

# EXISTING STRUCTURE

- [-] ← [i] signaling
  - [+] ← [i] behavioral signaling
  - [+] ← [i] cell-cell signaling
  - [+] ← [i] extracellular matrix-cell signaling
  - [+] ← [i] motogenic signaling initiating cell movement in cerebral cortex
    - ← [i] motogenic signaling involved in interneuron migration from the subpallium to the cortex
    - ← [i] motogenic signaling involved in postnatal olfactory bulb interneuron migration

- [-] ← [i] signaling pathway
  - [+] ← [i] carbohydrate mediated signaling
  - [+] ← [i] cell surface receptor linked signaling pathway
  - [+] ← [i] chemoreceptor signaling pathway involved in regulation of blood pressure
    - ← [i] defense response signaling pathway, resistance gene-dependent
    - ← [i] defense response signaling pathway, resistance gene-independent
  - [+] ← [i] hormone-mediated signaling pathway
    - ← [i] hydrogen peroxide mediated signaling pathway
  - [+] ← [i] immune response-regulating signaling pathway
  - [+] ← [i] intracellular signaling pathway
  - [+] ← [i] jasmonic acid mediated signaling pathway
  - [+] ← [i] lipoprotein mediated signaling
  - [+] ← [i] negative regulation of signaling pathway
  - [+] ← [i] nitric oxide mediated signal transduction
  - [+] ← [i] osmosensory signaling pathway
  - [+] ← [i] positive regulation of signaling pathway
  - [+] ← [i] red or far-red light signaling pathway
  - [+] ← [i] regulation of signaling pathway
  - [+] ← [i] salicylic acid mediated signaling pathway
  - [+] ← [i] sphingolipid signaling pathway

- [-] ← [i] signaling process
  - [+] ← [i] consequence of signal transmission
  - [-] ← [i] generation of a signal involved in cell-cell signaling
    - [+] ← [i] creation of an inductive signal
    - [+] ← [i] signal release
  - [+] ← [i] initiation of signal transduction
  - [+] ← [i] receptor recycling
  - [+] ← [i] regulation of signaling process
  - [+] ← [i] signal release
- [-] ← [i] signal transmission
  - [+] ← [i] signal release
  - [+] ← [i] signal transduction
    - ← [i] signal transmission via air
    - ← [i] signal transmission via conformational transition
    - [+] ← [i] signal transmission via diffusible molecule
    - [+] ← [i] signal transmission via phosphorylation event
      - ← [i] signal transmission via transcytosis
    - [+] ← [i] signal transmission via vascular system
    - [+] ← [i] transmission of nerve impulse
    - [+] ← [i] two-component signal transduction system (phosphorelay)
  - [+] ← [i] termination of signal transduction

