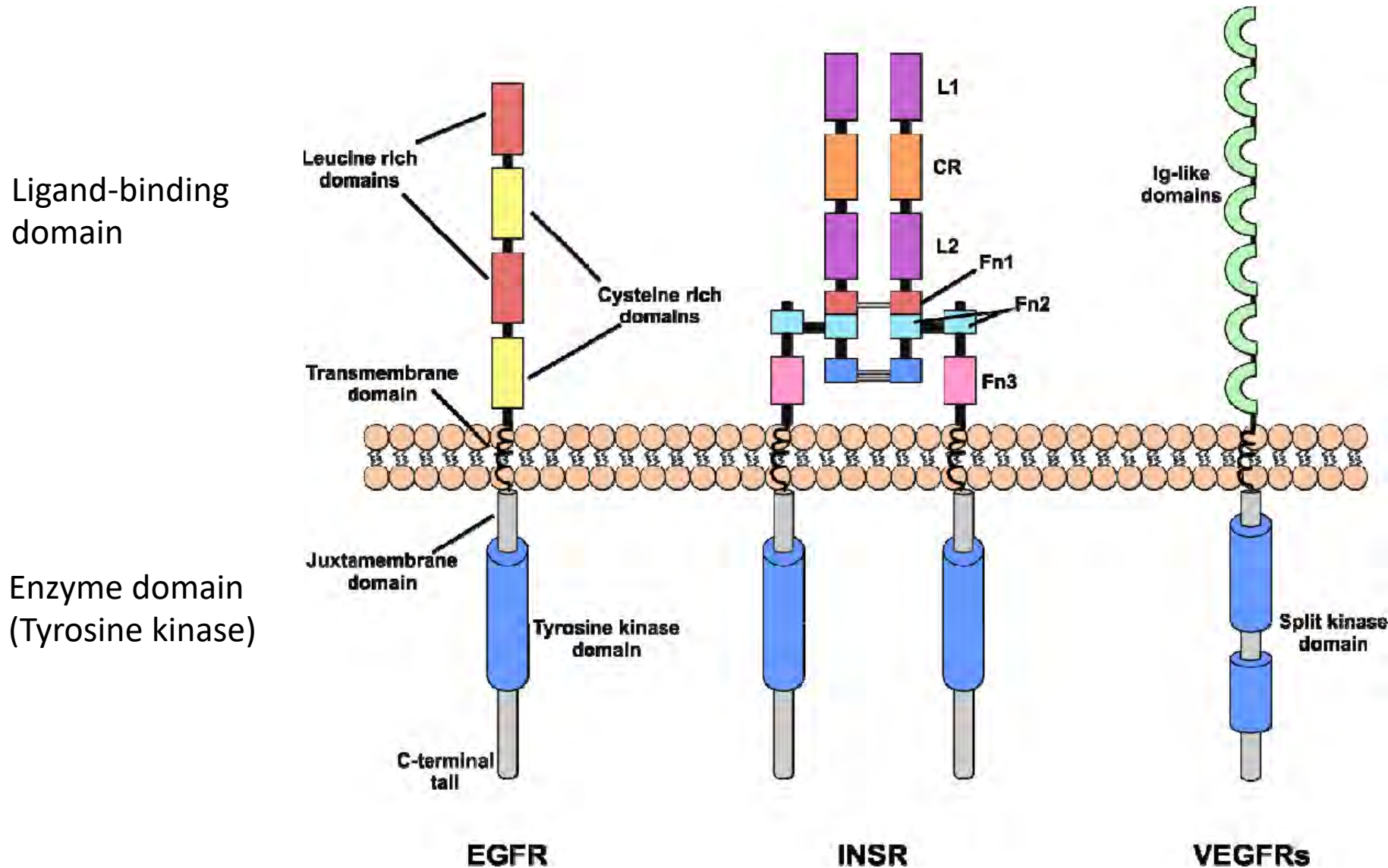


Signal transduction 3

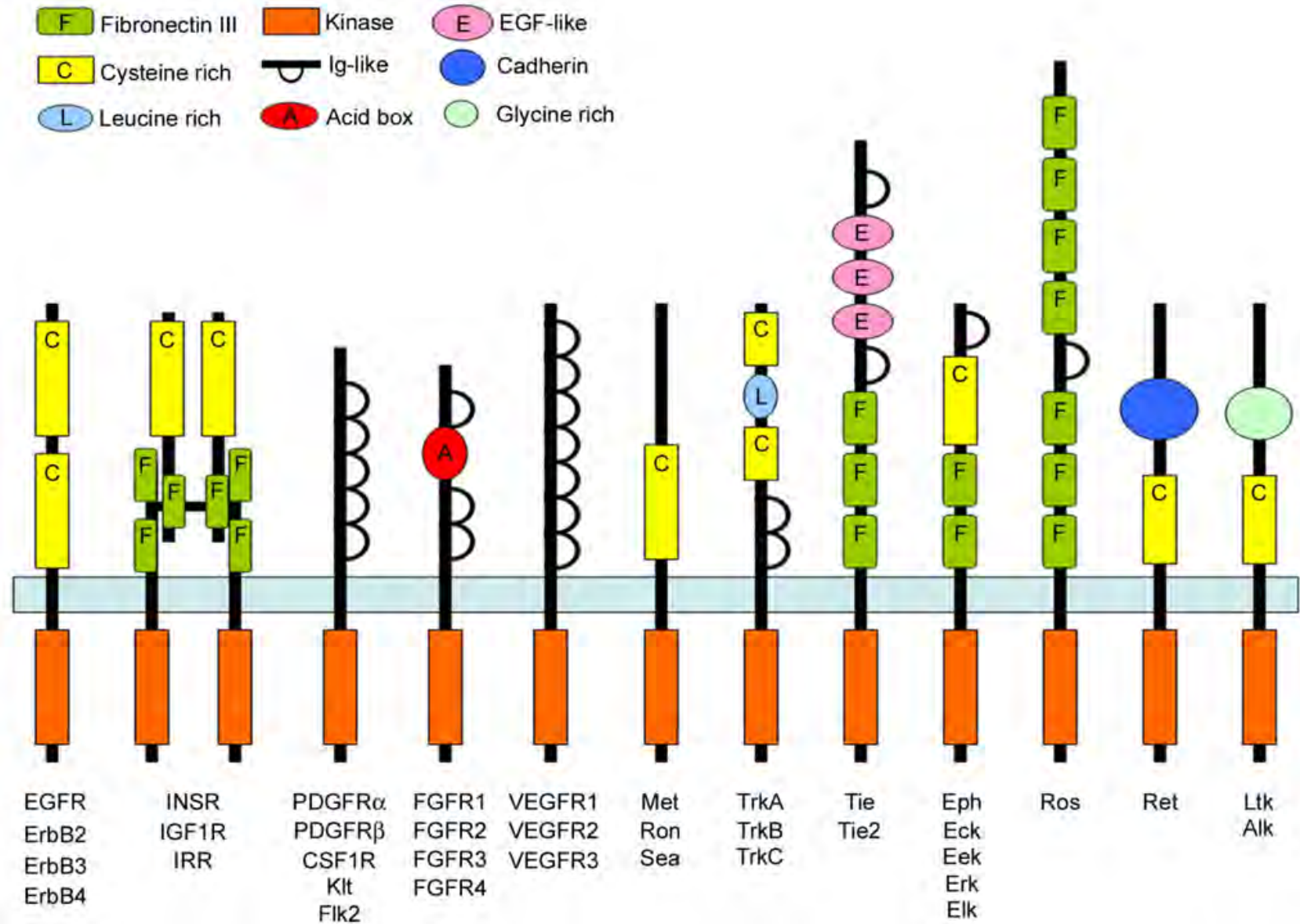
Receptor types

1. Nuclear receptors
2. G protein-coupled receptors
3. Receptor tyrosine kinases (RTK)
