

The Minimum Information about a Molecular Interaction Causal Statement (MI2CAST)

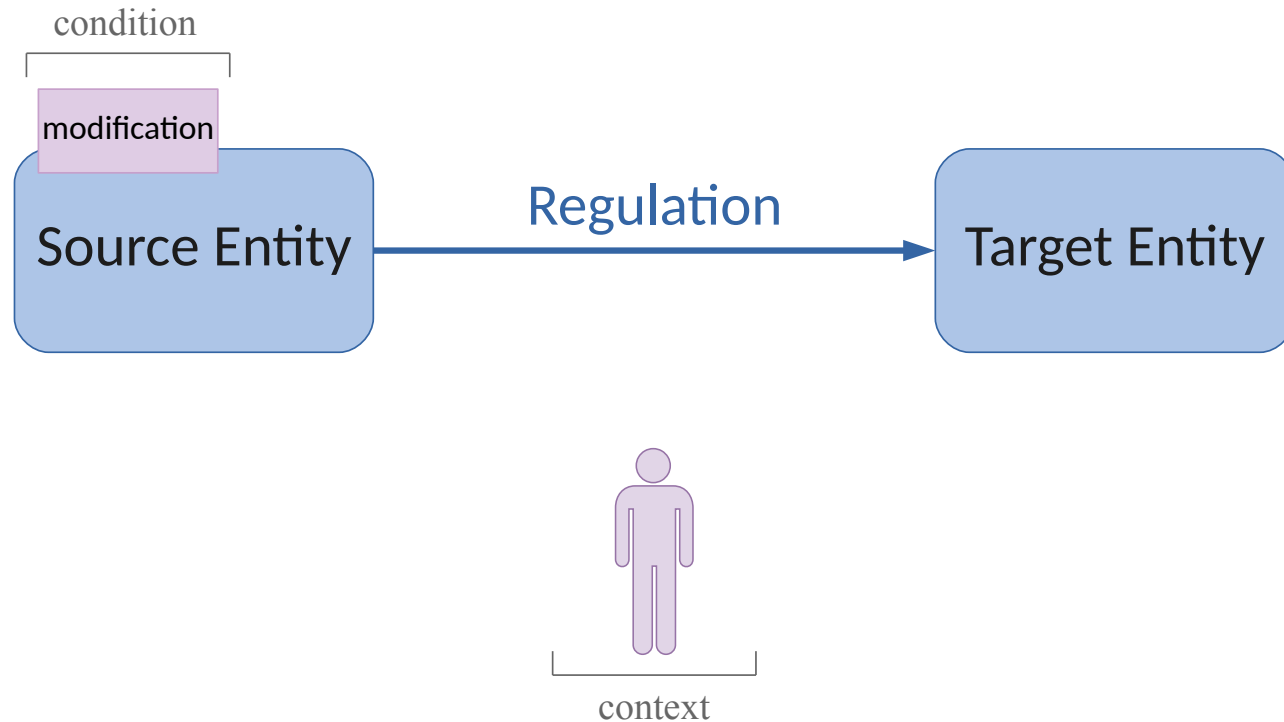
BC² WS2 - Annotation and curation of computational models in biology

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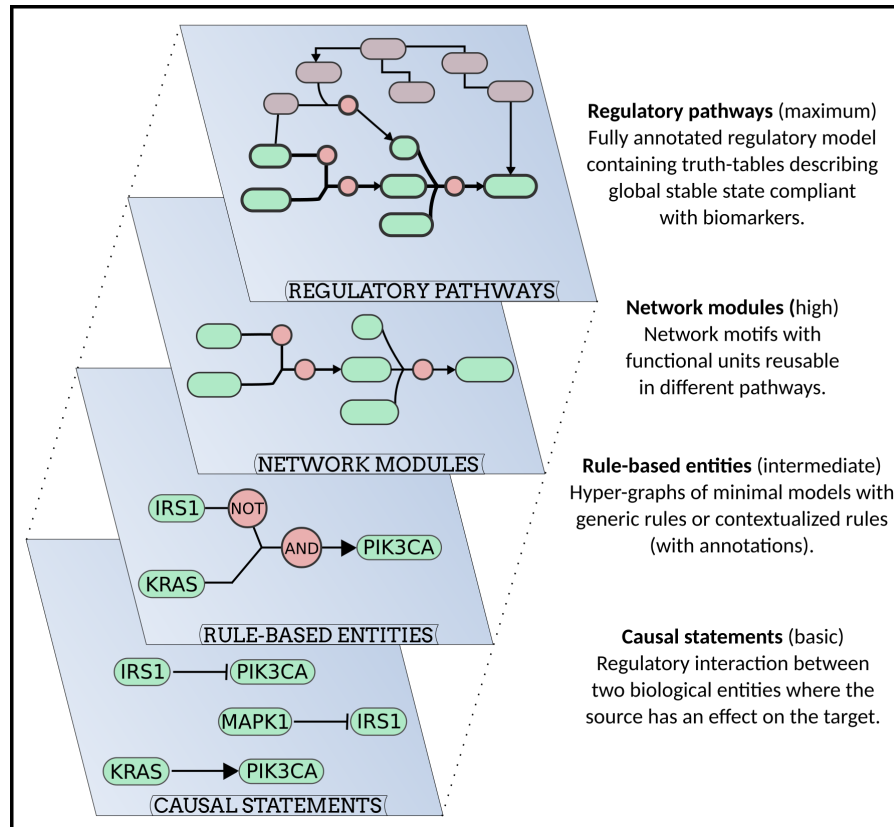
09/09/2019