'signaling pathway' & 'signaling process' are siblings

'signaling pathway' and 'signal transduction' aren't connected

# PROPOSAL

- ← signaling
  - ← cell-cell signaling
    - ← extracellular matrix-cell signaling
    - ← generation of a signal involved in cell-cell signaling
      - ← creation of an inductive signal
      - ← signal maturation NEW
        - ← epidermal growth factor ligand processing
          - ← patched ligand maturation
        - ← signal release
      - ← motogenic signaling initiating cell movement in cerebral cortex
      - ← motogenic signaling involved in interneuron migration from the subpallium to the cortex
      - ← motogenic signaling involved in postnatal olfactory bulb interneuron migration
    - ← multi-organism signaling NEW
    - ← multicellular organismal signaling NEW
    - ← endocrine signaling NEW
    - ← transmission of nerve impulse
    - ← negative regulation of signaling
    - ← positive regulation of signaling
    - ← regulation of signaling
  - ← signal transduction
    - ← carbohydrate mediated signaling pathway
    - ← cell surface receptor linked signaling pathway
    - ← chemoreceptor signaling pathway involved in regulation of blood pressure
      - ← chloroplast-nucleus signaling pathway
      - ← defense response signaling pathway, resistance gene-dependent
      - ← defense response signaling pathway, resistance gene-independent
    - ← DNA replication checkpoint
    - ← ER-nucleus signaling pathway
    - ← hormone-mediated signaling pathway
      - ← hydrogen peroxide mediated signaling pathway
    - ← immune response-regulating signaling pathway
    - ← initiation of signal transduction
    - ← intracellular receptor mediated signaling pathway
    - ← intracellular signal transduction
    - ← jasmonic acid mediated signaling pathway
    - ← lipoprotein mediated signaling
    - ← meiotic cell cycle checkpoint
    - ← mitochondria-nucleus signaling pathway
    - ← mitotic cell cycle checkpoint
    - ← negative regulation of signal transduction
      - ← neuronal signal transduction
    - ← nitric oxide mediated signal transduction
    - ← osmosensory signaling pathway
    - ← phototransduction
    - ← positive regulation of signal transduction
      - ← red or far-red light signaling pathway
    - ← regulation of conjugation with cellular fusion by signal transduction
    - ← regulation of floral organ abscission by signal transduction
    - ← regulation of signal transduction
    - ← salicylic acid mediated signaling pathway
    - ← signal transducer activity
      - ← signal transduction involved in conjugation with mutual genetic exchange
      - ← signal transduction involved in filamentous growth
    - ← signal transduction involved in regulation of gene expression
      - ← signal transduction via conformational change
      - ← signal transduction via phosphorylation event
    - ← sphingolipid signaling pathway
    - ← termination of signal transduction
    - ← two-component signal transduction system (phosphorelay)