4. Receptors with associated kinases

Receptor Types



Receptor Types



Activation of Receptor tyrosine kinases

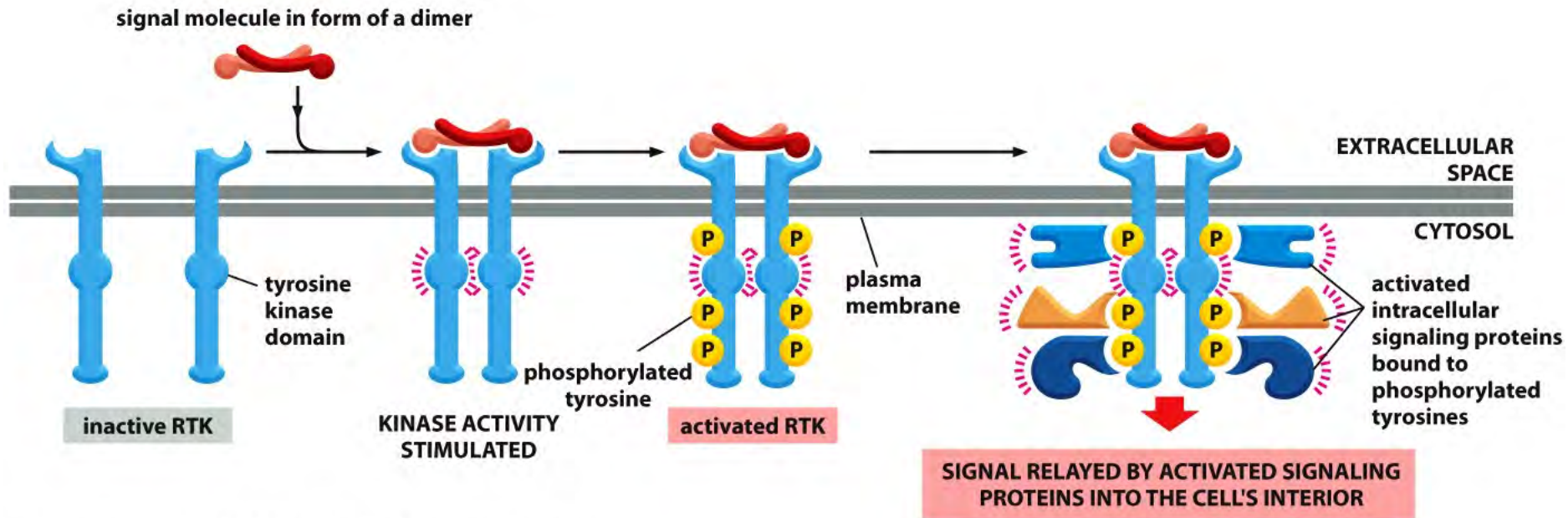
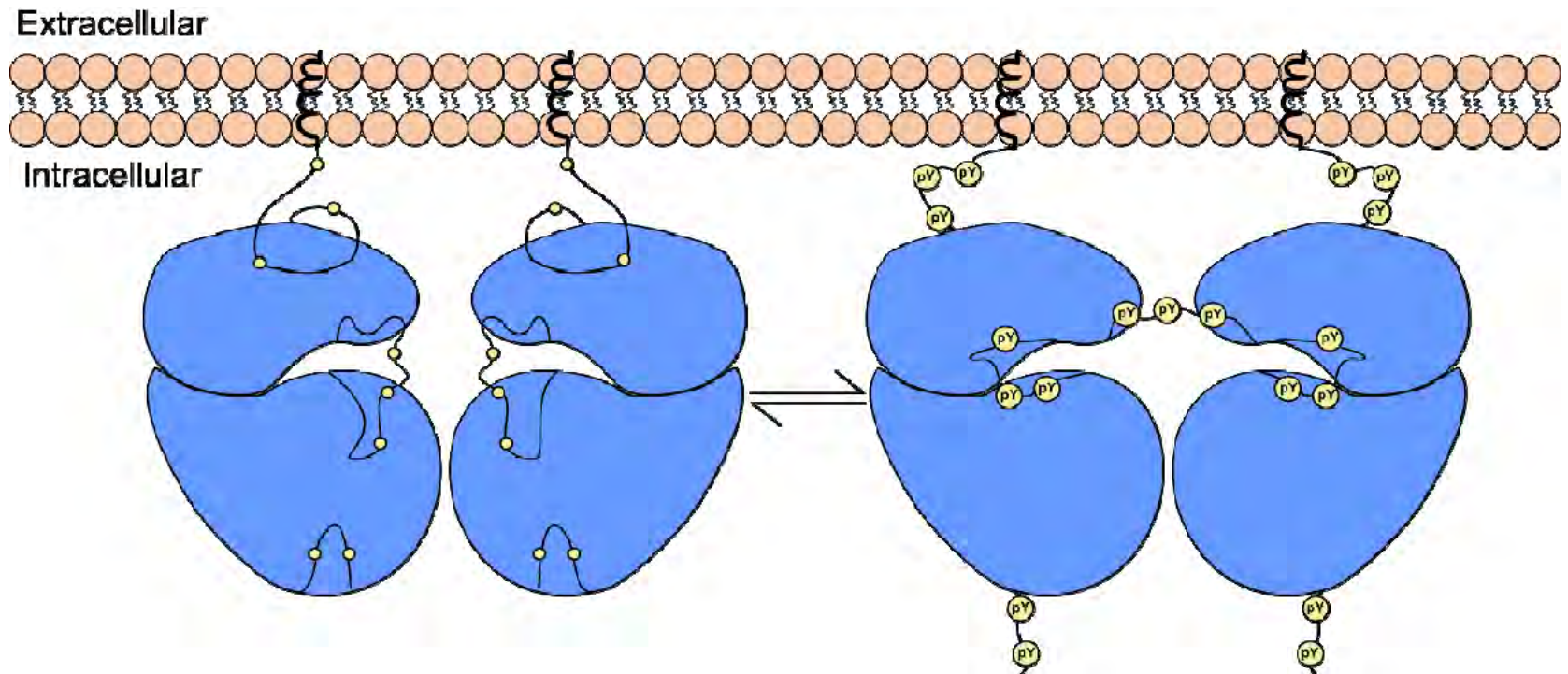


