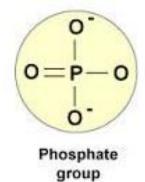
3.B. Conformational Changes from Covalent Modification - 1. PHOSPHORYLATION

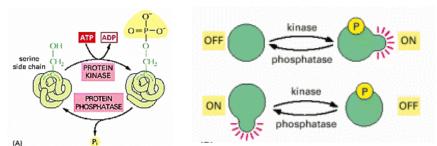


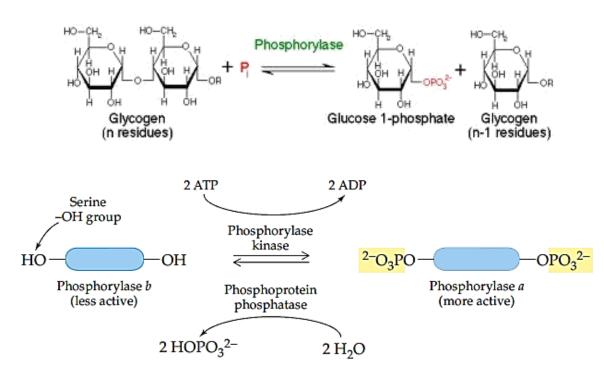
Why is it effective?

- Adds two negative charges: new electrostatic interactions and accordingly conformation
- Can form three or more hydrogen bonds: specific interactions with hydrogen-bond donors
- Can take place in less than a second or over a span of hours
- Often causes highly amplified effects

3.B. Conformational Changes from Covalent Modification - 1. PHOSPHORYLATION

- Rapid and transient regulation of enzyme activity REVERSIBLE
- Phosphorylation: (Ser, Thr, & Tyr)
 - ✓ Mostly, ATP is the donor
 - ✓ Kinases vs. phosphatases
 - Phosphorylation does not lead always to activation of enzymes
 - ✓ Glycogen
 phosphorylase reaction (two forms; a
 & b). Ser is away from
 the active site

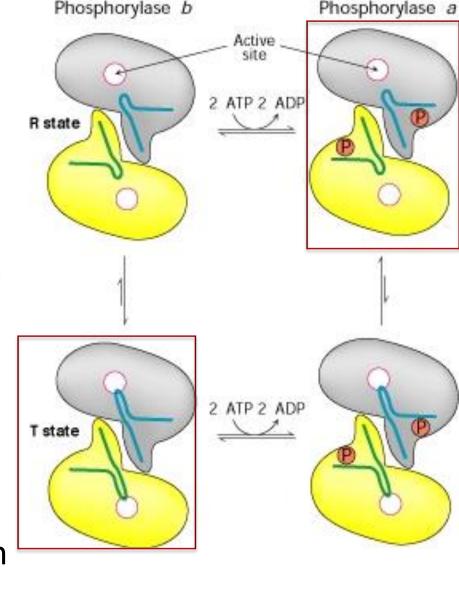




The two forms of the enzyme

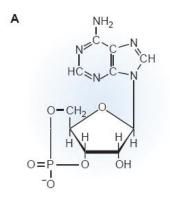
- Both phosphorylase b and phosphorylase a exist as equilibria between an active R state and a less-active T state
- Phosphorylase b is usually inactive because the equilibrium favors the T state
- Phosphorylase a is usually active because the equilibrium favors the R state

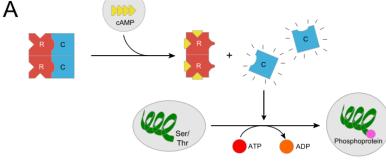
The transition of phosphorylase b between the T and the R state is controlled by the energy charge of the muscle cell.



Protein kinase A (PKA)

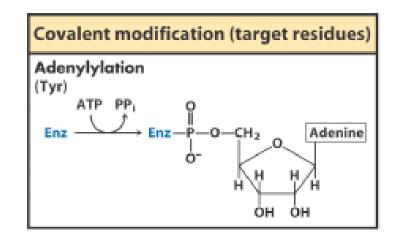
- Protein kinase A (PKA): refers to a family of enzymes whose activity is dependent on cellular levels of cyclic AMP (cAMP)
- cAMP: referred to as a hormonal 2nd messenger
- Has several functions in the cell, & lipid metabolism
- Either dedicated or not B including regulation of glycogen, sugar, **PDE**
- \rightarrow Adrenaline (epinephrine) $\rightarrow \uparrow$ cAMP \rightarrow activates protein kinase A \rightarrow phosphorylates & activates glycogen phosphorylase kinase → phosphorylates & activates glycogen phosphorylase
- Phosphorylation cascade