NEW TERMS

REHOUSED

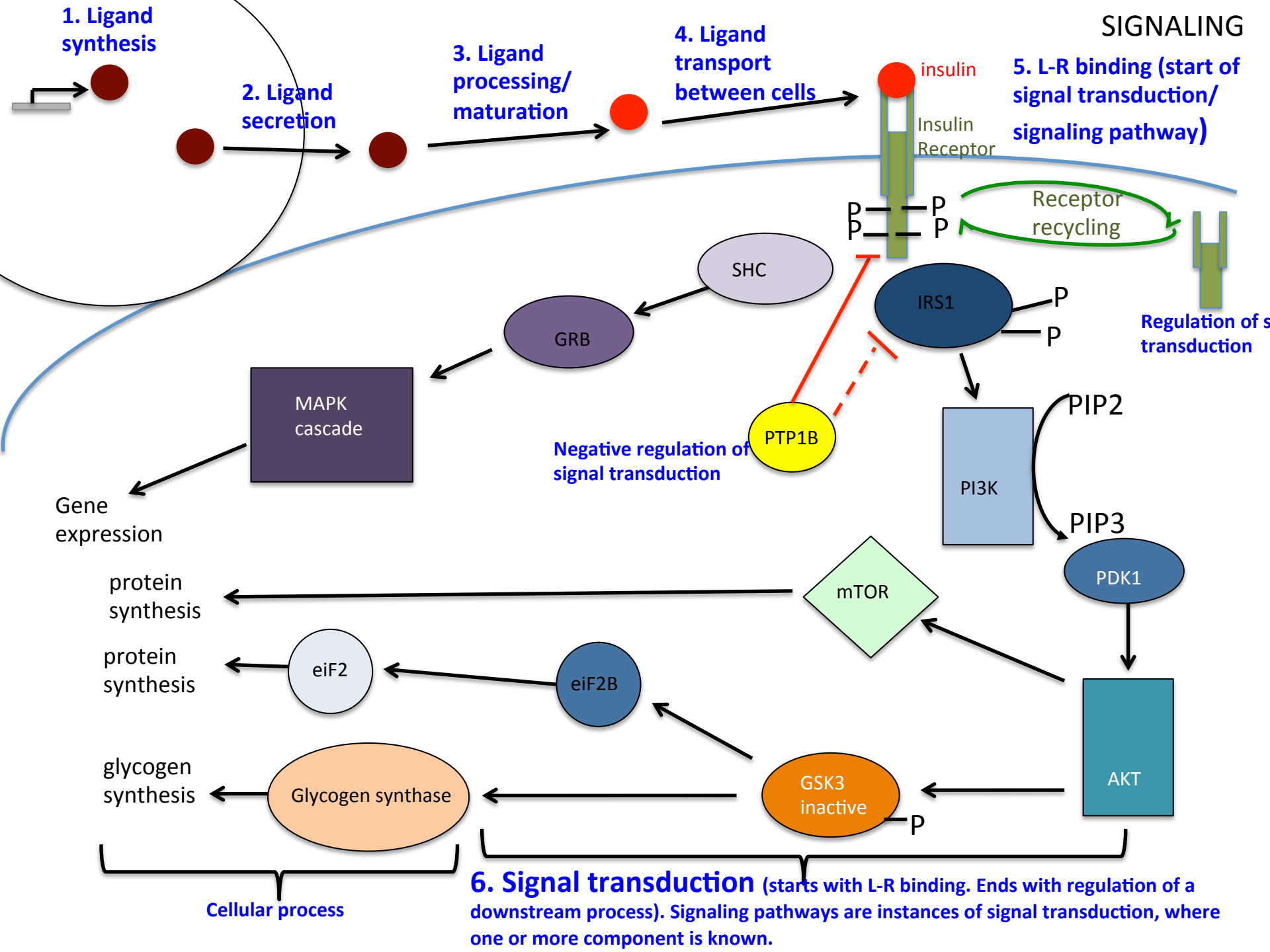
RENAMED

No generic 'pathway' term, but all the instances of the pathways are under signal transduction  
(all pathway terms will be given the synonym 'x signal transduction pathway')

Ligands are part of a signaling pathway, and can be annotated to 'signal transduction'.

The first step in a pathway would be ligand-receptor binding (or in case of light receptors, light being received by the receptor).

A pathway would end with regulation of a process.



# SUMMARY OF CHANGES

## NEW TERMS:

multi-organism signaling ; GO:NEW

The transfer of information between living organisms.

synonym: signaling with other organism

synonym: signaling between organisms

synonym: multi-organism signalling

GOC:go\_curators

is\_a: multi-organism process ; GO:0051704

is\_a: signaling ; GO:0023052

**NB: This term is intended to replace the obsoleted term 'signal transmission via air ; GO:0023070'.**

multicellular organismal signaling ; GO:NEW

The transfer of information occurring at the level of a multicellular organism.

GOC:go\_curators

is\_a: multicellular organismal process ; GO:0032501

is\_a: signaling ; GO:0023052

*part\_of child*: endocrine signaling ; GO:NEW

*is\_a child*: transmission of nerve impulse ; GO:0019226

endocrine signaling ; GO:NEW

Signaling between cells where the a cell producing an endocrine hormone acts on a distant receiving cell. The endocrine hormone is transported via the circulatory system (via blood, lymph or intercellular fluid) so that remote regions of an organism can be reached.

is\_a: cell-cell signaling ; GO:0007267

part\_of: endocrine process ; GO:50886

part\_of: multicellular organismal signaling ; GO:NEW

*part\_of child*: endocrine hormone secretion ; GO:0060986

ISBN:3527303782

ISBN:0199264678

**NB: This term is intended to replace the obsoleted 'signal transmission via vascular system ; GO:0023066' terms, and its children.**

**Q: Can this be used for plants? (ISBN:0199264678 suggests it can)**

**Q: Do we want a split between endocrine/paracrine/autocrine signaling in GO?**

## NEW TERMS (CONT)

paracrine signaling ; GO:NEW

The transfer of information between cells where the signal producing cell is in the vicinity of the receiving cell, and the signal reaches the receiving cell by passive diffusion.

ISBN:3527303782

is\_a: cell-cell signaling ; GO:0007267

NB: This term is intended to replace the obsoleted term 'signal transmission via diffusible molecule ; GO:0023017'.

