CONCEPT: INSULIN RECEPTOR

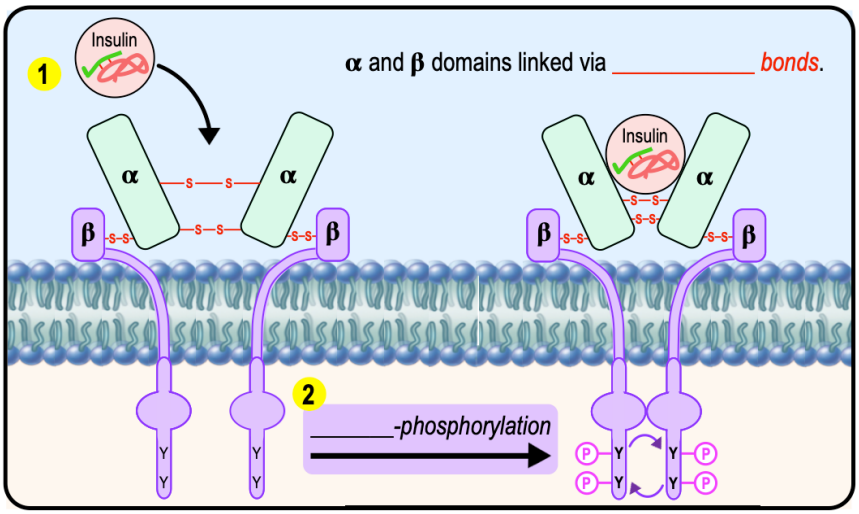
●Insulin signaling beings with _____ steps:

1 *Ligand Binding*: Insulin does _____ enter cells, but instead binds an *insulin* _____.

- □ **Ins**ulin **R**eceptor (_____): a specific type of RTK activated by *insulin* binding.
  - □ INSR has _____ protein subunits (2 α & 2 β) linked via _____ *bonds*.
  - □ Unusual because even in the *unliganded* state, INSR already exists as two αβ _____.

2 *INSR Auto-phosphorylation*: tyrosine kinase domains in the INSR _____ subunits cross-phosphorylate each other.

EXAMPLE: Insulin Receptor.



EXAMPLE: For the insulin receptor to transduce the signal inside the cell:

a) The G-alpha subunit needs to bind GTP to activate adenylate cyclase.
b) The G-alpha subunit needs to bind GTP to activate phosphodiesterase.
c) It needs to activate its tyrosine kinase domains via autophosphorylation, after binding the insulin ligand.
d) It needs to recruit a tyrosine kinase to auto-phosphorylate the cytoplasmic domain after dimerization.
e) It needs to recruit a tyrosine phosphatase to phosphorylate the cytoplasmic domain after dimerization.

PRACTICE: The insulin receptor is an example of a _____:

a) G-protein coupled receptor.
b) Receptor tyrosine kinase.
c) Receptor tyrosine phosphatase.
d) Membrane channel protein.
e) Receptor threonine kinase.

CONCEPT: INSULIN RECEPTOR

INSR Substrates (IRS)

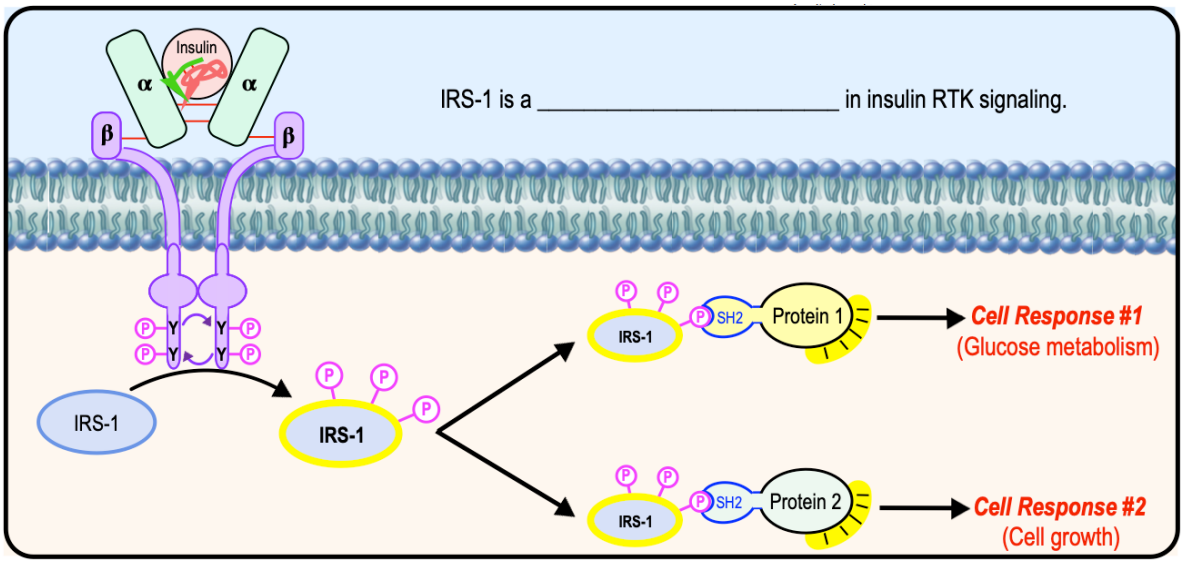
●***I**nsulin **R**eceptor **S**ubstrates* (_____): peptides that are the main targets of fully active autophosphorylated INSR.

□ *IRS-1*: a *secondary messenger* that transmits the insulin receptor signal as an _____ *protein*.

□ *Adapter proteins*: _____ enzymatic activity & serve mainly as a _____ to bring other proteins together.

●Depending on the cell type & conditions, IRS-1 can induce _____ other signaling pathways.

□ Insulin's *RTK signaling pathway* results in *IRS-1 activation*, but then _____ at this point.



PRACTICE: insulin binds to a receptor that:

a) I, III and V.
b) II and IV.
c) I, II and V.
d) II, IV and V.
e) IV and V.

I. Is coupled to a G protein.

II. Possesses tyrosine kinase activity.

III. Possesses serine/threonine phosphatase activity.

IV. Interacts with the adapter protein IRS-1.

PRACTICE: Which of the following is TRUE concerning the interaction between the insulin receptor and IRS-1:

a) The IRS protein phosphorylates the insulin receptor.
b) The β-subunits of the receptor bind to insulin, where each subunit has a separate insulin binding site.
c) Each β-subunit acts as a serine kinase and auto-phosphorylates the other subunit.
d) IRS is phosphorylated by the tyrosine kinase domains in the β-subunits of the insulin receptor.
e) IRS contains phosphorylated threonine residues that directly bind to insulin.