

**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
    - ← [R] receptor signaling protein tyrosine kinase activator activity
    - ← [R] 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

- Replace existing 'receptor signaling protein x kinase activity' terms with broader 'signal transducing x kinase activity' terms.
- Place the enzymatic receptor terms under the new 'signal transducing x kinase activity' terms.
- Merge the old 'receptor signaling protein x kinase activity' terms into the new broader terms.

*NB: merged rather than obsoleted so curators don't have to spend time re-mapping their annotations.*

## 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
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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
  - [-] ← [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

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.

# 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).



**MERGE INTO SIGNAL TRANSDUCER ACTIVITY: receptor signaling protein activity ; GO:0005057**

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

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

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

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

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

Merge into: signal transducing protein tyrosine kinase activity ; GO:NEW

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

Merge into: signal transducing protein tyrosine phosphatase activity ; GO:NEW

NB: Have created new terms rather than renaming the old terms, because the meaning of the new terms is broader so deserves a new ID.

NB: Haven't obsoleted the old terms, to save curators having to remap lots of their annotations. A new ID should flag that the definition is changed so they can look at them IF THEY HAVE TIME, but it's not compulsory.

TM receptor AND receptor  
signaling protein proposals  
combined

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