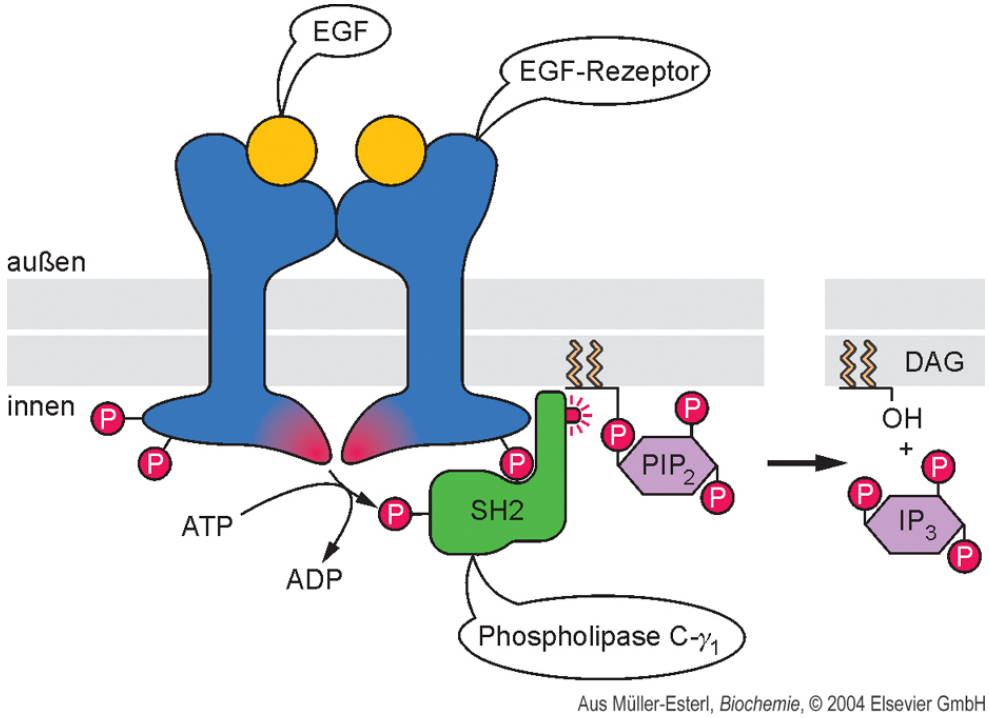


Figure 15-30
Molecular Cell Biology, Sixth Edition

Short term effects on cell metabolism and movement
Long term effects on gene expression

