



















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

**December 2010**

- ☐ ←  receptor signaling protein activity
  - ☐ ←  receptor signaling protein serine/threonine kinase activity
    - ⊕ ←  MAP kinase activity
    - ⊕ ←  MAP kinase kinase kinase activity
    - ⊕ ←  MAP kinase kinase kinase kinase activity
    - ⊕ ←  NF-kappaB-inducing kinase activity
    - ←  polo kinase kinase activity
    - ←  receptor signaling protein serine/threonine phosphatase activity
  - ☐ ←  receptor signaling protein tyrosine kinase activity
    - ←  receptor signaling protein tyrosine kinase activator activity
    - ←  receptor signaling protein tyrosine kinase inhibitor activity
    - ←  receptor signaling protein tyrosine phosphatase activity
  - ☐ ←  transforming growth factor beta receptor, cytoplasmic mediator activity
    - ←  transforming growth factor beta receptor, common-partner cytoplasmic mediator activity
    - ←  transforming growth factor beta receptor, inhibitory cytoplasmic mediator activity
    - ←  transforming growth factor beta receptor, pathway-specific cytoplasmic mediator activity
  - ←  two-component response regulator activity
  - ←  two-component sensor activity

# PROBLEMS

- 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 + receptor signaling protein serine = ADP + receptor signaling protein serine phosphate, and ATP + receptor signaling protein threonine = ADP + receptor signaling protein threonine phosphate.*

- The definition is for 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 signaling proteins THAT POSSESS ser/thr kinase activity.

Therefore, I'd like to propose the following:

## 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
    - [+] ← [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] 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
  - [-] ← [I] signal transducing protein tyrosine phosphatase activity NEW
    - ← [I] transmembrane receptor protein tyrosine phosphatase activity ←
  - [+] ← [I] transforming growth factor beta receptor, cytoplasmic mediator activity
  - ← [I] two-component response regulator activity

Receptor terms  
are children of  
the new signal  
transducing  
terms

If we go the HAS\_PART route for receptors, we could (re)name the new terms:

protein histidine kinase signal transducer activity ; GO:NEW

HAS\_PART protein histidine kinase activity

is\_a signal transducer activity

## Proposed Revisions: OBSOLETIONS

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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  - ← [I] histidine phosphotransfer kinase activity
  - [+] ← [I] receptor activity
  - [-] ← [I] signal transducing protein histidine kinase activity NEW
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