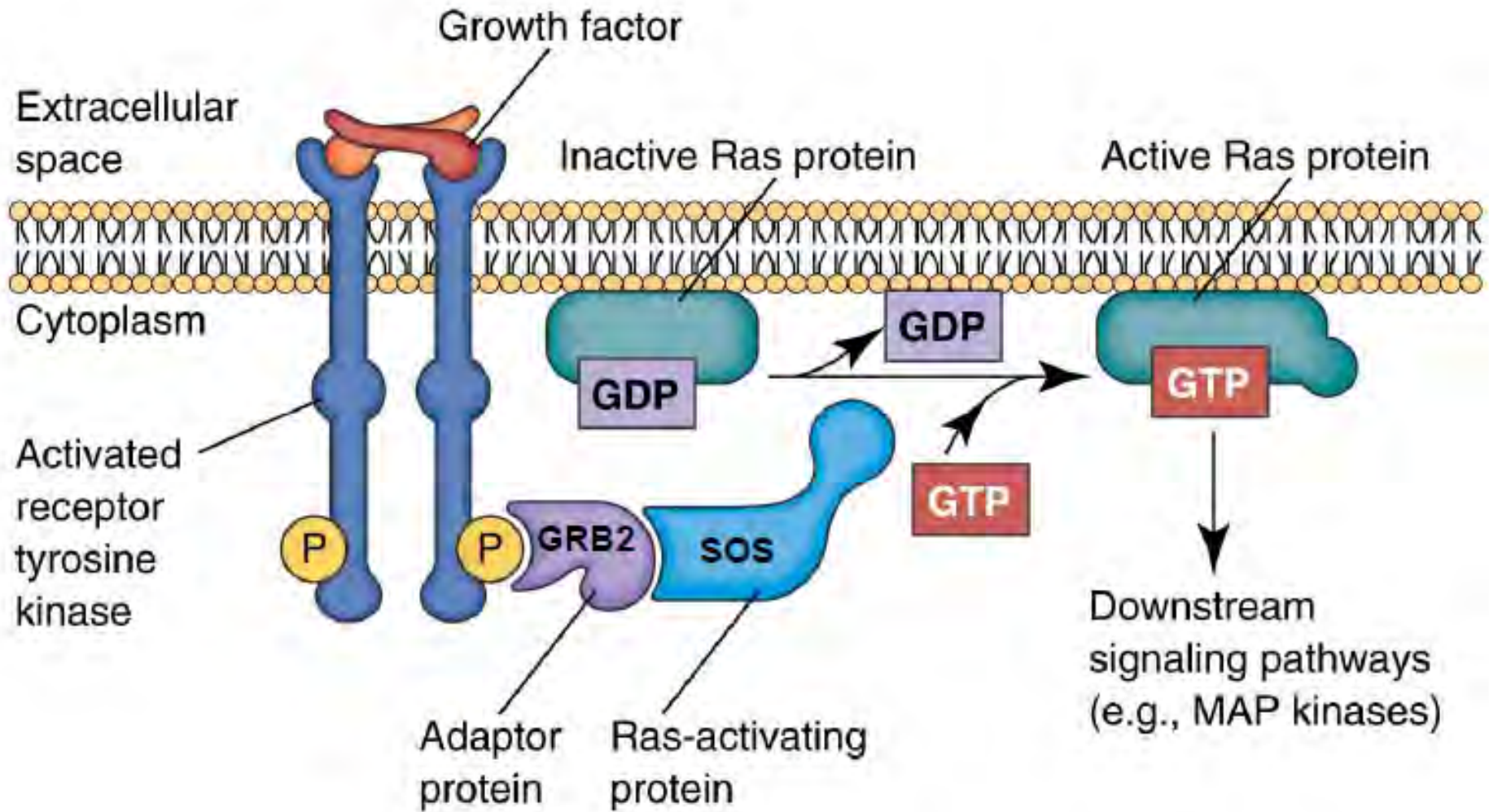
Figure 16-30 Essential Cell Biology 3/e (© Garland Science 2010)