NB: Will remove 'paracrine signaling' as synonym of 'cell-cell signaling ; GO:0007267'.

signal maturation; GO:NEW

Any process leading to the attainment of the full functional capacity of a signal. A signal is a physical entity or change in state that is used to transfer information to trigger a response.

Related synonym: ligand maturation

part\_of: generation of a signal involved in cell-cell signaling ; GO:0003001

is\_a: cellular process ; GO:0009987

is\_a child: epidermal growth factor ligand processing ; GO:0007174

is\_a child: patched ligand maturation ; GO:0007225

## OBSOLETIONS:

signal transmission ; GO:0023060 (0 direct annotations)

Comment: This term was made obsolete because it was an unnecessary grouping term.  
consider: signaling ; GO:0023052

signal transmission via air ; GO:0023070 (0 annotations)

Comment: This term was made obsolete because the meaning of the term is ambiguous.  
consider: multi-organism signaling ; GO:NEW

signal transmission via diffusible molecule ; GO:0023017 (0 direct annotations)

Comment: This term was made obsolete because the meaning of the term is ambiguous.  
consider: paracrine signaling ; GO:NEW

signaling via chemical mediator ; GO:0023044 (0 direct annotations)

Comment: This term was made obsolete because the meaning of the term is ambiguous.  
consider: signaling ; GO:0023052  
consider: signal transduction ; GO:0007165

(NB: although 'chemical' isn't well defined in GO at the moment- GOCHE will fix this).

signaling via ionic flux ; GO:0023040 (0 direct annotations)

Comment: This term was made obsolete because the meaning of the term is ambiguous.  
consider: signaling ; GO:0023052  
consider: signal transduction ; GO:0007165

signaling via lipid mediator ; GO:0023043 (0 direct annotations)

Comment: This term was made obsolete because the meaning of the term is ambiguous.  
consider: signaling ; GO:0023052  
consider: phosphoinositide 3-kinase cascade ; GO:0014065

signaling via protein/peptide mediator ; GO:0023042 (0 annotations)

Comment: This term was made obsolete because the meaning of the term is ambiguous.  
consider: signaling ; GO:0023052  
consider: signal transduction ; GO:0007165

NB: Obsoleted because most signaling molecules are proteins or peptides.

T cell activation of signal transmission via diffusible molecule ; GO:0023018 (0 annotations)

Comment: This term was made obsolete because the meaning of the term is ambiguous.  
consider: signaling ; GO:0023052  
consider: signal transduction ; GO:0007165  
consider: paracrine signaling ; GO:NEW

The signal transmission terms are up for obsolescence because they are ambiguous. They cover everything from signal release through to the end of signal transduction in the receiving cell.

From the existing terms, it's unclear whether the ligand can be annotated, and whether the 'mediators' are ligands or downstream signaling molecules.

If you know what step a gene product is involved in, you can use a more specific term. If not, you can use the top level 'signaling' term.

The new 'endocrine signaling' and 'paracrine signaling' terms were created to replace some of the transmission terms.

## OBSOLETIONS (CONT):

signal transmission via transcytosis ; GO:0023062

transcytosis involved in signal transduction ; GO:0023062

The directed movement of endocytosed material through the cell and its exocytosis from the plasma membrane at the opposite side, that contributes to signal transduction.

consider: transcytosis ; GO:0045056

**NB: The current term isn't connected to 'transcytosis ; GO:0045056'.**

signal transmission via vascular system ; GO:0023066 (0 annotations)

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

consider: endocrine signaling ; GO:NEW

consider: vascular transport ; GO:0010232

signal transmission via blood ; GO:0023065 (0 annotations)

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

consider: endocrine signaling ; GO:NEW

consider: vascular transport ; GO:0010232

signal transmission via lymphatic system ; GO:0023067 (0 annotations)

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

consider: endocrine signaling ; GO:NEW

consider: vascular transport ; GO:0010232

signal transmission via phloem ; GO:0023068 (0 annotations)

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

consider: endocrine signaling ; GO:NEW

consider: phloem transport ; GO:0010233

signal transmission via xylem ; GO:0023069

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

consider: endocrine signaling ; GO:NEW

consider: vascular transport ; GO:0010232

consequence of signal transmission ; GO:0023050

Comment: This term was made obsolete because the term is no longer needed.

