

**PROPOSAL TO CLEAN UP
RECEPTOR SIGNALING PROTEIN
ACTIVITY**

January 2011

Receptors, and
receptor
signaling
proteins are
SIBLINGS

- [-] ← [i] signal transducer activity
 - ← [i] histidine phosphotransfer kinase activity
 - [+] ← [i] receptor activity
 - [-] ← [i] receptor signaling protein activity
 - [-] ← [i] receptor signaling protein serine/threonine kinase activity
 - [+] ← [i] MAP kinase activity
 - [+] ← [i] MAP kinase kinase kinase activity
 - [+] ← [i] MAP kinase kinase kinase kinase activity
 - [+] ← [i] NF-kappaB-inducing kinase activity
 - ← [i] polo kinase kinase activity
 - ← [i] receptor signaling protein serine/threonine phosphatase activity
 - [-] ← [i] receptor signaling protein tyrosine kinase activity
 - ← [i] receptor signaling protein tyrosine kinase activator activity
 - ← [i] receptor signaling protein tyrosine kinase inhibitor activity
 - ← [i] receptor signaling protein tyrosine phosphatase activity
- [-] ← [i] transforming growth factor beta receptor, cytoplasmic mediator activity
 - ← [i] transforming growth factor beta receptor, common-partner cytoplasmic mediator activity
 - ← [i] transforming growth factor beta receptor, inhibitory cytoplasmic mediator activity
 - ← [i] transforming growth factor beta receptor, pathway-specific cytoplasmic mediator activity
- ← [i] two-component response regulator activity
- ← [i] two-component sensor activity

PROBLEMS

- It's unclear what the function of a 'receptor signaling protein' is.
- receptor signaling protein activity ; GO:0005057 (and its children) has been used to annotate both receptors and downstream molecules. Its (recently added) definition is intended for the latter:

Conveys a signal from an upstream receptor or intracellular signal transducer, converting the signal into a form where it can ultimately trigger a change in the state or activity of a cell.

- Part of the problem is the definition of the children:

E.g. receptor signaling protein serine/threonine kinase activity ; GO:0004702

Catalysis of the reaction: $ATP + \text{receptor signaling protein serine} = ADP + \text{receptor signaling protein serine phosphate}$, and $ATP + \text{receptor signaling protein threonine} = ADP + \text{receptor signaling protein threonine phosphate}$.

- The definition describes phosphorylation OF a receptor signaling protein (Many receptors phosphorylate receptor signaling proteins, so would be included in this definition).
- BUT I think the term is intended for annotation of downstream signaling proteins THAT POSSESS ser/thr kinase activity.

PROPOSAL

OUTLINE OF PROPOSAL

- Obsolete existing 'receptor signaling protein x kinase activity' terms, and replace them with broader 'signal transducing x kinase activity' terms.
- Place the enzymatic receptor terms under the new 'signal transducing x kinase activity' terms.

Proposed Revisions

- [-] ← [I] signal transducer activity
 - ← [I] histidine phosphotransfer kinase activity
 - [+] ← [I] receptor activity
 - [-] ← [I] signal transducing protein histidine kinase activity NEW
 - [+] ← [I] transmembrane receptor histidine kinase activity ←
 - ← [I] two-component sensor activity
 - [-] ← [I] signal transducing protein serine/threonine kinase activity NEW
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 - [+] ← [I] transmembrane receptor protein serine/threonine kinase activity ←
 - ← [I] signal transducing protein serine/threonine phosphatase activity NEW
 - [-] ← [I] signal transducing protein tyrosine kinase activity NEW
 - [+] ← [R] signal transducing protein tyrosine kinase activator activity RENAME
 - [+] ← [R] signal transducing protein tyrosine kinase inhibitor activity RENAME
 - [+] ← [I] transmembrane receptor protein tyrosine kinase activity
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 - ← [I] two-component response regulator activity

Enzymatic receptors are children of the new signal transducing terms

If we go the HAS_PART route for receptors, we could also use HAS_PARTs for these terms (and rename the new terms to 'protein histidine kinase signal transducer activity ; GO:NEW')

HAS_PART protein histidine kinase activity

is_a signal transducer activity

NB: The proposal would remove the distinction between receptors and the molecules that signal downstream of them.

I'm not sure this distinction (E.g. where the gene product lies in a pathway) belongs in function.

This distinction can be captured by annotating to 'intracellular signal transduction ; GO:0035556' for the downstream molecules.

