



SELVENTA™

Analyze. Accelerate. Clarify.

Reverse Causal Reasoning (RCR)

Analysis of Omics Data Using Reverse Causal Reasoning (RCR) in an Integrated Analysis Environment

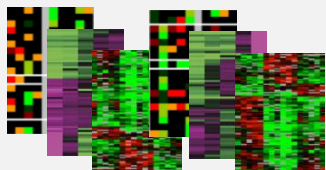
Dexter Pratt, VP Innovation, Selventa

Tech Talk 3

CSHALS 2011

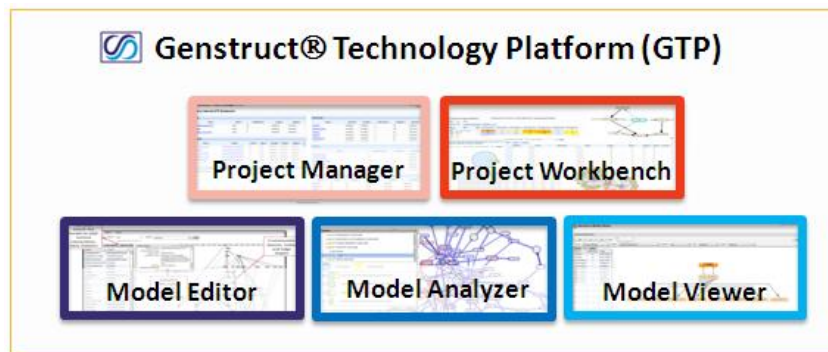
February 24th, 2011

RCR Overview

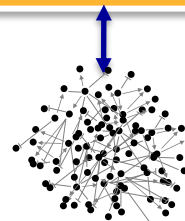


Complex Biological Data

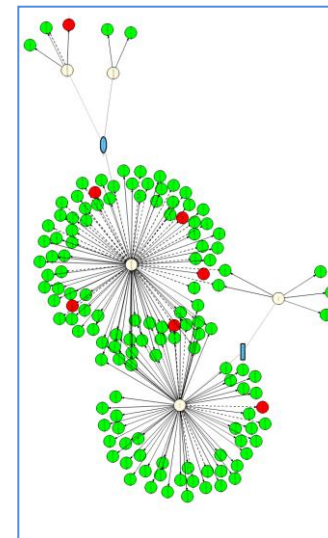
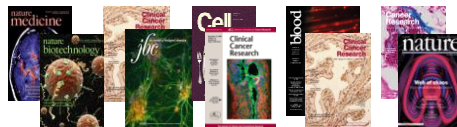
transcriptomic, RNA-Seq, proteomic, metabolomic, etc.