**NB: With the x signaling pathway terms involved in x, and regulation of y by 'x signaling pathway' terms, the consequence terms are not required (and don't make ontological sense).**

**signal initiation by chemical mediator ; GO:0023047**

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

consider: initiation of signal transduction ; GO:0023036

## MERGES:

MERGED behavioral signaling ; GO:0023032

into:

behavioral interaction between organisms ; GO:0051705

[and removed the signaling parent]

MERGED signaling pathway ; GO:0023033

into:

signal transduction ; GO:0007165

MERGED regulation of signaling pathway ; GO:0035466

into:

regulation of signal transduction ; GO:0009966

MERGED negative regulation of signaling pathway ; GO:0035467

into:

negative regulation of signal transduction ; GO:0009968

MERGED positive regulation of signaling pathway ; GO:0035468

into:

positive regulation of signal transduction ; GO:0009967

MERGED signaling process ; GO:0023046

into:

signaling ; GO:0023052

MERGED intracellular signaling pathway ; GO:0023034

Into:

intracellular signal transduction ; GO:0035556

New synonym: secondary signal transduction

Moved the following children of GO:0023034 to be direct children of 'signal transduction ; GO:0007165'

GO:0010019 : chloroplast-nucleus signaling pathway

GO:0006984 : ER-nucleus signaling pathway

GO:0030522 : intracellular receptor mediated signaling pathway

GO:0031930 : mitochondria-nucleus signaling pathway



**MOVED:**

MOVED: transmission of nerve impulse ; GO:0019226

WAS: child of signal transmission ; GO:0023060

NOW: child of multicellular organismal signaling ; GO:NEW

MOVED: two-component signal transduction system (phosphorelay) ; GO:0000160

WAS: is\_a child of signal transmission ; GO:0000160

NOW: is\_a child of signal transduction ; GO:0000160

MOVED: patched ligand maturation ; GO:0007225

WAS: part\_of smoothed signaling pathway ; GO:0007224

NOW: part\_of regulation of smoothed signaling pathway ; GO:0045880

NOW: is\_a child of 'signal maturation ; GO:NEW'

**NB: moved under 'regulation of signaling pathway' because the signaling pathway begins with receptor-ligand binding, and this step is upstream.**

MOVED: termination of signal transduction ; GO:0023021 (0 annotations)

WAS: is\_a signaling process

NOW: is\_a negative regulation of signal transduction ; GO:0009968

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**RENAMED:**

(keeping old names as synonyms)

RENAMED: regulation of signaling process ; GO:0023051

TO: regulation of signaling ; GO:0023051

RENAMED: negative regulation of signaling process ; GO:0023057

TO: negative regulation of signaling ; GO:0023057

RENAMED: positive regulation of signaling process ; GO:0023056

TO: positive regulation of signaling ; GO:0023056

RENAMED: signal transmission via phosphorylation event ; GO:0023014

TO: signal transduction via phosphorylation event ; GO:0023014

[and rehoused under signal transduction]

RENAMED: regulation of gene expression as a consequence of signal transmission ; GO:0023019

TO: signal transduction involved in regulation of gene expression ; GO:0023019

WAS: is\_a regulation of gene expression ; GO:0010468

NOW: part\_of regulation of gene expression ; GO:0010468

[and rehoused under signal transduction]

RENAMED: signal transmission via conformational change ; GO:0023045

TO: signal transduction via conformational transition ; GO:0023045

REDEFINED FROM: The process whereby a signal is conveyed via a conformational transition

TO: The process whereby a signal is passed on within a cell by triggering a conformational change in the molecule that is receiving the signal.

[and rehoused under signal transduction]

## REDEFINED

### **signal transduction ; GO:0007165**

#### *FROM:*

The process whereby a signal is converted into a form where it can ultimately trigger a change in the state or activity of a cell. A signal is a physical entity or change in state that is used to transfer information in order to trigger a response.