Activation of Receptor tyrosine kinases



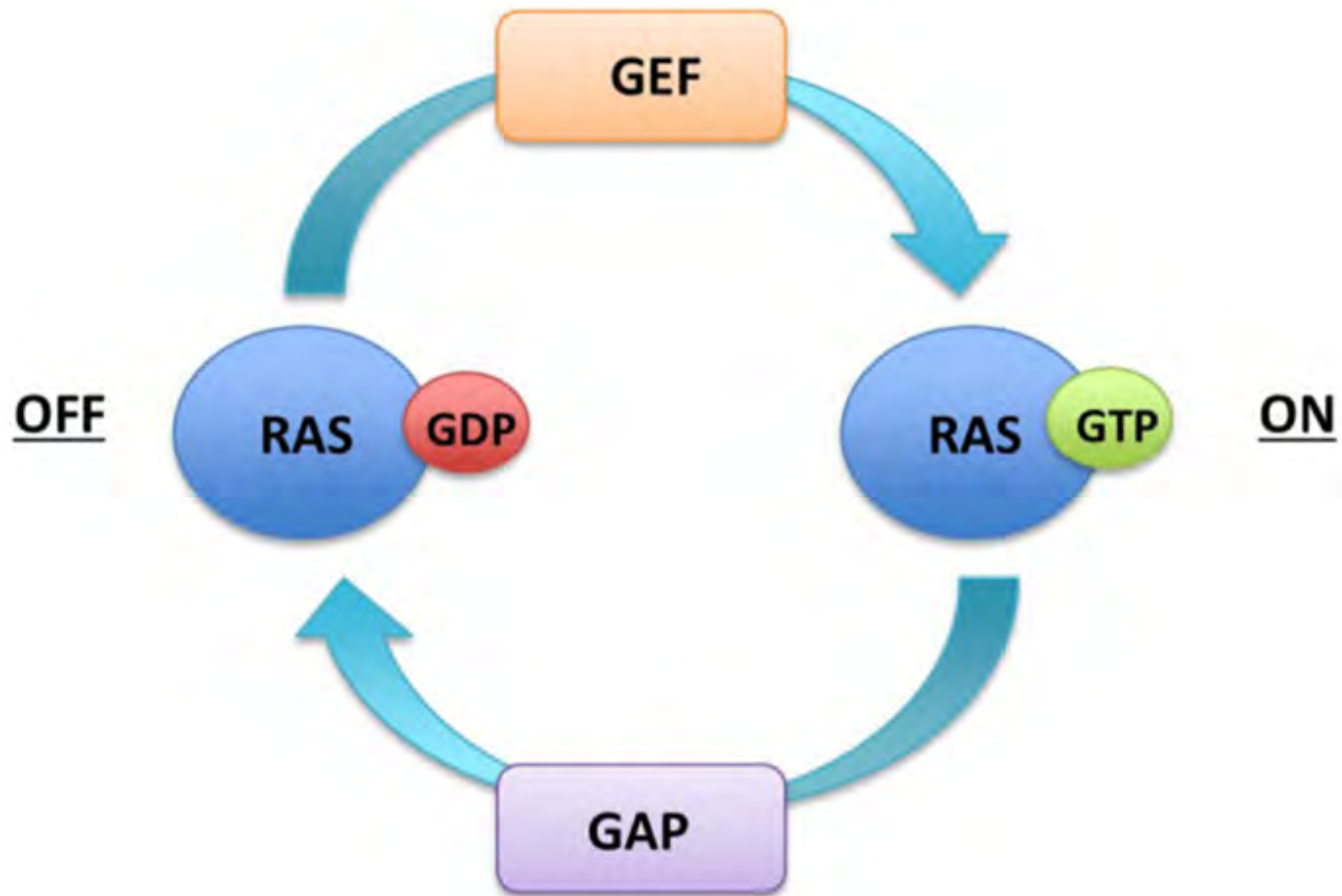
EGF Receptor – Signaling pathway

GTP/GDP Exchange



EGF Receptor – Signaling pathway

GTP/GDP Exchange