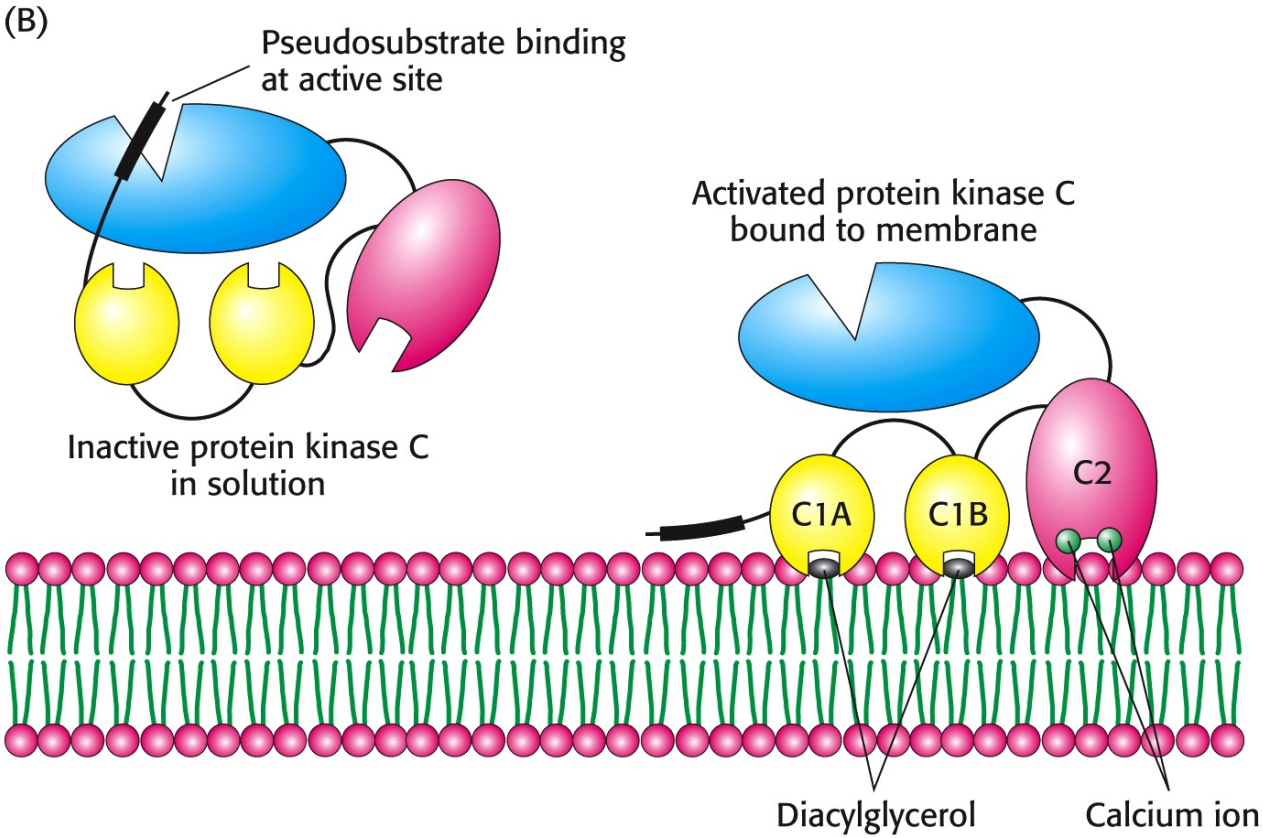
PLCγ_1 is an effector targeted by RTKs

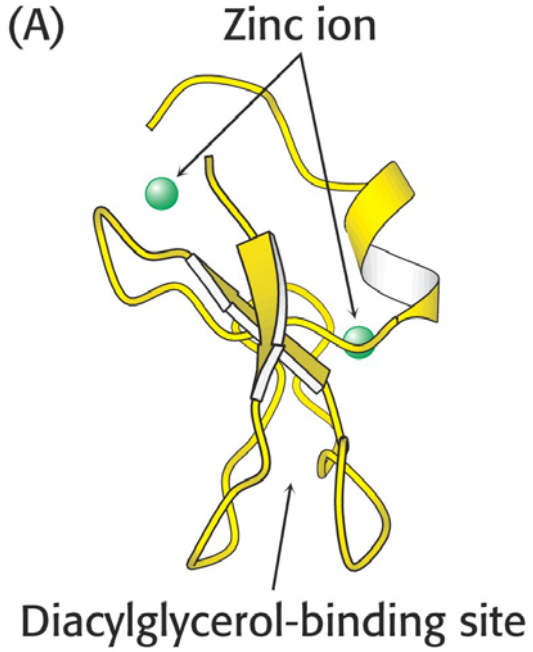


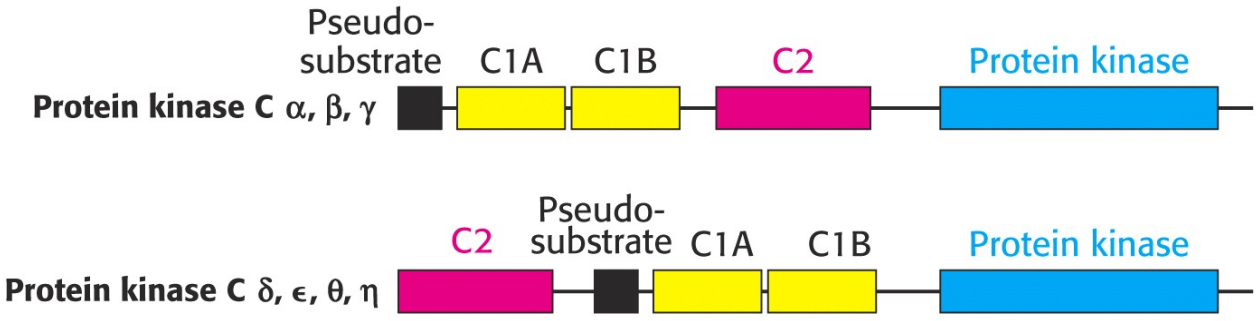
The activated EGF-receptor recruits the cytosolic phospholipase C-γ_1 (substrate PIP_2) via its **SH2-domain** and activates the enzyme by phosphorylation.