BEL Enabled Applications

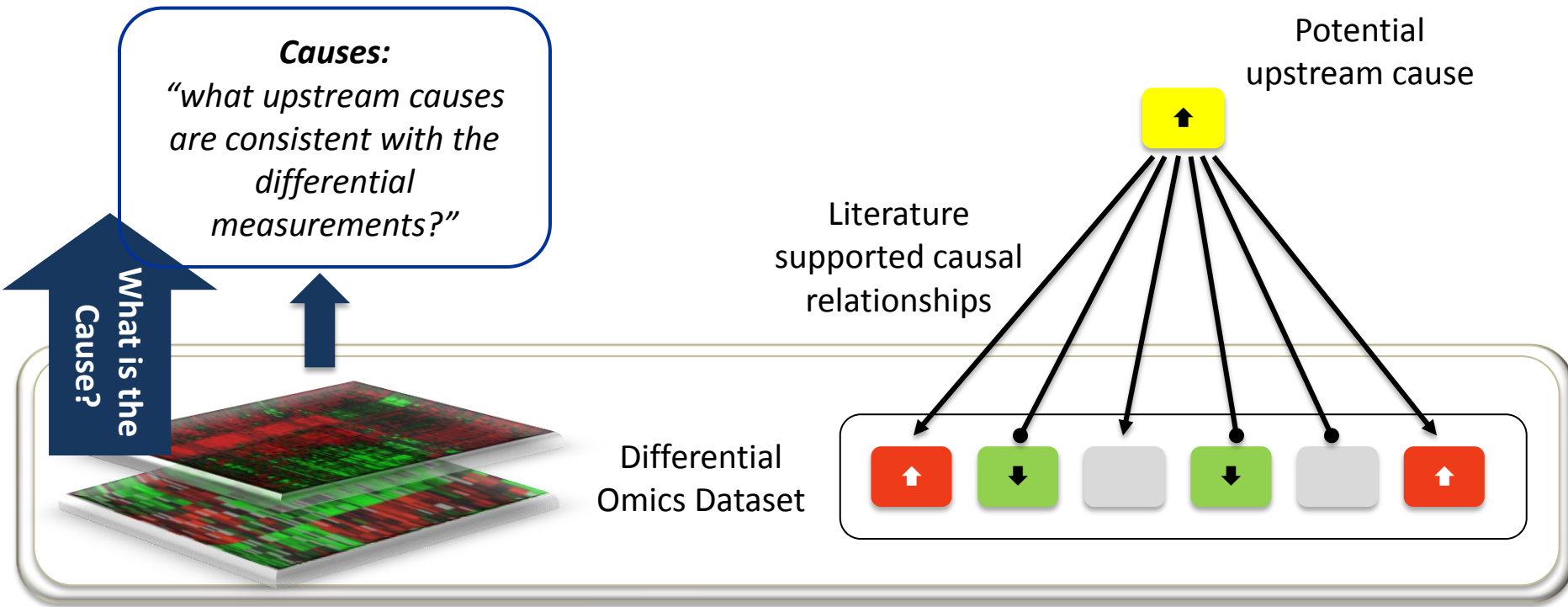


Structured Knowledge in the BEL Framework

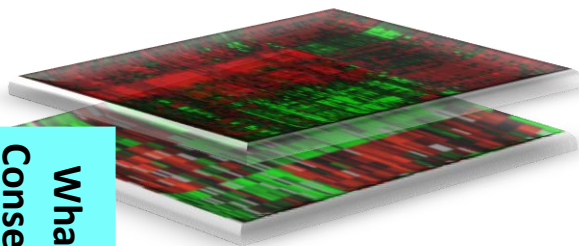


Understanding at the level of process and mechanism

Knowledge based Evaluation of Potential Causes



Comparison to Pathway Analysis



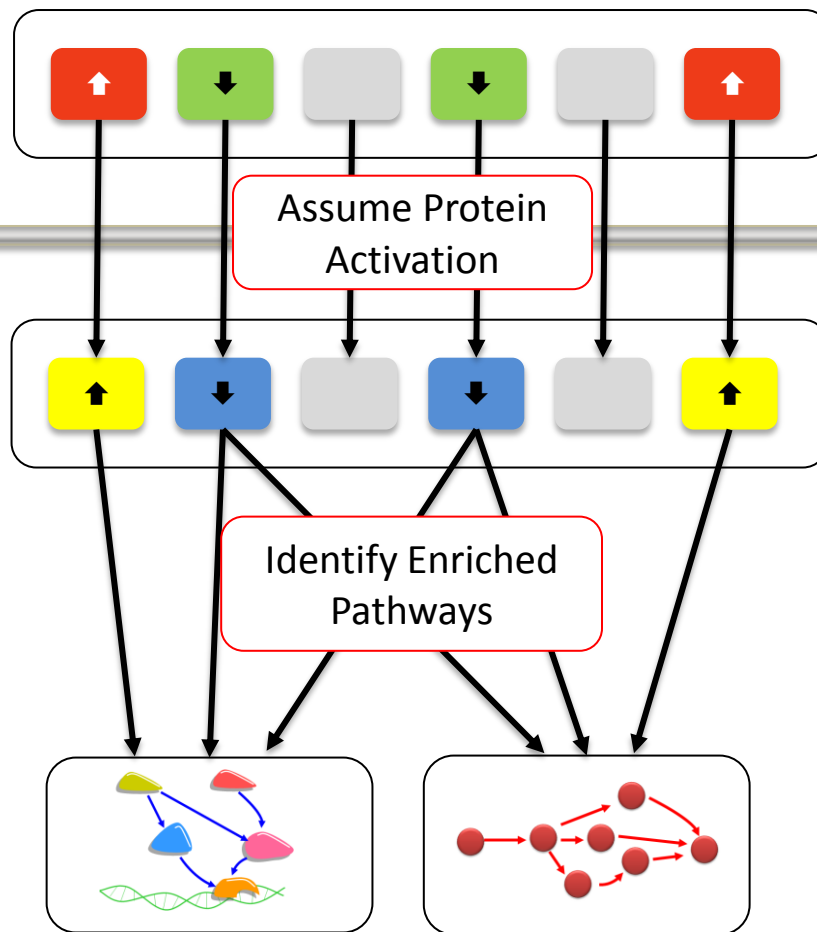
Differential RNA expression

What is the
Consequence?