#### *TO:*

The process whereby a signal is passed across a cell to trigger a change in the activity or state of a cell. Signal transduction begins with reception of a signal and ends with regulation of a downstream process. Signal transduction covers signaling from receptors located on the surface of the cell, and signaling via molecules located within the cell. For signaling between cells, signal transduction is restricted to events at and within the receiving cell.

Comment: signal transduction is defined broadly to include all events from a ligand interacting with a receptor, to a response being triggered. A change in form of the signal in every step is not necessary.

### **signal transducer activity ; GO:0004871**

#### *FROM:*

Converts a signal into a form where it can be further conveyed, or can trigger a change in the state or activity of a cell. A signal is a physical entity or change in state that is used to transfer information in order to trigger a response.

Comments: Ligands do NOT have the molecular function 'signal transducer activity'.

#### *TO:*

Conveys a signal across a cell to trigger a change in cell function or state. A signal is a physical entity or change in state that is used to transfer information in order to trigger a response.

Comments: Ligands do not have the molecular function 'signal transducer activity'.

# PROPOSAL FOR 'INVOLVED IN' SIGNALING TERMS

- signaling pathways end with regulation of a downstream process (but do not include the downstream process itself).

To make this clearer in the ontology, we propose changing:

- X signaling pathway involved in y process

TO:

- X signaling pathway involved in REGULATION OF y process
- Where 'regulation of y process' terms already exist, I will move the signaling term.
- Where 'regulation of y process' term does NOT exist, I will create one, then move the signaling term.

E.g.

- BMP signaling pathway involved in forebrain neuron fate commitment
- Wnt receptor signaling pathway involved in somitogenesis
- transforming growth factor beta receptor signaling pathway involved in determination of left/right asymmetry

TO:

- BMP signaling pathway involved in regulation of forebrain neuron fate commitment
- Wnt receptor signaling pathway involved in regulation of somitogenesis
- transforming growth factor beta receptor signaling pathway involved in regulation of determination of left/right asymmetry

Q: Any terms that shouldn't get a 'regulation' child?

TIMING:

I'd like to do the commits this week (w/c January 10<sup>th</sup>) and next week (w/c January 17<sup>th</sup>) so they're in place for the signaling workshop mid-February.

# regulation of regulation....

regulation of BMP signaling pathway involved in heart jogging

regulation of canonical Wnt receptor signaling pathway involved in controlling pancreatic B cell proliferation

regulation of canonical Wnt receptor signaling pathway involved in neural crest cell differentiation

regulation of canonical Wnt receptor signaling pathway involved in neural plate anterior/posterior pattern formation

regulation of cell adhesion involved in heart morphogenesis by non-canonical Wnt signaling pathway

regulation of coreceptor activity involved in epidermal growth factor receptor signaling pathway

regulation of Notch signaling pathway involved in heart induction

regulation of octopamine signaling pathway involved in response to food

regulation of transforming growth factor beta receptor signaling pathway involved in determination of lateral mesoderm left/right asymmetry

regulation of transforming growth factor beta receptor signaling pathway involved in primitive streak formation

regulation of transforming growth factor receptor beta signaling pathway involved in determination of left/right asymmetry

regulation of Wnt receptor signaling pathway involved in digestive tract morphogenesis

regulation of Wnt receptor signaling pathway involved in dorsal/ventral axis specification

regulation of Wnt receptor signaling pathway involved in heart development

It would mean 'regulation of x signaling pathway involved in regulation of y process for some terms.....

## OUTSTANDING QUESTIONS AT THIS STAGE

1. Does it make sense to have the endocrine/paracrine/autocrine split?
  - The autocrine term already exists: autocrine signaling ; GO:0035425
  - The endocrine and paracrine terms were created to replace the 'signal transmission' terms that are up for obsolescence.
2. Can endocrine signaling be used in plants?
  - ISBN:0199264678 suggests it can, but we're keen to hear from curators.