

Datums: a knowledge base and representation system for experimental findings concerning cellular response to stimuli.



Merrill Knapp, Tim McCarthy, Carolyn Talcott

SRI International, Menlo Park, CA. USA

What is a datum?

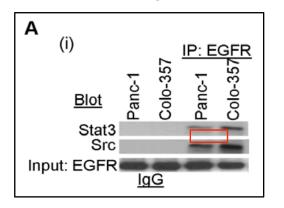
- a formal, computable representation of experimental findings
- a manageable chunk of information, sufficient to unambiguously describe an experimental finding, expressed using concepts readily understood by biologists

Two types of Datum

- a **state datum** describes the state of something (protein, gene) in a defined system
 - present/absent, active/inactive
 - a protein-protein interaction
- a **change datum** describes the change in the state of something in a system in response to a stimulus.

An Example of a State Datum

Stat3[Ab] copptby[WB] EgfR[Ab] is detectable cells: PANC1 in BMS source: 21573184-Fig-1a



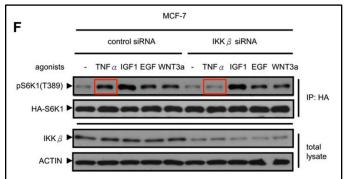
Information that this datum supplies:

- (1) PANC1 cells growing in medium with serum express endogenous Stat3 and EgfR.
- (2) Endogenous Stat3 and EgfR can coprecipitate in PANC1 cells growing in medium with serum.

An Example of a Change Datum with an Extra

xS6k1[tAb]IP phos(T412)[phosAb] is increased irt Tnf (30 min) cells: MCF7<xS6k1> in BMLS reqs: Ikk2 [RNAi]

source: 17693255-Fig-3f



Information that this datum supplies:

- (1) The phosphorylation of expressed S6k1 on T389 is increased in response to the addition of TNF to quiescent MCF7 cells for 30 min.
- (2) The response described in (1) is abrogated by removal of Ikk2 by RNAi.
- (3) Quiescent MCF7 cells overexpressing S6k1 in medium without serum express endogenous Ikk2.

Using Datums as input to design of Experiments

Q1: What proteins have been shown to be directly phosphorylated by Mekk1?

Result: Stat3, Mek1, Erk2, and Mkk4

Q2: Is expressed Ikk2 constitutively active? **Result**: Yes

Q3: What proteins have been shown to be required for the activation of Jnk kinase activity in response to IL1? **Result**: Irak1, Irak4, Mkk7, Myd88, Tak1, Traf6

Q4: What proteins have been shown to NOT be required for the activation of Jnk kinase activity in response to IL1? **Result**: Ripk1, Tab2, Traf2, Traf5,

Q5: How long should I treat cells with IL1 to maximize Jnk phosphorylation?

Result: between 10 and 15 minutes

Q6: What stimuli turn on Jun-gene transcription? **Result**: Egf, Ngf, PMA, IL2, Serum. Lps, Hypoxia, IL3, and UV

Q7: Do untreated HELA cells express endogenous Myc? **Result**: Yes

Q8: Where is endogenous Atf2 located in untreated cells? **Result**: in the nucleus and cytoplasm

Q9: What proteins have been shown to coprecipitate with Trka?

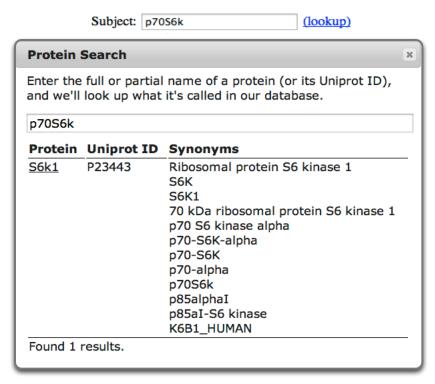
Result: Crk1, CrkL, Gab2, Ngf, Frs2, Sh2b1, Grb2, Abl1, Csk. Rgs19ip1, Shc1, Matk, Arms, Pik3r1, Plcg1, Rgs19, RasGrf1, Trpv1

Searching the Datum Knowledge Base

http://pl.csl.sri.com/datumkb.html

A searchable database of more than 39k datums collected as evidence for models of signal transduction in response to external stimuli

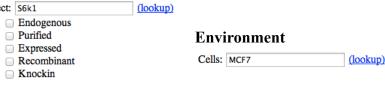
Protein Lookup



Sample Query

What proteins are required for an increase in phosphorylation of S6k1 on T412 in response to Tnf treatment in MCF7 cells?