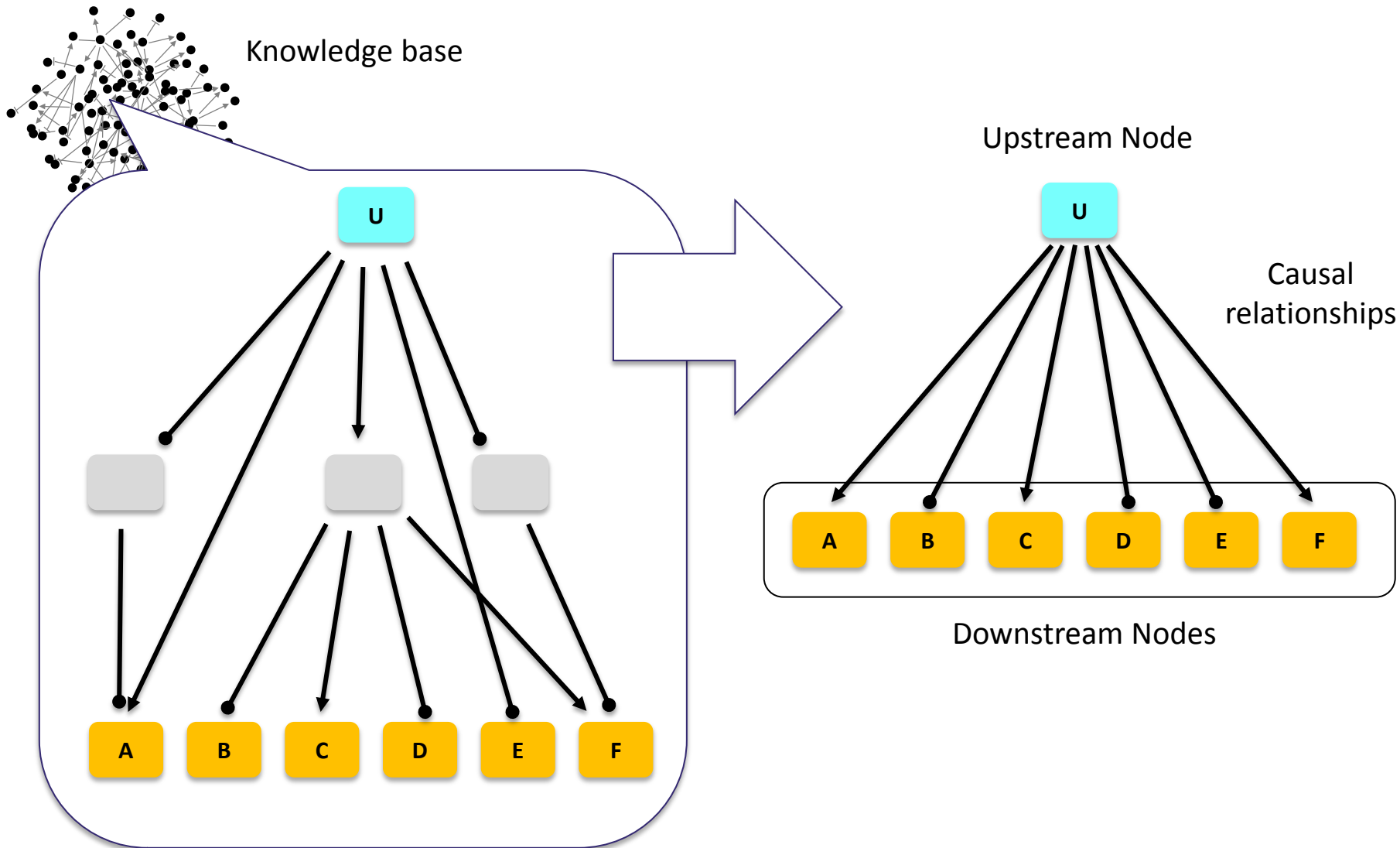
What is the
Consequence?

Pathway Analysis

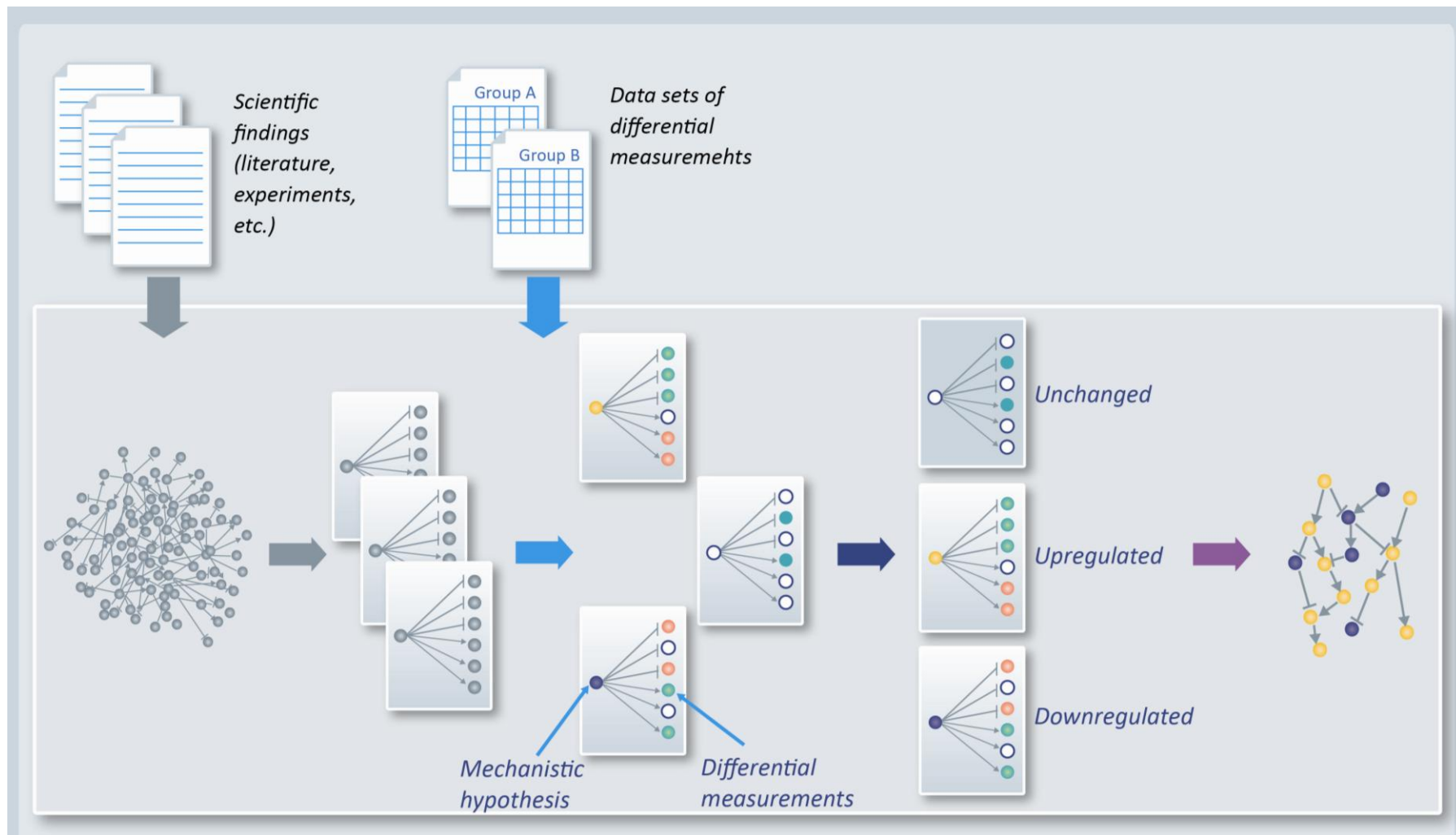
Consequences:
"what pathways could be affected
by the differential RNA
expression?"



