

Improving representation of biological responses

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Environment affects cells

- [-] **I** **GO:0050896 : response to stimulus [35839 gene products]** 
- [+] **I** GO:0007610 : behavior [3985 gene products]
- [+] **I** GO:0051716 : cellular response to stimulus [10559 gene products]
- [+] **I** GO:0051606 : detection of stimulus [2028 gene products]
- [+] **I** GO:0006955 : immune response [4117 gene products]
- [+] **R** GO:0048585 : negative regulation of response to stimulus [670 gene products]
- [+] **G** GO:0048584 : positive regulation of response to stimulus [1352 gene products]
- [+] **R** GO:0048583 : regulation of response to stimulus [2928 gene products]
- [+] **I** GO:0009628 : response to abiotic stimulus [4419 gene products]
- [+] **I** GO:0014823 : response to activity [76 gene products]
- [+] **I** GO:0009607 : response to biotic stimulus [4800 gene products]
- [+] **I** GO:0042221 : response to chemical stimulus [15182 gene products]
- [+] **I** GO:0002021 : response to dietary excess [46 gene products]
- [+] **I** GO:0009719 : response to endogenous stimulus [3063 gene products]
- [+] **I** GO:0009605 : response to external stimulus [4897 gene products]
- [+] **I** GO:0014854 : response to inactivity [6 gene products]
- [+] **I** GO:0014874 : response to stimulus involved in regulation of muscle adaptation [9 gene products]
- [+] **I** GO:0006950 : response to stress [19906 gene products]

GO definition of 'response to'

- Response to stimulus:
A change in state or activity of a cell or an organism (in terms of movement, secretion, enzyme production, gene expression, etc.) as a result of a stimulus

Challenges with responses

1. Definition is very wide
2. Specific terms can be very informative
3. Not all groups understand the definition the same way, leading to inconsistencies
4. Expression experiments are sometimes incorrectly annotated to IDA



1. Definition is very wide

Concern about high level terms:

- GO:0050896 : response to stimulus
- GO:0051716 : cellular response to stimulus
- GO:0009628 : response to abiotic stimulus
- GO:0009607 : response to biotic stimulus
- GO:0042221 : response to chemical stimulus
- GO:0009719 : response to endogenous stimulus
- GO:0009605 : response to external stimulus
- GO:0006950 : response to stress

What stimulus?

What stress?

- [-] I GO:0006950 : response to stress [19906 gene products] 
- [+] I GO:0033554 : cellular response to stress [7738 gene products]
- [+] I GO:0006952 : defense response [5795 gene products]
- [+] I GO:0033555 : multicellular organismal response to stress [162 gene products]
- [+] I GO:0003299 : muscle hypertrophy in response to stress [4 gene products]
- [-] I GO:0009271 : phage shock [17 gene products]
- [-] P GO:0010610 : regulation of mRNA stability involved in response to stress [6 gene products]
- [+] R GO:0080134 : regulation of response to stress [1717 gene products]
- [+] I GO:0034059 : response to anoxia [11 gene products]
- [-] I **GO:0009409 : response to cold [506 gene products]** 

Stats about high level terms

- GO:0050896 : response to stimulus ~ 150 direct EXP
- GO:0051716 : cellular response to stimulus ~ 5 direct EXP
- GO:0009628 : response to abiotic stimulus ~ 30 direct EXP
- GO:0009607 : response to biotic stimulus ~ 15 direct EXP
- GO:0042221 : response to chemical stimulus ~ 150 direct EXP
- GO:0009719 : response to endogenous stimulus
- GO:0009605 : response to external stimulus ~ 10 direct EXP
- GO:0006950 : response to stress ~ 300 direct EXP

Proposal 1

Quality Control check: High level 'response to' terms should not directly be used for annotation

2. Specific terms can be very informative

- We want to keep 'response to' terms, and annotate to the most specific ones, e.g.:
 - response to insulin stimulus
 - cell cycle arrest in response to pheromone
 - pigment accumulation in response to UV light
 - regulation of translation in response to stress



Proposal 2

Encourage the use of granular terms for 'responses' (update documentation)

3. Inconsistencies in RT annotations

Groups either:

- only capture mediators
- capture targets (often by IEP)
- annotate mediators by IDA even though the experiment is an IEP

Proposal 3

Update 'response to' definition

- Current: A change in state or activity of a cell or an organism (in terms of movement, secretion, enzyme production, gene expression, etc.) as a result of a stimulus.

- Proposed: **ANY PROCESS THAT RESULTS IN** a change in state or activity of a cell or an organism (in terms of movement, secretion, enzyme production, gene expression, etc.) as a result of a stimulus.