OBSOLETE: receptor signaling protein activity ; GO:0005057

Comment: This term was made obsolete because its meaning is ambiguous.

Consider: [signal transducer activity ; GO:0004871](#)

Consider: [intracellular signal transduction ; GO:0035556](#)

OBSOLETE: receptor signaling protein serine/threonine kinase activity ; GO:0004702

Comment: This term was made obsolete because its meaning is ambiguous.

Replaced with: [signal transducing protein serine/threonine kinase activity ; GO:NEW](#)

Consider: [intracellular signal transduction ; GO:0035556](#)

OBSOLETE: receptor signaling protein serine/threonine phosphatase activity ; GO:0009400

Comment: This term was made obsolete because its meaning is ambiguous.

Replaced with: [signal transducing protein serine/threonine phosphatase activity ; GO:NEW](#)

Consider: [intracellular signal transduction ; GO:0035556](#)

OBSOLETE: receptor signaling protein tyrosine kinase activity ; GO:0004716

Comment: This term was made obsolete because its meaning is ambiguous.

Replaced with: [signal transducing protein tyrosine kinase activity ; GO:NEW](#)

Consider: [intracellular signal transduction ; GO:0035556](#)

OBSOLETE: receptor signaling protein tyrosine phosphatase activity ; GO:0004728

Comment: This term was made obsolete because its meaning is ambiguous.

Replaced with: [signal transducing protein tyrosine phosphatase activity ; GO:NEW](#)

Consider: [intracellular signal transduction ; GO:0035556](#)

NB: Obsoleting terms rather than renaming, because the new terms have a broader meaning, and some annotations could be transferred to the more specific receptor terms.

Proposed Revisions: NEW TERMS

signal transducing protein serine/threonine kinase activity ; GO:NEW

Functions to pass on a signal by catalysis of the reaction: $\text{ATP} + \text{protein serine} = \text{ADP} + \text{protein serine phosphate}$, and $\text{ATP} + \text{protein threonine} = \text{ADP} + \text{protein threonine phosphate}$. A signal is a physical entity or change in state that is used to transfer information in order to trigger a response. The phosphate group can be transferred to itself or a downstream protein.

Comment: For gene products that signal downstream of a receptor, consider also annotating to 'intracellular signal transduction ; GO:0035556'.

signal transducing protein serine/threonine phosphatase activity ; GO:NEW

Functions to pass on a signal by catalysis of the reaction: $\text{protein serine phosphate} + \text{H}_2\text{O} = \text{protein serine} + \text{phosphate}$, and $\text{protein threonine phosphate} + \text{H}_2\text{O} = \text{protein threonine} + \text{phosphate}$. A signal is a physical entity or change in state that is used to transfer information in order to trigger a response. The phosphate group can be removed from itself or a downstream protein.

Comment: For gene products that signal downstream of a receptor, consider also annotating to 'intracellular signal transduction ; GO:0035556'.

signal transducing protein tyrosine kinase activity ; GO:NEW

Functions to pass on a signal by catalysis of the reaction: $\text{ATP} + \text{a protein tyrosine} = \text{ADP} + \text{protein tyrosine phosphate}$. A signal is a physical entity or change in state that is used to transfer information in order to trigger a response. The phosphate group can be transferred to itself or a downstream protein.

Comment: For gene products that signal downstream of a receptor, consider also annotating to 'intracellular signal transduction ; GO:0035556'.

signal transducing protein tyrosine phosphatase activity ; GO:NEW

Functions to pass on a signal by catalysis of the reaction: $\text{protein tyrosine phosphate} + \text{H}_2\text{O} = \text{protein tyrosine} + \text{phosphate}$. A signal is a physical entity or change in state that is used to transfer information in order to trigger a response. The phosphate group can be removed from itself or a downstream protein.

Comment: For gene products that signal downstream of a receptor, consider also annotating to 'intracellular signal transduction ; GO:0035556'.

signal transducing protein histidine kinase activity ; GO:NEW

Functions to pass on a signal by catalysis of the reaction: $\text{ATP} + \text{protein L-histidine} = \text{ADP} + \text{protein phospho-L-histidine}$. A signal is a physical entity or change in state that is used to transfer information in order to trigger a response. The phosphate group can be removed from itself or a downstream protein.

Comment: For gene products that signal downstream of a receptor, consider also annotating to 'intracellular signal transduction ; GO:0035556'.

(NB: This term is not to replace an existing term, but is needed to complete the set).

TM receptor AND receptor
signaling protein proposals
combined

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