What is a Causal Statement?



Causal statements in modeling

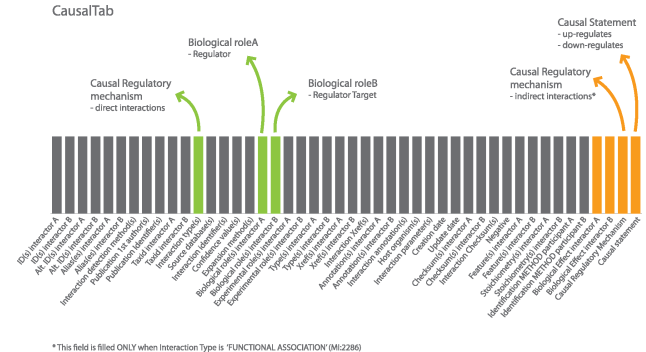


Current representations of causal statements

• SIF

AKT1 -I FOXO3
ILK -> AKT1
STAT3 -> CASP3
BIRC6 -I CASP3

• MITAB2.8



source: [Perfetto et al. 2019](#)

• BEL

SET Citation = ["PubMed","Distinct angiogenic mediators are required for basic fibroblast Growth factor- and vascular endothelial growth factor-induced angiogenesis: the role of cytoplasmic tyrosine kinase c-Abl in tumor angiogenesis.",
"Molecular biology of the cell; Vol. 19; Iss. 5","2008-05-01",
"Wei Yan|Brooke Bentley|Rong Shao","18353972"]

SET Evidence = "In contrast, the physical interaction between integrin beta 5 and Flk-1/KDR was detectable only by stimulation with VEGF."

SET Cell = "endothelial cell"

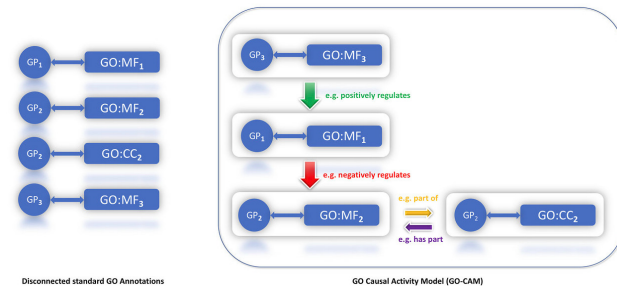
Context annotation

p(HGNC:VEGFA) -> complex(p(HGNC:ITGB5),p(HGNC:KDR))

BEL statement

source: [Fluck et al. 2016](#)