Extras ✓ Effect: Phosphorylation Inhibited by: (lookup) □ Total Enhanced by: (lookup) S-only Reversed by: (lookup) □ T-only ST-only Unaffected by: (lookup) Requires: (lookup) Site: T412 Does not require:

Treatment No Treatment

✓ Addition of Something to Cell Supernatants

Something specific: Tnf (lookup)

Protein Expression

Expressed Protein 1: (lookup)

Expressed Protein 2: (lookup)

Protein Removal

Removed Protein 1: (lookup)

Removed Protein 1: (lookup)

Removed Protein 2: (lookup)

Stress
Specfic stress: (lookup)

Addition of Something to Cell Free Reaction
Something specific: (lookup)

Sample Query Result: Ikk2, Nemo, and Mtor

Change

Increased

Decreased

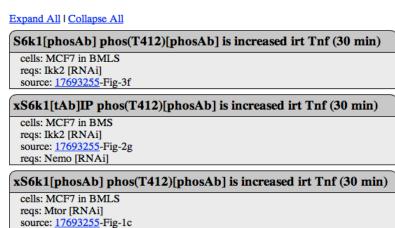
Detectable

Unchanged

Undetectable

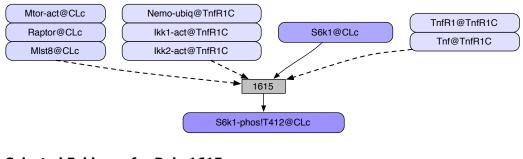
Screen Shot of Datum Result Page

Showing 3 of 3 matching datums



Using Datums as evidence for rules in signal transduction networks

Rule 1615 from the Tnf Signaling Network



Selected Evidence for Rule 1615

Requirement for Ikk2

xS6k1[tAb]IP phos(T412)[phosAb] is increased irt Tnf (30 min) cells: MCF7<xS6k1> in BMLS reqs: Ikk2 [RNAi] source: 17693255-Fig-3f

Requirement for Mtor

xS6k1[phosAb] phos(T412)[phosAb] is increased irt Tnf (30 min) cells: MCF7<xS6k1> in BMLS reqs: Mtor [RNAi] source: 17693255-Fig-1c

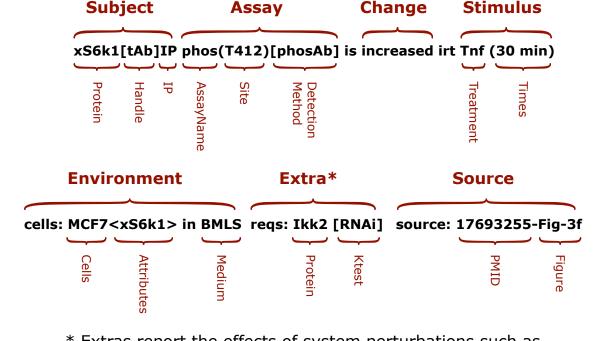
Requirement for Nemo

xS6k1[tAb]IP phos(T412)[phosAb] is increased irt Tnf (30 min) cells: MCF7<xS6k1> in BMS reqs: Nemo [RNAi] source: 17693255-Fig-2g

Other Possible Uses for Datums

- a notebook to record and organize results of literature search
- input for computing influence diagrams
- a way to categorize experimental results stored in databases

What are the parts of a datum?



* Extras report the effects of system perturbations such as knockout or mutation of a protein or addition of inhibitors.

Under the Hood