The HYP

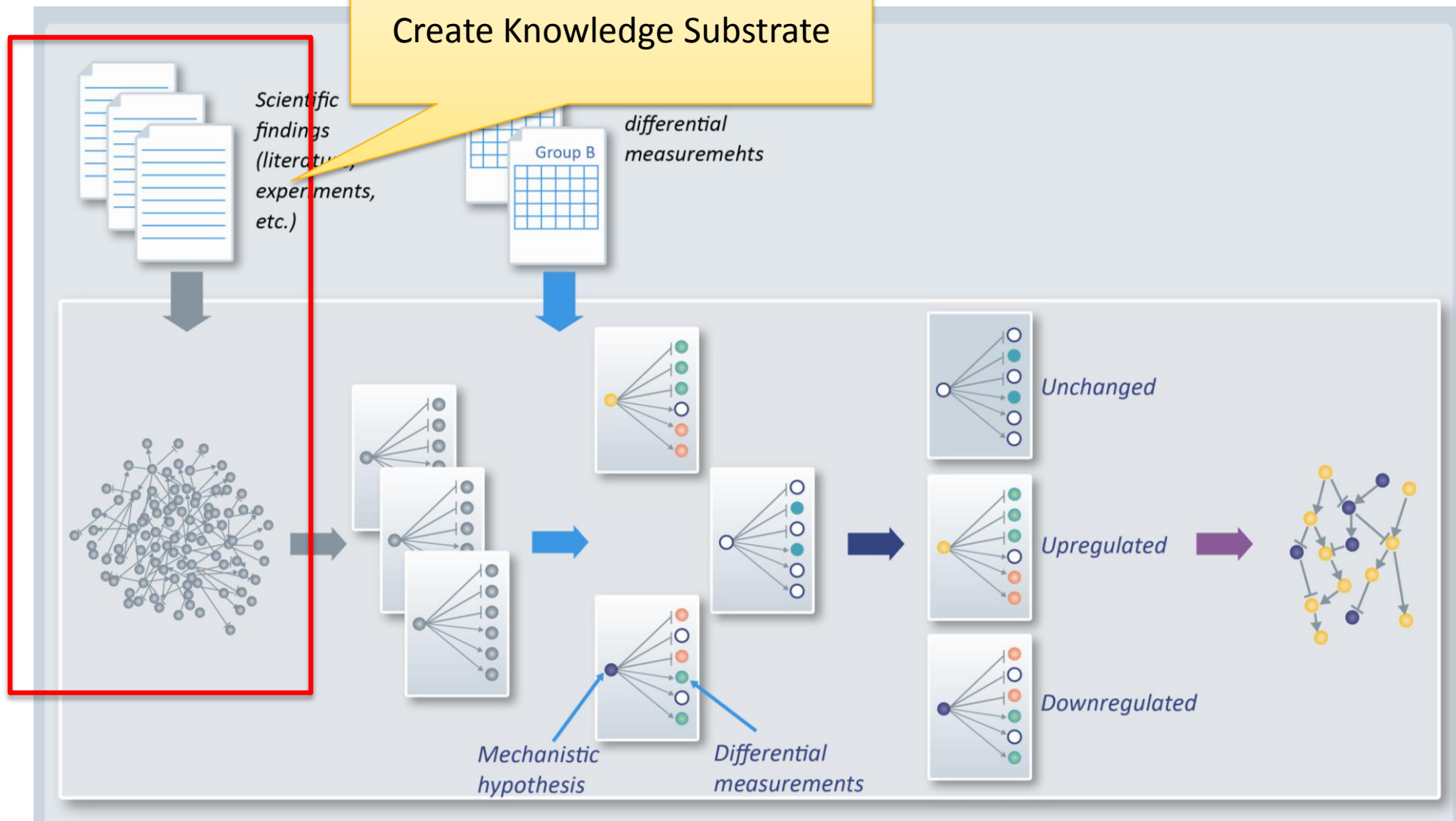


RCR Workflow

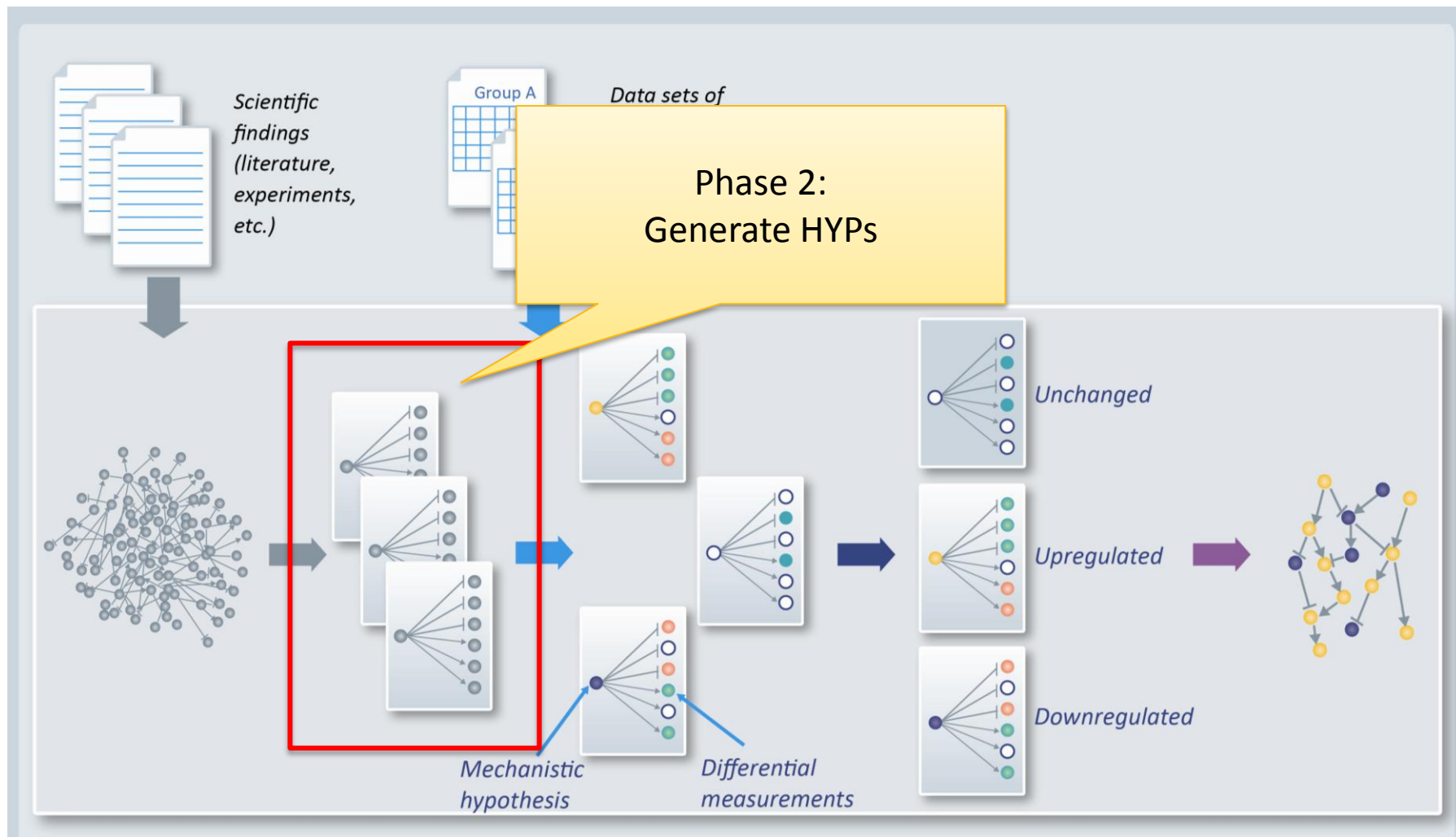


RCR Workflow

Phase 1: Create Knowledge Substrate



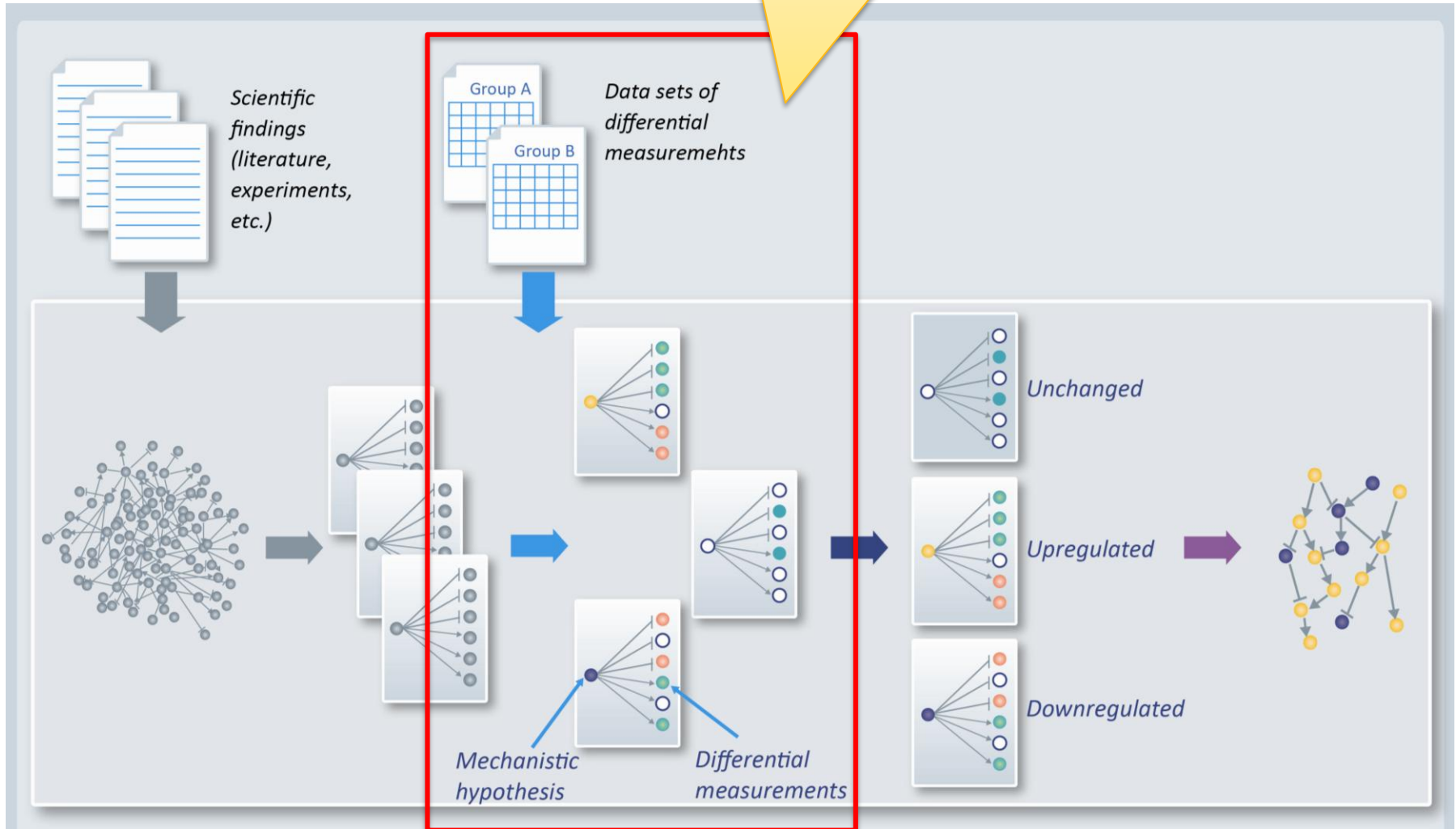
RCR Workflow



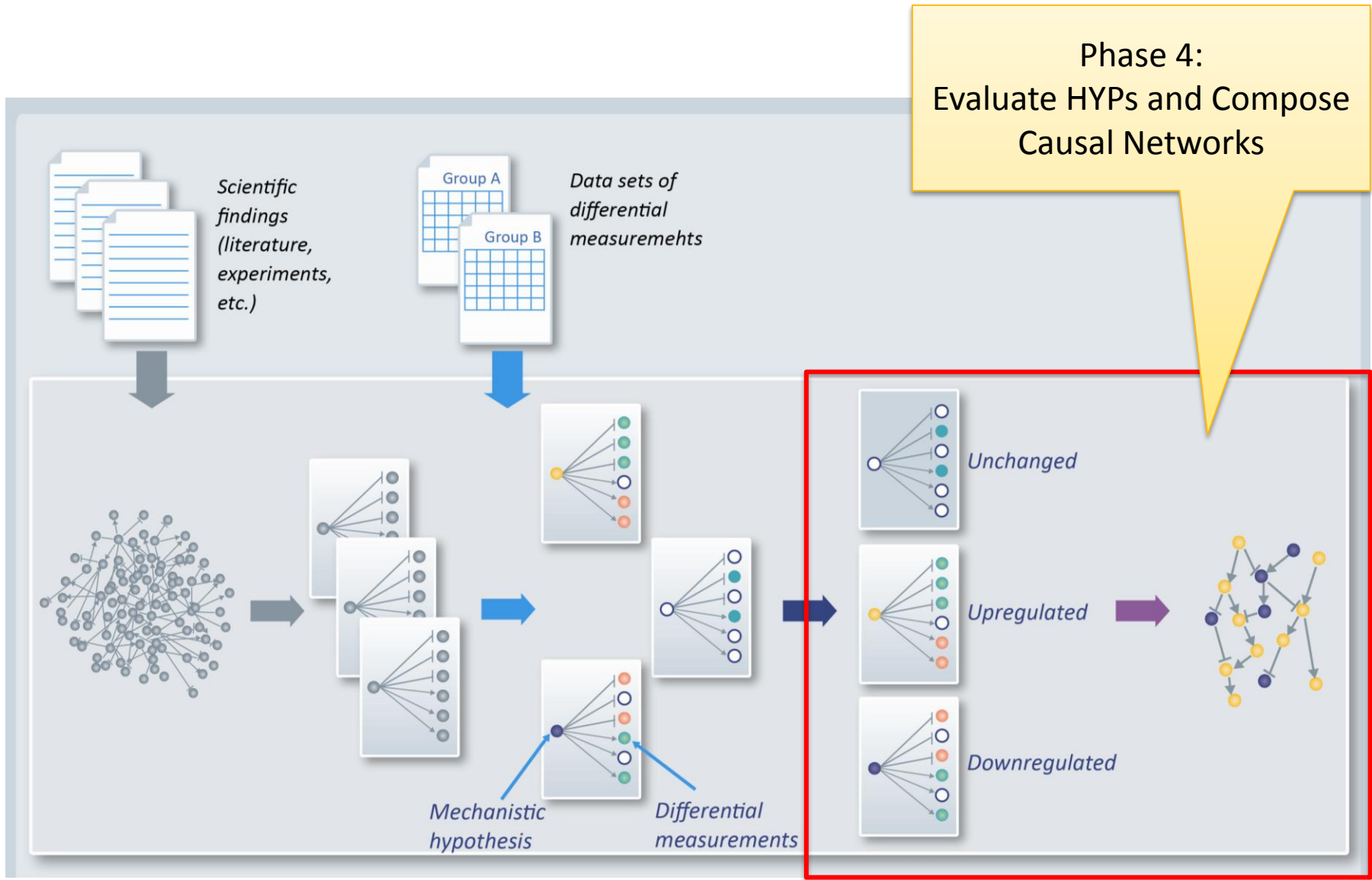
RCR Workflow



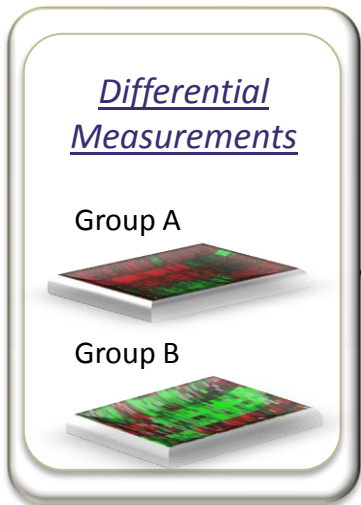
Phase 3:
Apply Data and Compute
HYP Statistics



RCR Workflow



HYP Significance Statistics



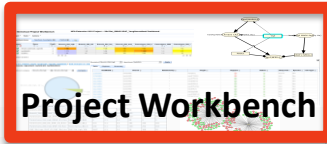
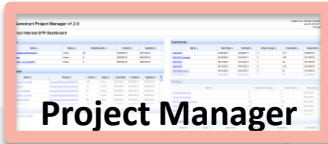
- Evaluate thousands of HYPs
- Each represents a potential casual explanation