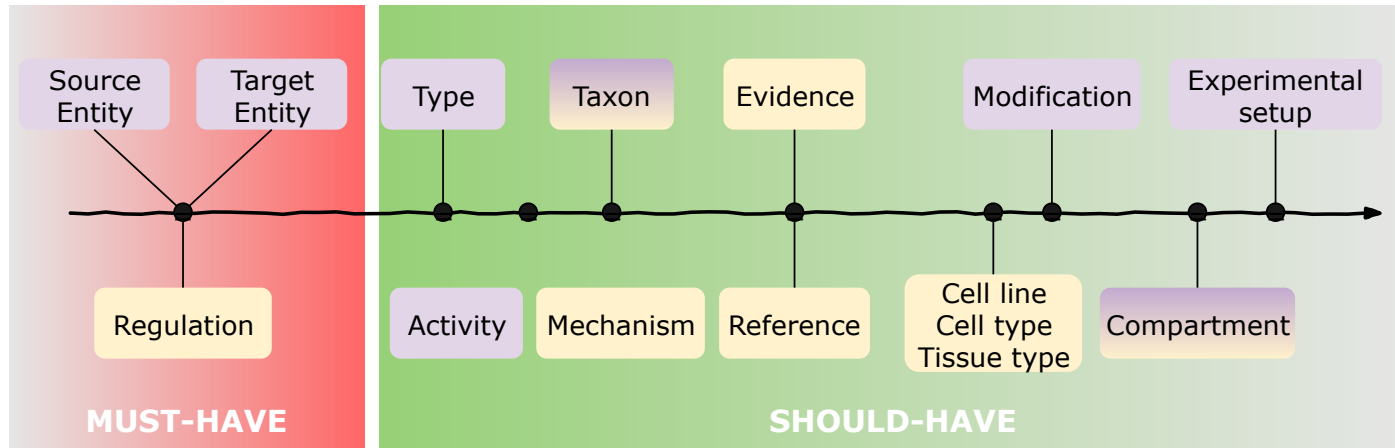
• GO-CAM



source: [GO-CAM website](#)

MI2CAST: from a checklist to guidelines

List of data to annotate about a causal interaction



➔ Arranged in guidelines with ontologies & CVs recommendations

MI2CAST guidelines defines 4 rules

Rule 1. Source and Target entity must be annotated

Rule 2. Regulation sign must be annotated

Rule 3. Origin of interaction should be annotated

Rule 4. Context of interaction should be specified

➔ MI2CAST on GitHub 🔗 : [vtoure/MI2CAST](https://github.com/vtoure/MI2CAST)

➔ Manuscript in preparation!

Coverage of MI2CAST

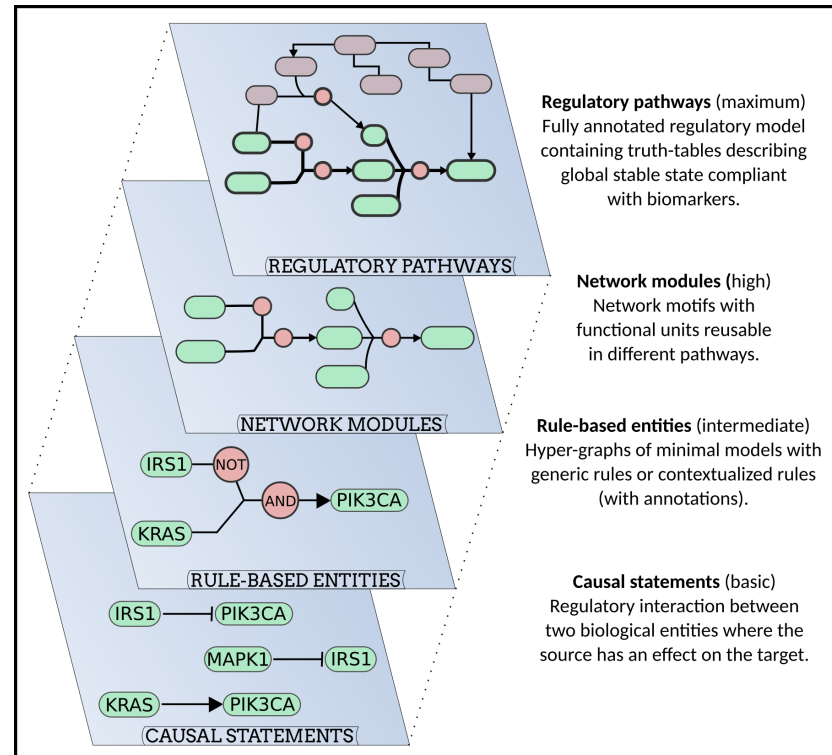
Term	SIF	MITAB2.8	BEL	GO-CAM
source entity	*	*	*	*
target entity	*	*	*	*
regulation sign	*	*	*	*
reference		*	*	*
evidence		*	*	*
biological activity		*	*	*
biological mechanism		*		*
biological type		*	*	
taxon entity		*		*
experimental setup		*		
biological modification		*	*	
taxon interaction		*	*	
cell line			*	
tissue type				*
cell type			*	*
compartment			*	*