Phosphatases terminate this process.

Proteinkinase C







Berg, Tymoczko, Stryer: Biochemistry,

PI-3 kinase generates phosphatidylinositol 3-phosphates, which are binding sites for various signal-transduction proteins, usually triggering survival.

PTEN phosphatase has a broad specificity but its major function in cells is to reverse the PI-3 kinase catalyzed reaction.

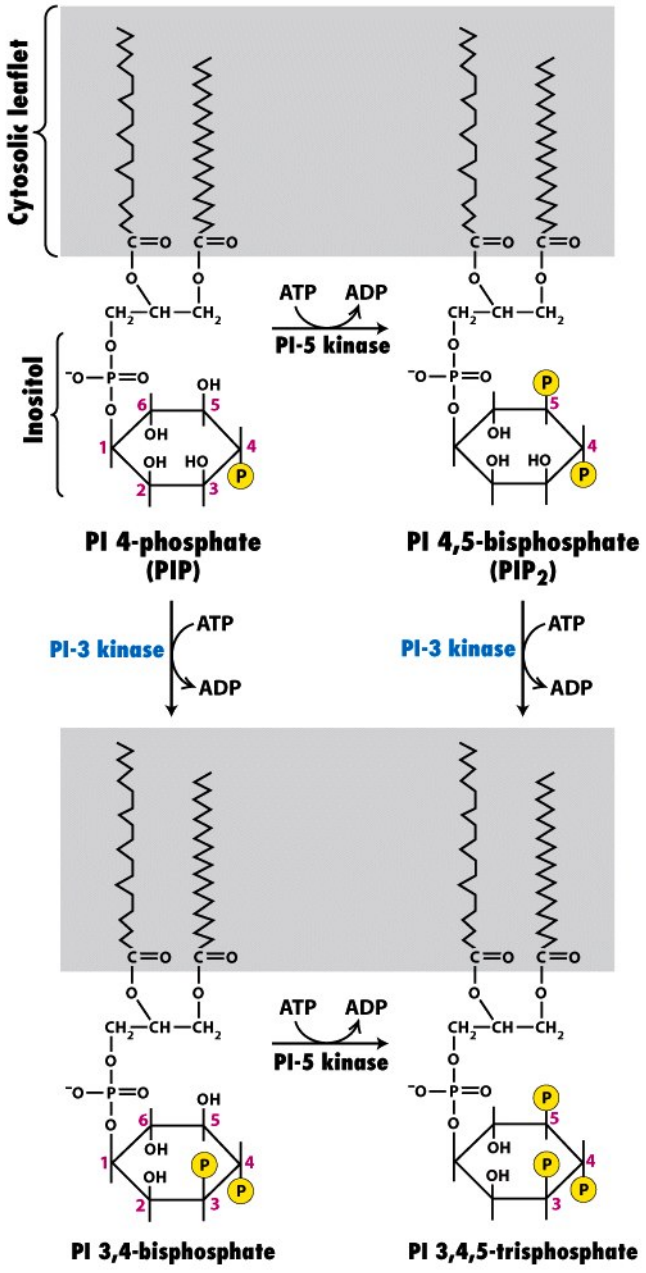


Figure 16-29
Molecular Cell Biology, Sixth Edition

PI 3-phosphates recruit and activate protein kinase B (PKB)

