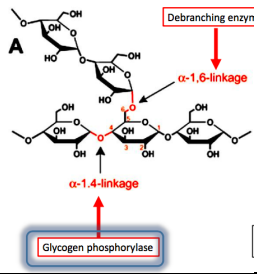
BCMB30004: MID SEMESTER TEST 1 REVISION
Lectures 1-16

Lecture 1/2

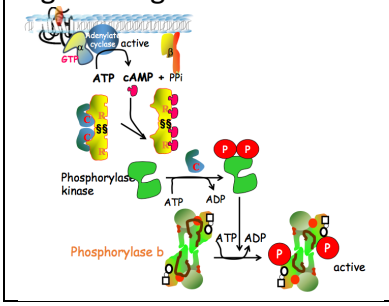
Cell Signalling	- Temporally sensing external stimuli by cells (of external cues)
How?	• Receptors - Extracellular environment; Growth Factor; GPCR; ion channels; gap junctions; steroid hormones - Induce biochemical changes in cells
Hormones or neurotransmitters	Event 1: - Ca++ inc; cAMP; phospholipid messengers Event 2: - Protein phosphorylation; - Leads to physiological effects

Glycogen metabolism

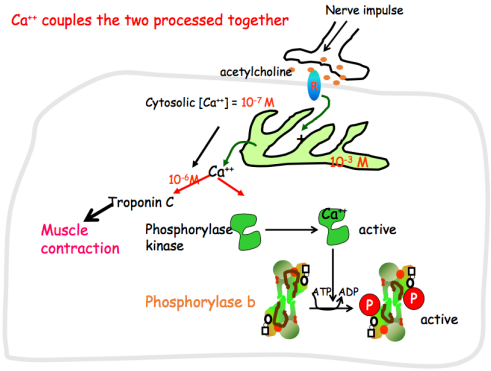
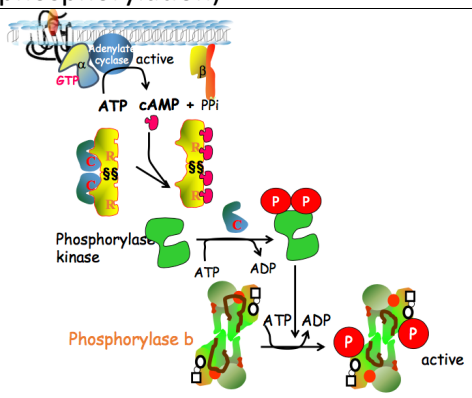
Why study glycogen metabolism?	1956: Kreb and Fischer: Phosphorylase – the first protein kinase – discovered. 1962: Sutherland - cAMP as second messenger of adrenaline on glycogenolysis 1968: Walsh and Krebs - PKA discovered (phosphorylation not only for glycogen metabolism) 1972: Rodbell – Gp as transducers → adenylate cyclase (and signal transduction)
Structure of glycogen 	- Polymer of glucose molecules; - Linked at C1 to C4 (α-1,4-glycosidic bond) → makes LONG CHAINS of glucose polymers - Linked at C1 to C6 (α-1,6- linkage) → for BRANCHING
Enzymes cutting GLYCOGEN:	1. C1→ C4 (α-1,4-glycosidic bond): GLYCOGEN PHOSPHORYLASE - Requires inorganic phosphate (Pi) from intracellular compartment of cell - Leads to one less glucose molecule on glycogen - Rate limiting enzyme; subject to regulation. Glycogen (n) + Pi → G1P + Glycogen (n-1) 2. C1→C6 (α-1,6-): DEBRANCHING ENZYME

	conformation (so Ser14 can interact with E501)
AMP bound vs G6P bound (considering NO phosphorylation)	• G6P binding: - S14 AWAY from interface - 280s loop occluding active site - near the interface – for G6P binding (as well as AMP) • AMP - Definitely near the interface - 280s loop disordered and out of place - Ser14 NEAR THE INTERFACE (so pSer14 can interact with R69 if it is phosphorylated!)

Another way to induce glycogenolysis through phosphorylation of phosphorylase kinase

Fight or flight: adrenaline 	Binds to adrenaline receptor; GPCR; Adenylate cyclase makes cAMP; PKA recruited; PKA then phosphorylates phosphorylase kinase; Phosphorylase kinase able to phosphorylate phosphorylase b!

THEREFORE to regulate phosphorylase kinase:

Through Ca++ (transient/allosteric reg)	Through adrenaline (covalent phosphorylation)
 Ca++ is an allosteric regulator of phosphorylase kinase. Allosteric – so transient – dependent on amount of Ca++ available.	 PKA able to phosphorylate phosphorylase kinase! More permanent. This mechanism amplifies signals of adrenaline

<u>Lecture 4</u>

Activation-inactivation cycle of trimeric G protein

1. β adrenergic receptor binds to agonist	Exposes region on receptor which can bind the Gα subunit