EGF Receptor Mitogen-activated Signal transduction

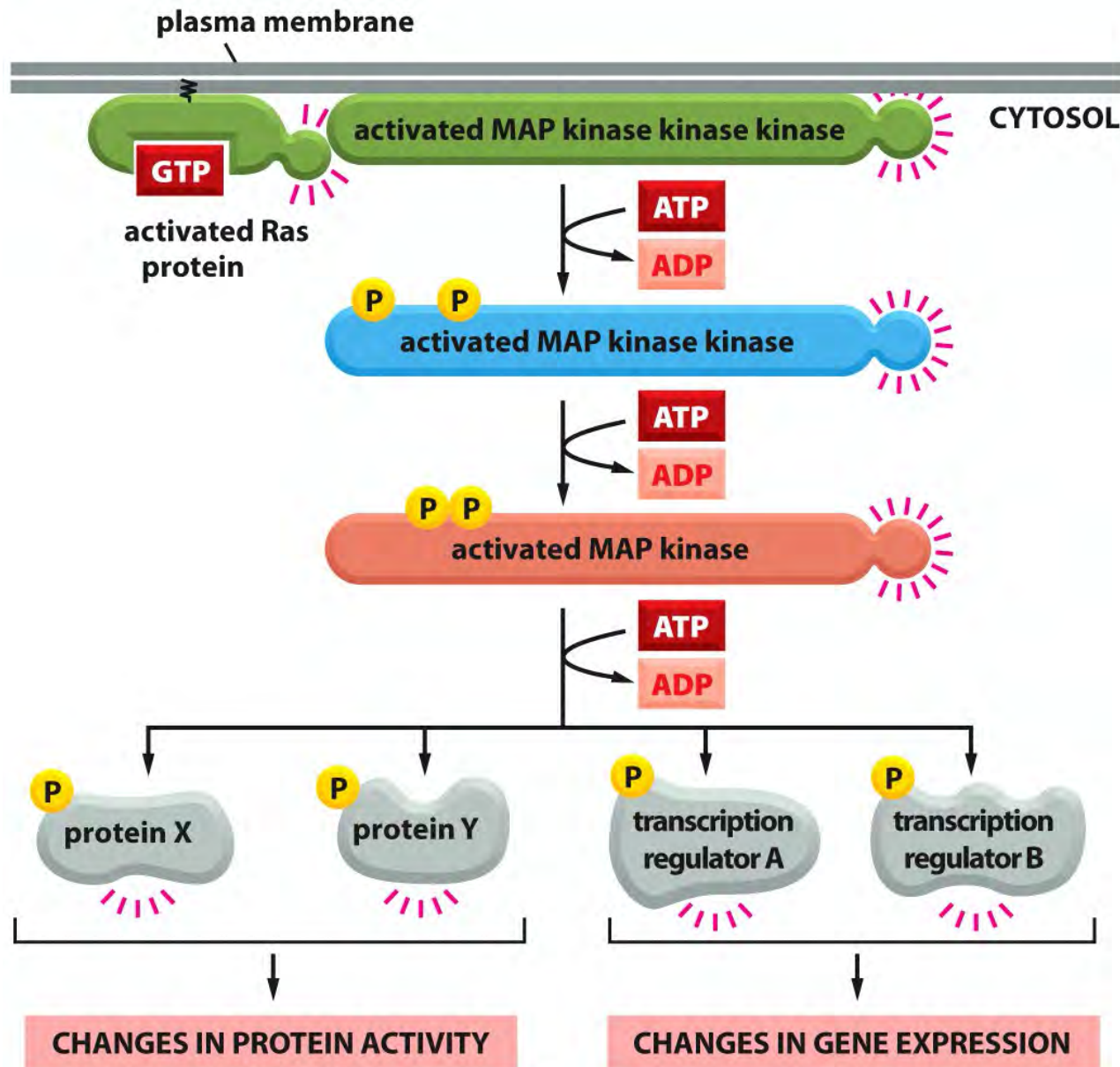
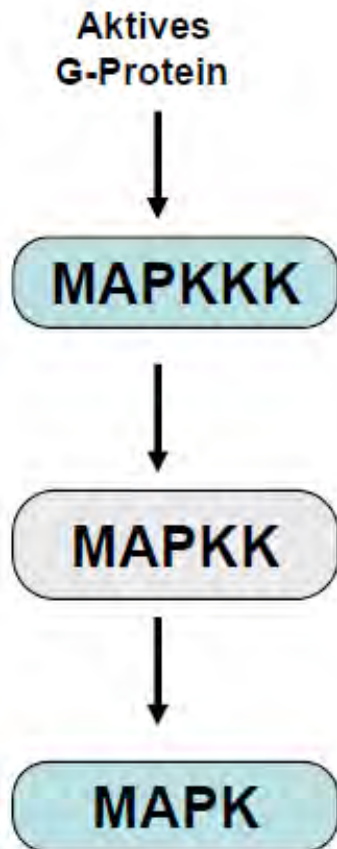


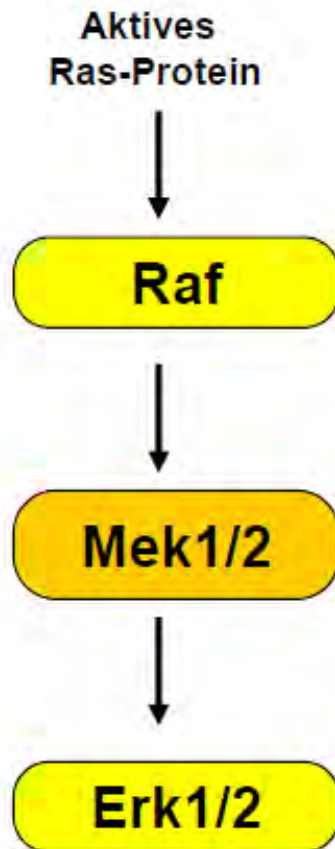
Figure 16-32 Essential Cell Biology 3/e (© Garland Science 2010)