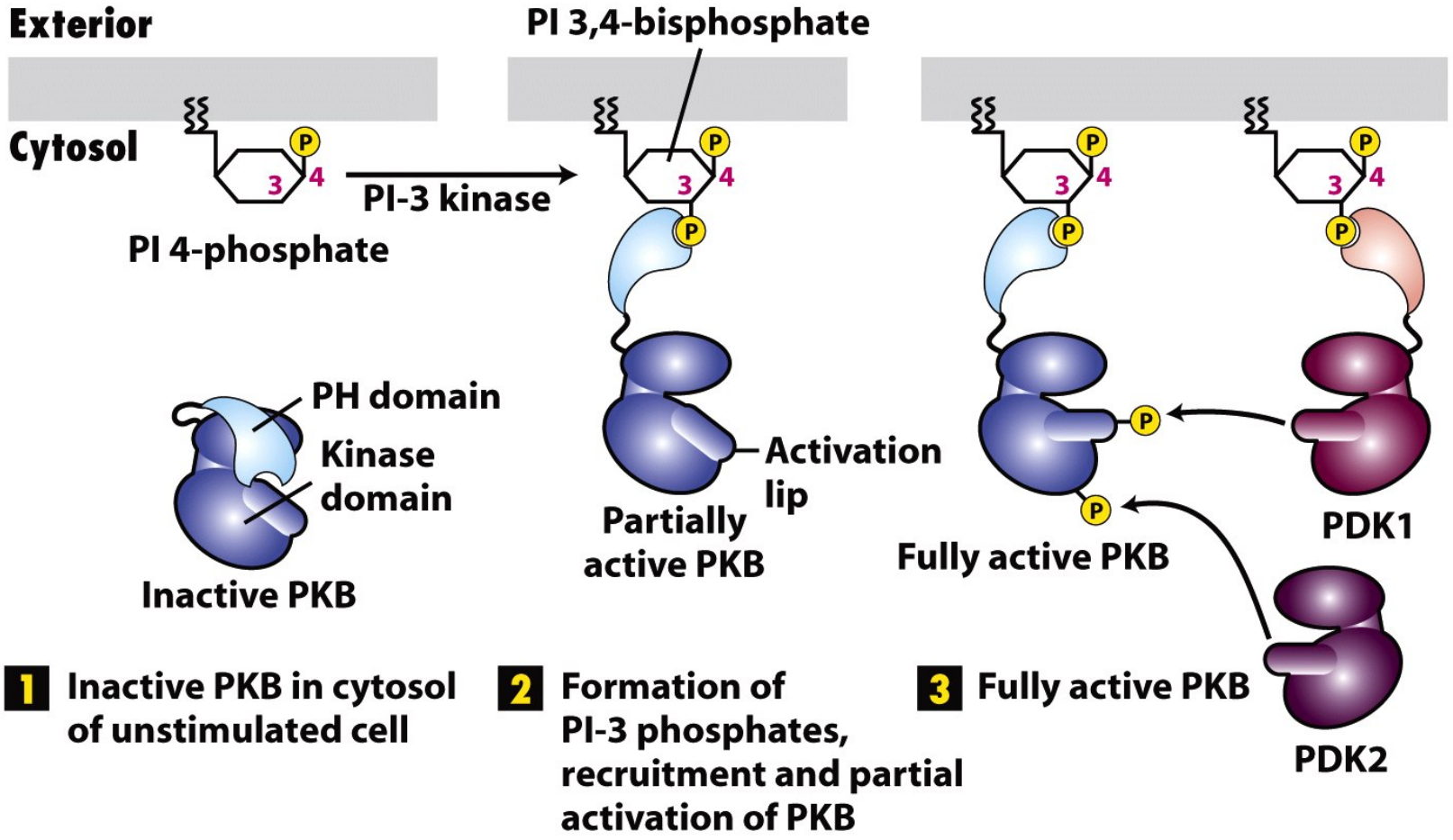


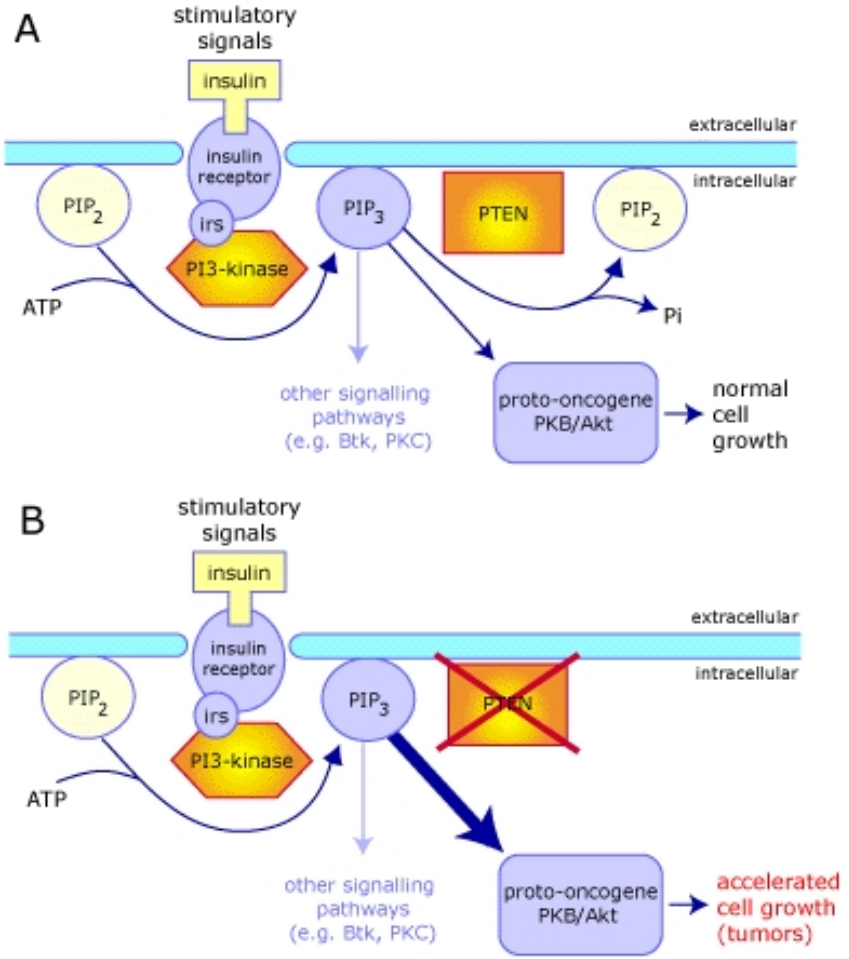
Figure 16-30
Molecular Cell Biology, Sixth Edition