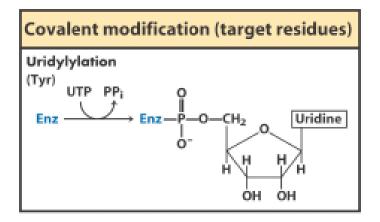




Other covalent modifiers

- Adenylylation (addition of adenylyl group). AMP (from ATP) is transferred to a Tyr hydroxyl by a phosphodiester linkage. The addition of bulky AMP inhibits certain cytosolic enzymes
- Uridylylation (addition of uridylyl group)



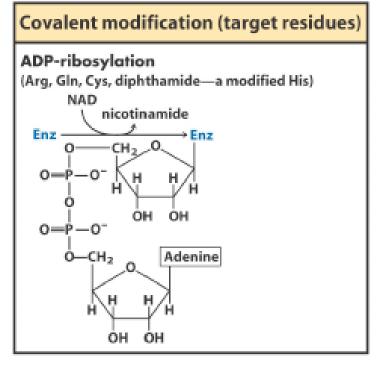


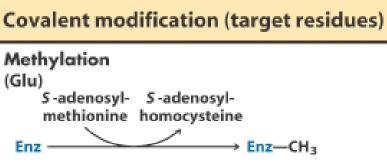
Other covalent modifiers

 ADP-ribosylation: inactivates key cellular enzymes

 Methylation: masks a negative charge & add hydrophobicity on carboxylate side chains

 Acetylation: masks positive charges when added to lysine residues



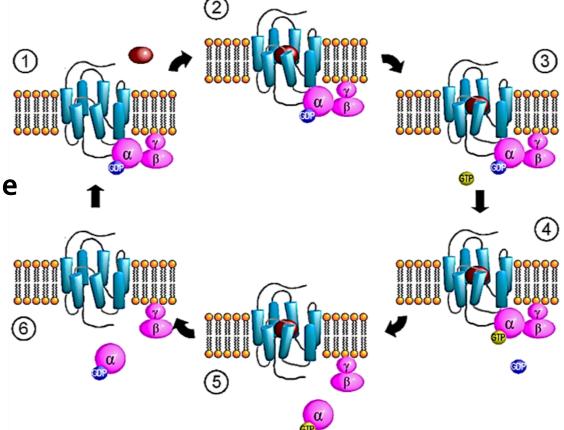


3.C. Conformational Changes from Protein-Protein Interactions

➤ G protein: a family of trans-membrane proteins causing changes inside the cell. They communicate signals from hormones, neurotransmitters, and other signaling factors

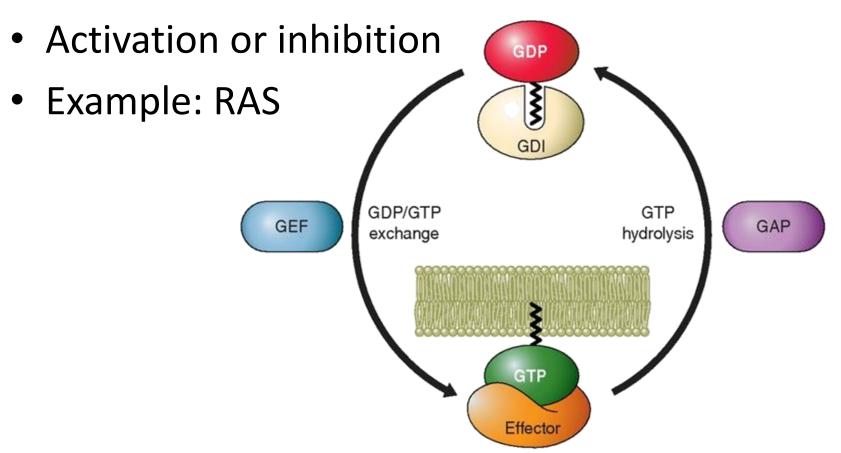
When they bind guanosine triphosphate (GTP), they are 'on', and, when they bind guanosine diphosphate (GDP), they are 'off'

α-Subunit can be stimulatory or inhibitory



Monomeric G proteins

- Same as Gα
- Hydrolysis vs. exchange



3.D. Proteolytic Cleavage Zymogens (Pro- or -gen)

- Irreversible cut usually at the Nterminus
- Trypsin, chymotrypsin, pepsin (trypsinogen, pepsinogen chymotrypsinogen)
 - ✓ Chymotrypsinogen: single polypeptide chain (245 residues), 5 (S—S) bonds

Ca2+

phospholipid

Prothrombin

FXa

- Blood clotting
 - ✓ The soluble protein fibrinogen is converted to the insoluble protein fibrin