- Calculate significance statistics for each HYP

Richness

p-value characterizing the **enrichment** of the predictions of the HYP in the observed differences

Concordance

p-value characterizing the **accuracy** of the HYP, whether observed directions of difference are consistent with the predictions of the HYP



Project Tools Actions

For example

Hypothesis Scores

Select	Name	Depth	R vs NR	NR vs R
<input type="checkbox"/>	kaof(EGFR)	2	-8	+6
<input type="checkbox"/>	bile duct ligation	2	-16	+16
<input type="checkbox"/>	SOCS3	2	+7	-7
<input type="checkbox"/>	response to wounding	2	+25	-25
<input type="checkbox"/>	MAT1A	2	+10	-10
<input type="checkbox"/>	VEGFA	2	-21	+21
<input type="checkbox"/>	Nickel	2	-26	+26
<input type="checkbox"/>	PDGFB	2	-8	+8
<input type="checkbox"/>	Histamine	2	-8	+8
<input type="checkbox"/>	BMP7	2	+4	-4
<input type="checkbox"/>	12-O-Tetradecanoylphorbol 13-a...	2	-16	+16
<input type="checkbox"/>	IFNB1	2	-13	+13
<input type="checkbox"/>	kaof(TGFB1)	2	-7	+7
<input type="checkbox"/>	CSF3	2	-19	+19
<input type="checkbox"/>	IL1B	2	-63	+63
<input type="checkbox"/>	taof(EPAS1)	2	-14	+14
<input type="checkbox"/>	JAK2	2	+18	-18
<input type="checkbox"/>	gtpof(HRAS)	2	-13	+13
<input type="checkbox"/>	tissue damage	2	-17	+17
<input type="checkbox"/>	taof(IRF3)	2	-14	+14
<input type="checkbox"/>	kaof(MAPK7)	2	-8	+8
<input type="checkbox"/>	And of Lipopolysaccharide and ...	2	-6	+6
<input type="checkbox"/>	cato(TLR4)	2	-39	+39
<input type="checkbox"/>	CD40LG	2	-31	+31
<input type="checkbox"/>	taof(RB1)	2	-30	+30
<input type="checkbox"/>	response to UV	2	-16	+16
<input type="checkbox"/>	taof(TP53)	2	-33	+33
<input type="checkbox"/>	GDNF	2	-4	+4