PTEN: the first tumour suppressor with phosphatase activity

PTEN phosphatase has a broad specificity but its major function in cells is to reverse the PI-3 kinase catalyzed reaction.

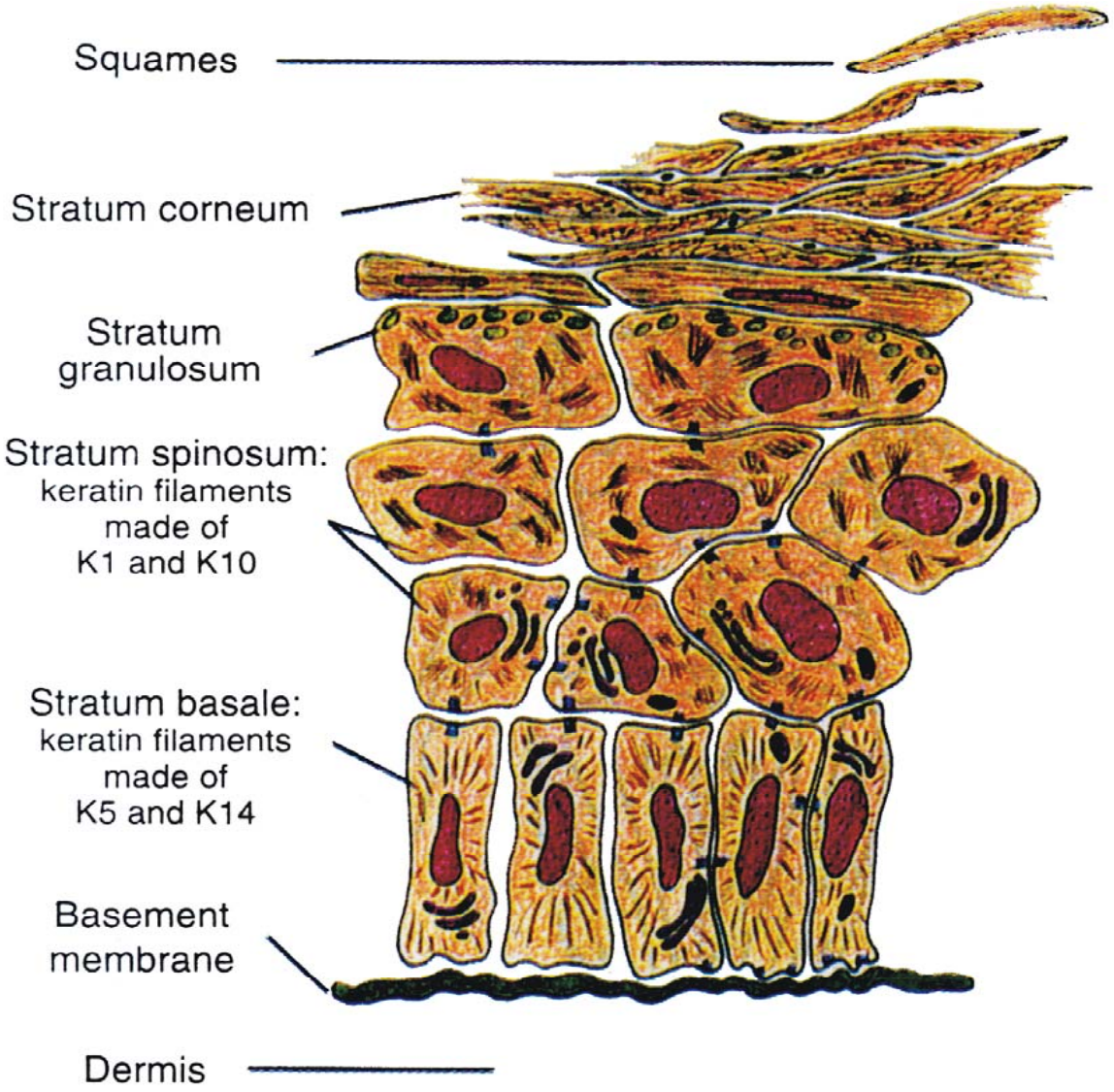
PTEN is deleted or mutated in multiple types of human cancer (glioblastoma, prostate cancer, endometrial tumour).