We need to distinguish between 'targets' and 'mediators' of responses

- Response to stimulus:
A change in state or activity of a cell or an organism (in terms of movement, secretion, enzyme production, gene expression, etc.) as a result of a stimulus
- ... do we want to annotate all **targets** of the response, or the biological molecules **mediating** the response?

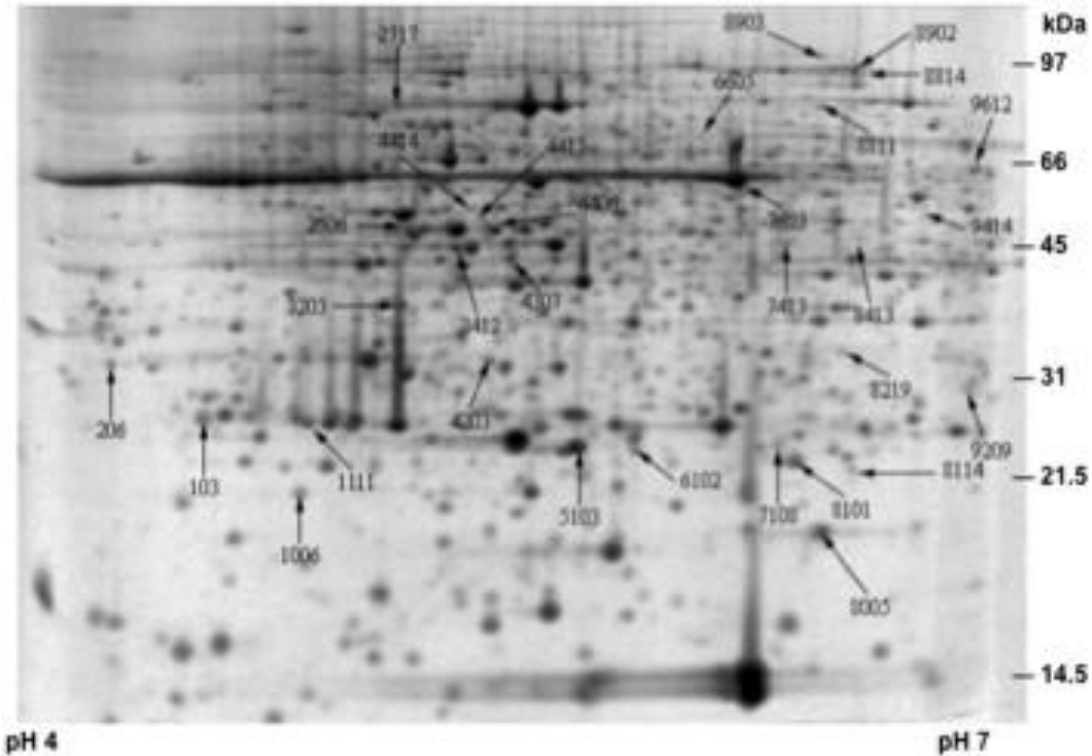
Example of targets: response to cadmium ion

A 1 week exposure to 1 μM Cd resulted in increased expression of 8 proteins

- Four of these proteins belong to the group related to oxidative stress: pathogenesis-related protein 5 (SSP-103), copper homeostasis factor (copper chaperone – CCH; SSP-1006), glutamine synthetase (SSP-4415) and stress-inducible protein (SSP-8219).
- two proteins are involved in the protein metabolism (a putative aspartic protease (SSP-206) and a putative 60S acidic ribosomal protein (SSP-3203)).

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Results



Sypro-stained 2-DE reference gel of *Arabidopsis thaliana* leaf protein. Identified spots that respond to Cd exposure are indicated by an arrow

Would you annotate the 8 proteins to 'response to cadmium ion'?

Survey results

No	42.9%	
Yes – IDA	7.1%	1
Yes – IMP	7.1%	1
Yes – IEP	42.9%	6
Yes - other evidence code	0.0%	

Concern about Microarrays (and 2D SDS PAGE)

- Not everything up-regulated by a stimulus plays a role in the DNA damage response
- Microarrays can be a nice way to test a mediator of a response:
e.g.: KO in gene A is unable to induce genes involved in a response to stimulus A
- Response to stimulus X, IMP
- Proposal 4:

Proposal 4

Microarray 'hits' should not be annotated to response to terms

Summary

1. High level 'response to' terms should not directly be used for annotation
2. Encourage the use of granular terms for 'responses' (update documentation)
3. Update definition of response to terms to "ANY PROCESS THAT CAUSES a change in state or activity of a cell or an organism (in terms of movement, secretion, enzyme production, gene expression, etc.) as a result of a stimulus"
4. Microarray 'hits' should not be annotated to response to terms