RTK - Mitogen-activated Signal transduction

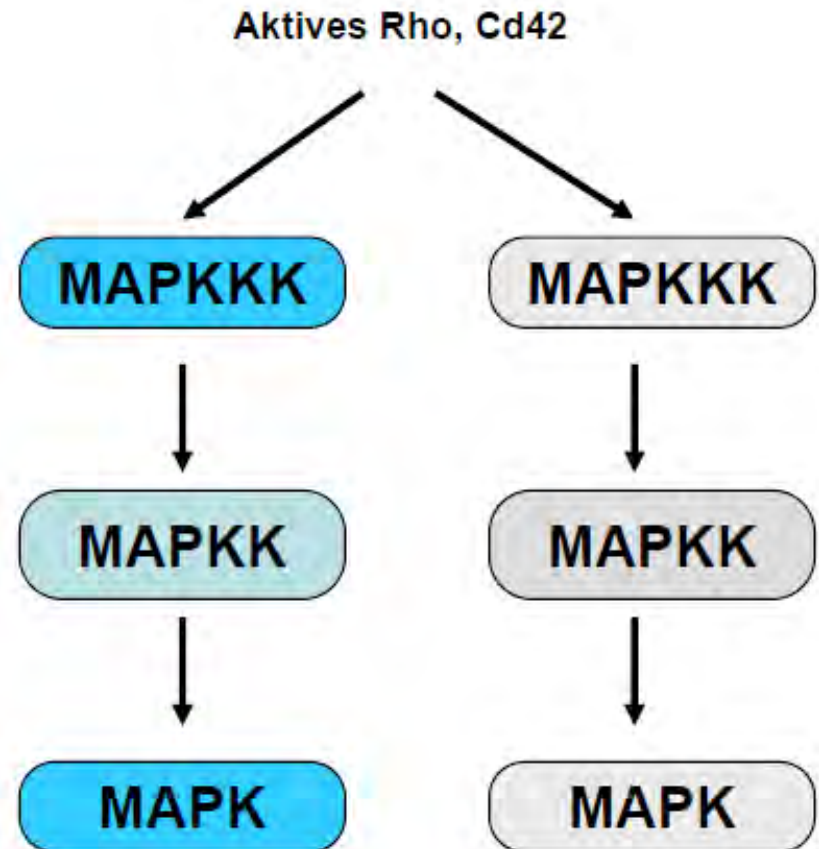
General



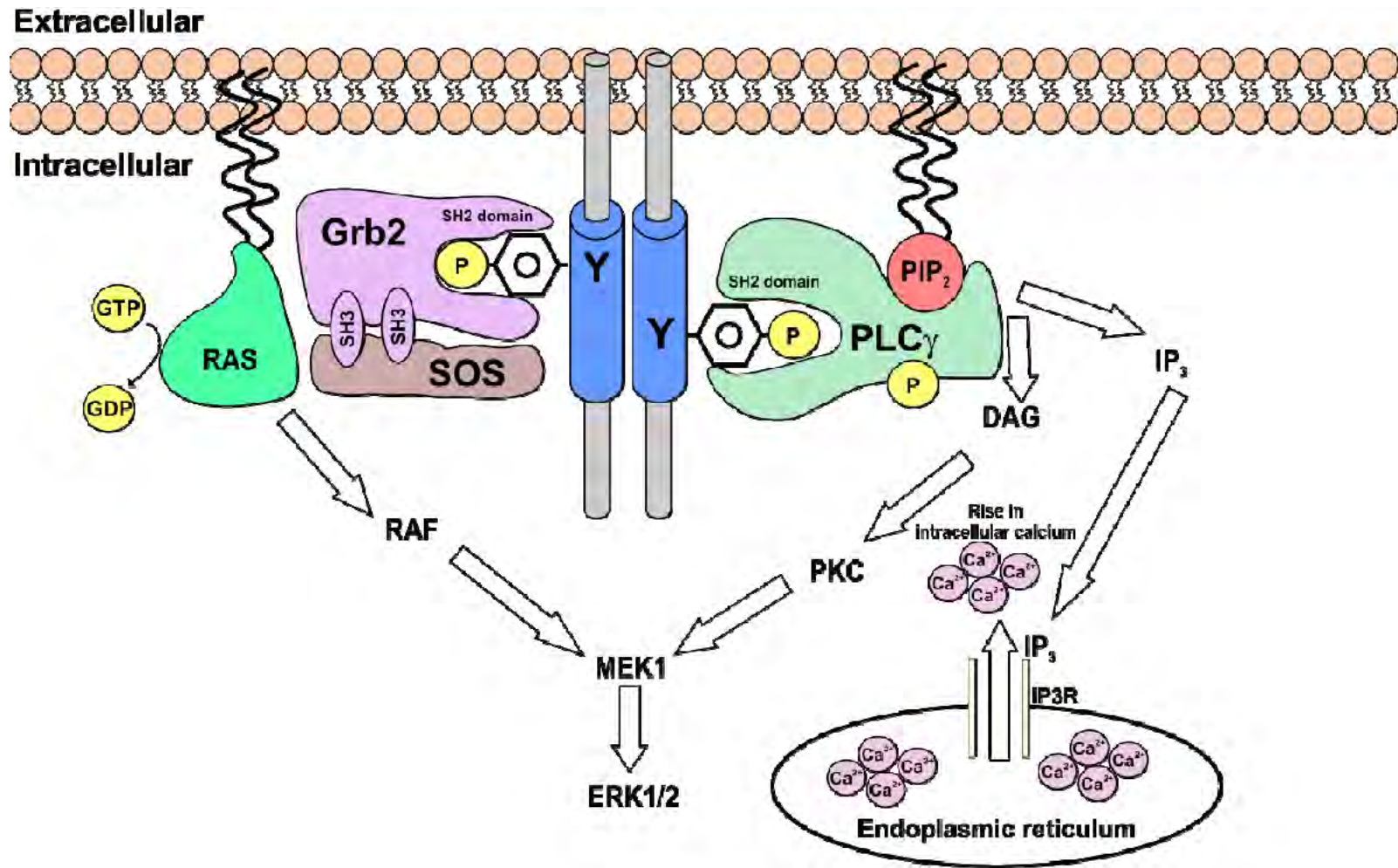
Growth factors



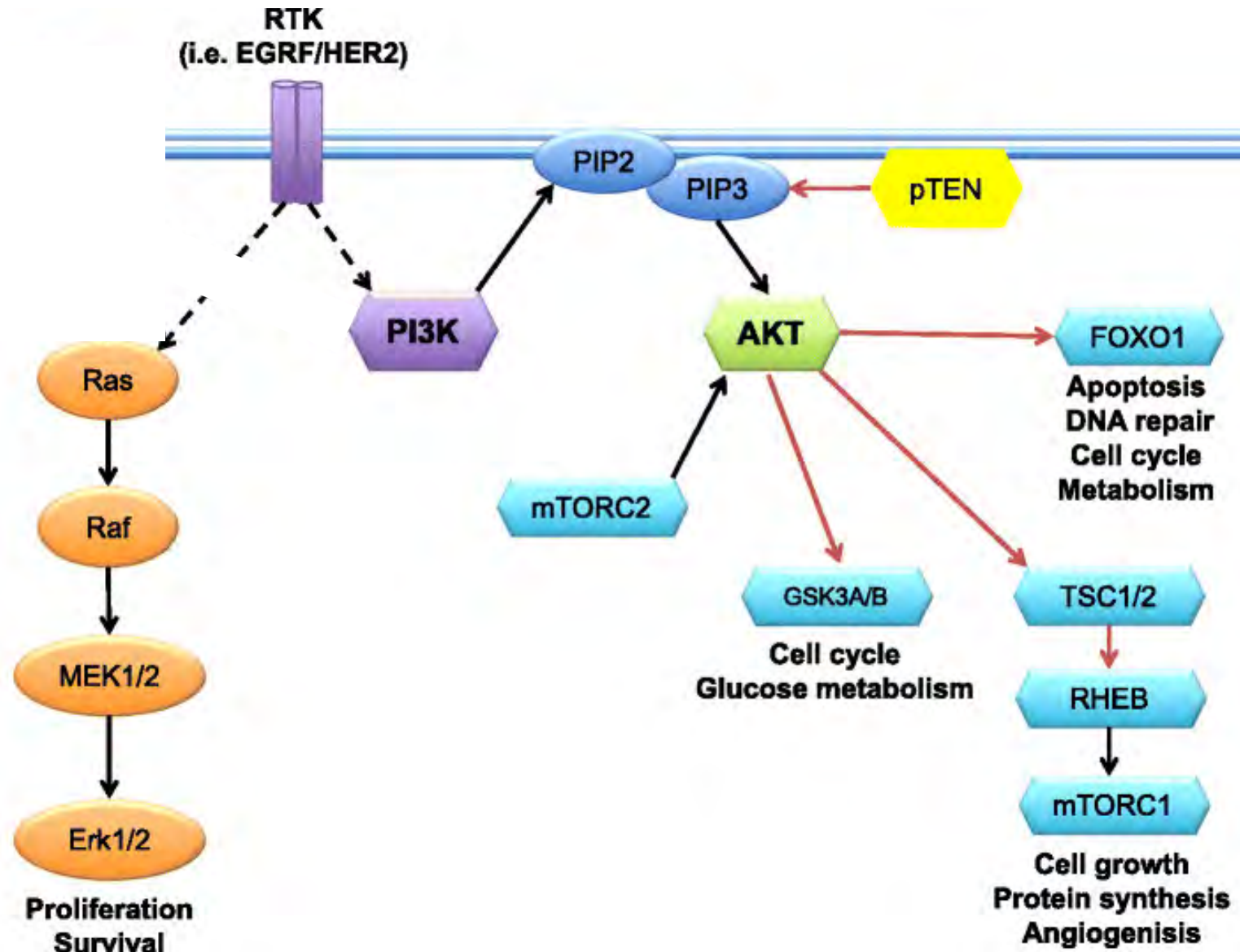
Cytokines



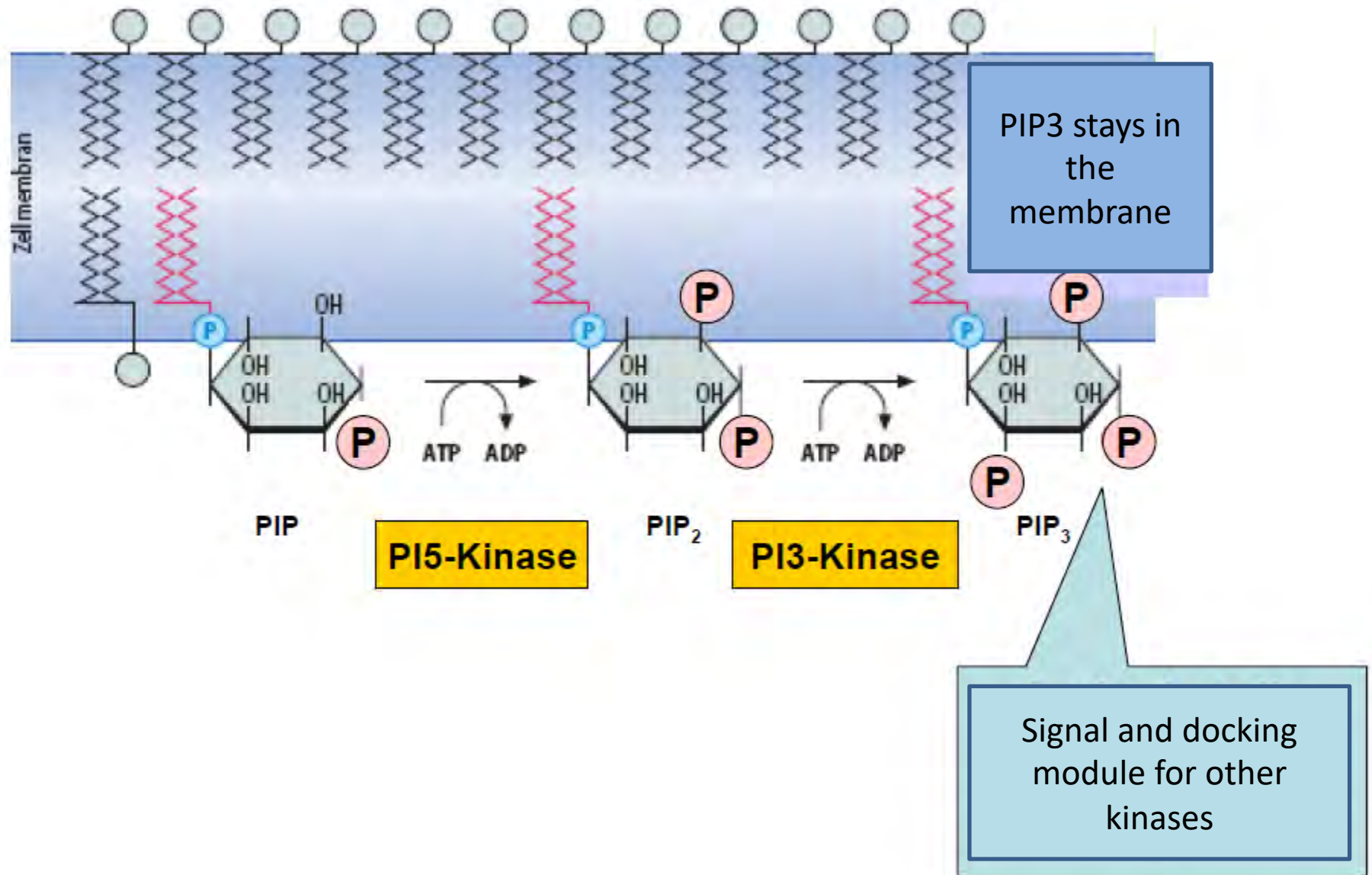
EGF Receptor Signal transduction



EGF Receptor Signal transduction



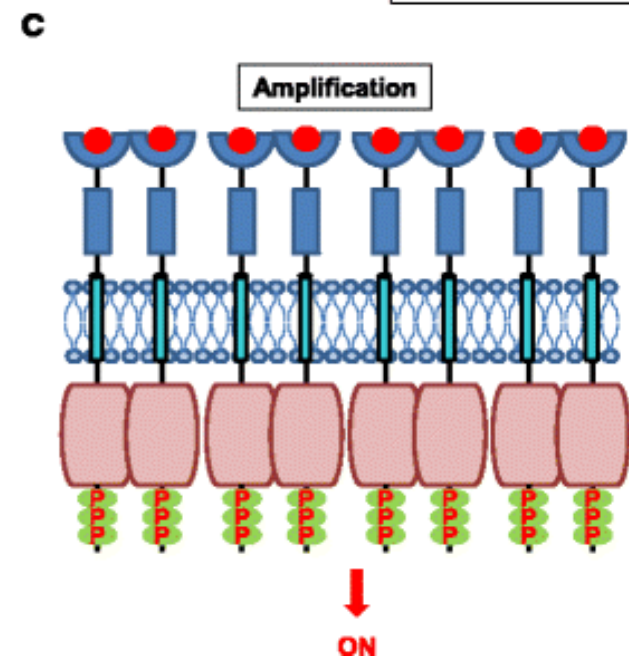
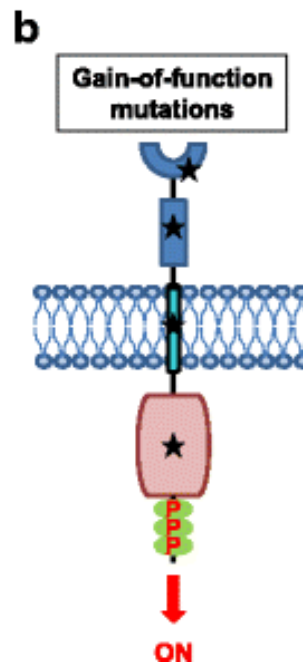
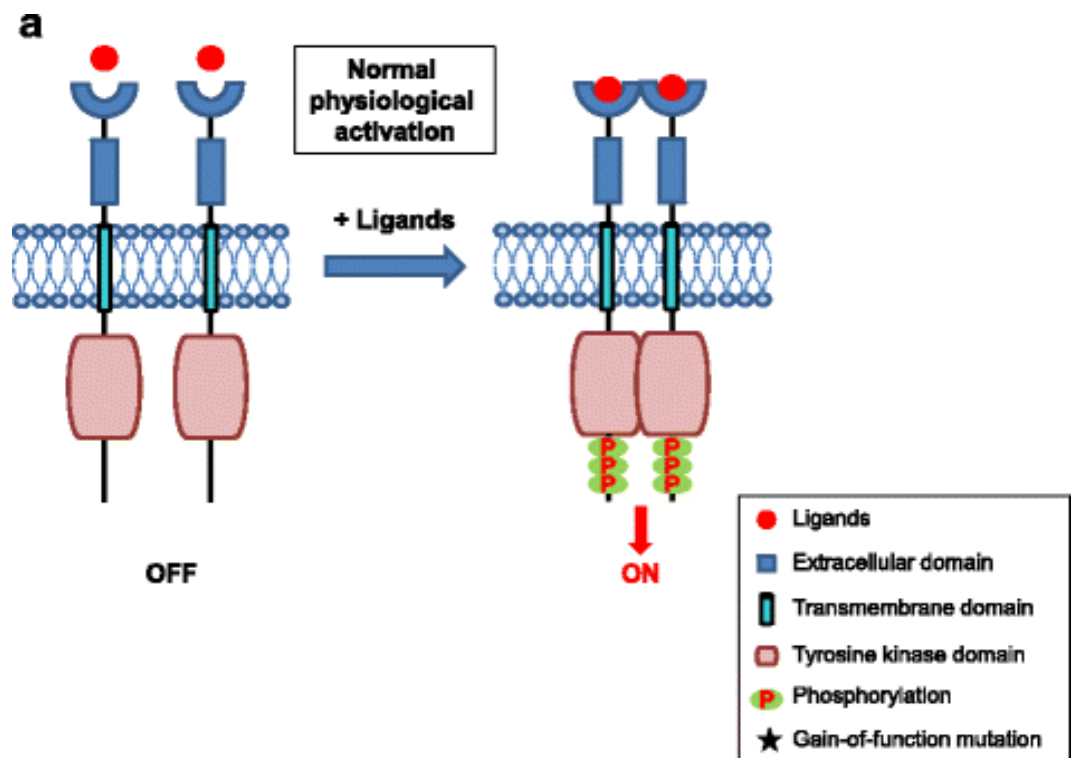
RTK - Signal transduction and PI3K



RTK Signal transduction

- Activation of Ras / MAP-Kinase-cascade
- Activation of Phospholipase C
- Activation of PI3-Kinase
- Activation of JAK / STAT-Signal pathway