Overexpression of PTEN promotes apoptosis in cultured mammalian cells.



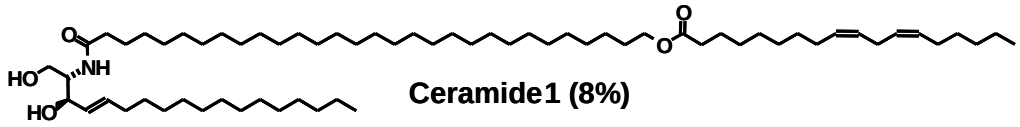
www.ncbi.nlm.nih.gov/bookshelf/picrender.fcgi...

The epidermal layers

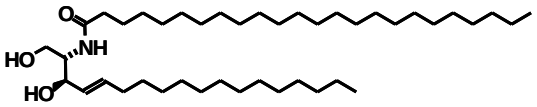


Lipid composition of the human Stratum corneum

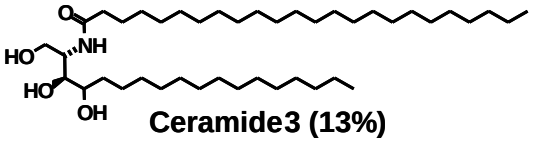
1. Ceramides 45%



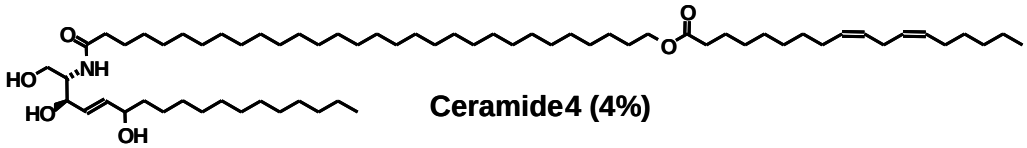
Ceramide1 (8%)



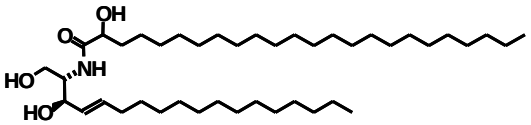
Ceramide2 (21%)



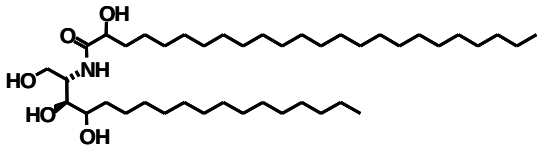
Ceramide3 (13%)



Ceramide4 (4%)



Ceramide5 (27%)



Ceramide6 (4%)

2. Cholesterol: 23%

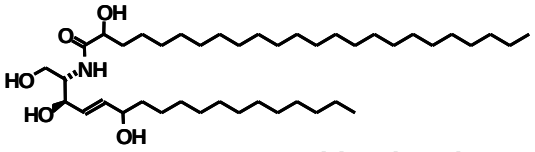
3. Free fatty acids: 10-12%

4. Cholesterolsulfate: 4%

5. Cholesterylester: 2%

6. Triglycerides: 1-2%

7. Sphingosine: 0,5%



Ceramide7 (22%)

Robson et al. (1994) *J. Lipid Res.* 35, 2060-2068