Scores 57 to 84 of 641

Evaluation of HYPs, Building Networks

Project Tools Actions

Hypothesis Scores

Select	Name	Depth	R vs NR	NR
<input type="checkbox"/>	kaof(EGFR)	2	-8	
<input type="checkbox"/>	bile duct ligation	2	-16	
<input type="checkbox"/>	SOC3	2	+7	
<input type="checkbox"/>	response to wounding	2	+25	
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<input type="checkbox"/>	Nickel	2	-26	
<input type="checkbox"/>	PDGFB	2	-8	
<input type="checkbox"/>	Histamine	2	-8	
<input type="checkbox"/>	BMP7	2	+4	
<input type="checkbox"/>	12-O-Tetradecanoylphorbol 13-a...	2	-16	+10
<input type="checkbox"/>	IFNB1	2	-13	+13
<input type="checkbox"/>	kaof(TGFBR1)	2	-7	+7
<input type="checkbox"/>	CSF3	2	-10	+19

Table Explorer Summary

PubMedId	Source
11883943	taof(AHR)
17502624	taof(AHR)
16214954	taof(AHR)
16214954	taof(AHR)
16214954	taof(AHR)
16214954	taof(AHR)
16214954	taof(AHR)
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Scores 57 to 84 of 641

Distinct biology in model 1

Shared biology between models 1 & 2

^	exp(Ppap2b)	✓	★	liver	Mm
^	exp(SLC25A28)	○	★	liver	Mm
-	exp(SUOX)	○	★	liver	Mm
^	exo(Ro4)	✓	★	liver	Mm

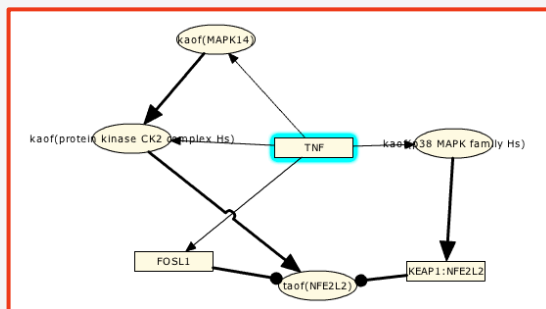
RCR Use Cases

Project Tools Actions

Hypothesis Scores

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Scores 57 to 84 of 641

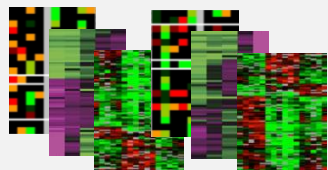


Molecular mechanisms of action

Molecular mechanisms for adverse events

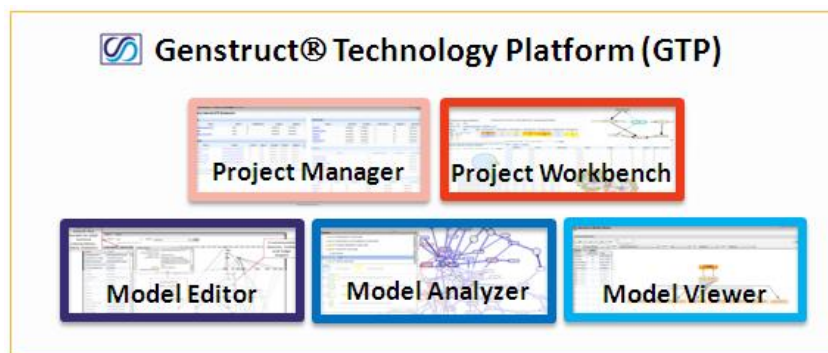
Molecular mechanisms of disease

Summary

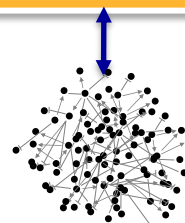


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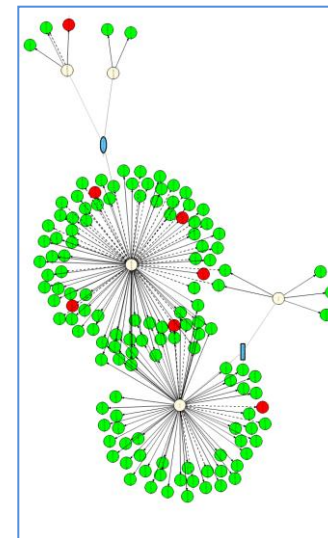
transcriptomic, RNA-Seq, proteomic, metabolomic, etc.



BEL Enabled Applications



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