RTK Pathology



RTK Pathology

Gene	Mutation	Disease
EGFRvIII	Extracellular domain	Glioblastoma, Ovarian tumor, Non small cell lung carcinoma
FGFR3	Extracellular domain	Multiple myeloma
BCR-ABL	Translocation t(9:22)	Chronic myeloid leukemia Acute lymphocytic leukemia
TEL-ABL	Translocation t(9:12)	Acute lymphocytic leukemia
TEL-PDGF	Translocation t(5:12)	Chronic myeloid monocytic leukemia
EGFR and EGF, TGF α	Autocrine-paracrine loop	Non small cell lung carcinoma Bladder cancer Glioblastoma multiforme
PDGFR and PDGF	Autocrine-paracrine loop	Glioma
IGFR and IGF I and II	Autocrine-paracrine loop	Breast cancer

RTK Pathology and therapy

Inhibitor	Target kinase(s)	Company	Cancer	Status
Small molecule inhibitors				
STI-571	Abl, c-kit, PDGFR	Novartis	CML, GIST	launched
ZD1839	EGFR	AstraZeneca	NSCLC, SCC	launched
OSI-774	EGFR	OSI/Genetech	SCC, BC, LC	Phase III
PKI-166	EGFR, Her-2	Novartis	general cancer	Phase II
PTK-787	VEGFR	Novartis	CR cancer	Phase III
SU5416	VEGFR	Sugen	solid tumor	Phase III
Monoclonal antibody				
Herceptin	Her-2/neu	Genetech	BC	FDA approved
MDX-H210	Her-2/neu	Madarex	BC	Phase I
2C4	Her-2/neu	Genetech	BC, PC, OC	Phase II
C225	EGFR	Imclone	Pan.C, BC, RenC	Phase III
Antisense				
ISIS 3521	PKC- α	ISIS	NSCLC, BC, Pan.C	Phase II
GEM 231	PKA	Hybridon	CR, Pan.C, LC	Phase I