MI2CAST's added-value

🔍 Guide curators for contextual annotation

📖 Guide biologists for experimental design

🔧 Data consistency for model building



Concrete biological examples

- Transcription factor target gene interaction

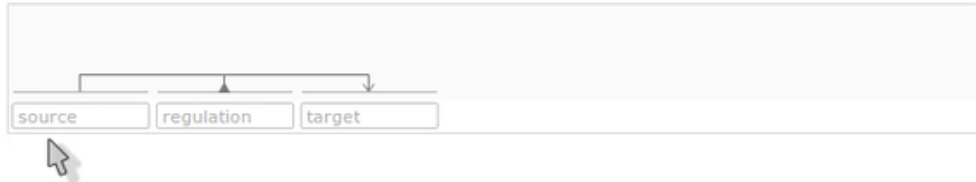
Term	Identifier	Name/Label	Database
source	A0AVK6	E2F8	Uniprot
target	898	CCNE1	Entrez gene
regulation sign	2240	down-regulates	PSI-MI
reference	16179649	"Characterization of E2F8, a novel..."	Pubmed
evidence 1	0000269	exp. evidence used in manual assertion	ECO
evidence 2	0001805	luciferase reporter gene assay evidence	ECO
biological mechanism	2247	transcription regulation	PSI-MI
compartment (interaction)	0005634	nucleus	GO:CC
taxon	9606	Homo sapiens	NCBI taxonomy
cell line	0001938	human osteosarcoma cell line	BTO
exp. setup source 1	0506	over expressed level	PSI-MI
exp. setup source 2	0331	engineered	PSI-MI
exp. setup target 1	0331	engineered	PSI-MI
exp. setup target 2	0001679	transcription_regulatory_region	SO

Concrete biological examples

- Protein kinase A regulation

Term	Identifier	Name/Label	Database
source	17489	3',5'-cyclic AMP	ChEBI
target	P17612	cAMP-dependent PKA catalytic	Uniprot
regulation sign	2236	up-regulates activity	PSI-MI
reference	26687711	"Protein kinase A catalytic subunit... "	Pubmed
evidence	0000302	author statement used in manual assertion	ECO
biological activity source	0034237	protein kinase A regulatory subunit binding	GO:MF
biological activity target	0004672	protein kinase activity	GO:MF
compartment of interaction	0005737	cytoplasm	GO:CC
taxon	9606	Homo sapiens	NCBI taxonomy

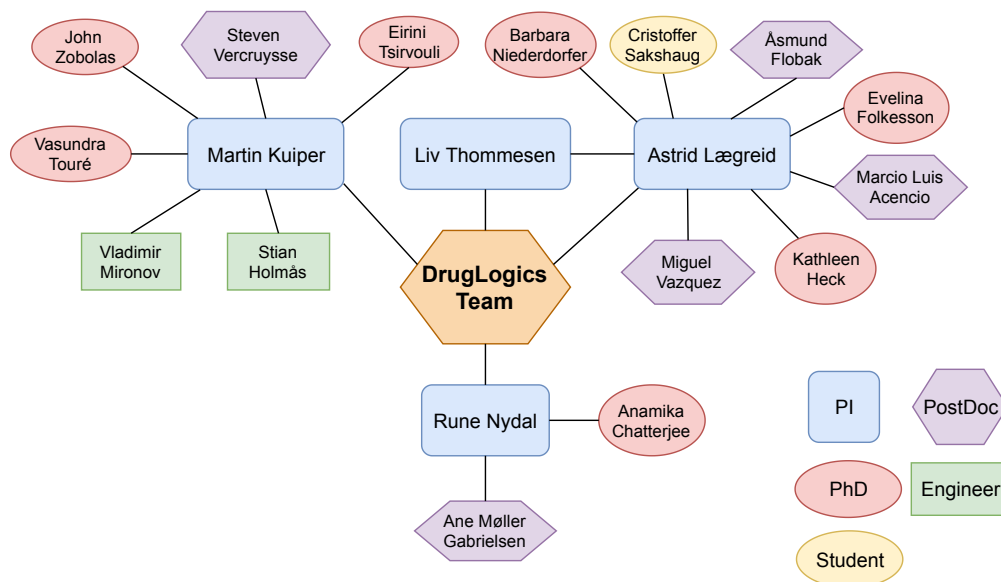
MI2CAST support with the **causalBuilder**



- Exports: causal-JSON + **MITAB2.8** (planned)
- Autocomplete for >800 ontologies with **VSM-dictionary-combiner**

Use of **VSM technology** & GitHub pages (**Jekyll Cayman theme**)

Acknowledgements



vtoure
 @Vsndr_T

Slides created via the R package **xaringan**.



 **NTNU**
 Norwegian University of
 Science and Technology

Tematisk satsingsområde 2014–2023

NTNU HELSE



 **cost**
 EUROPEAN COOPERATION
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ERACOSYS
MED

List of abbreviations

- MI2CAST Minimum Information about a Molecular Interaction Causal Statement
- BEL Biological Expression Language
- GO-CAM Gene Ontology Causal Activity Model
- PSI-MI Proteomics Standards Initiative Molecular Interactions
- RO Relation Ontology
- PMID Pubmed Identifier
- DOI Digital Object Identifier
- ECO Evidence and Conclusion Ontology
- GO:MF Gene Ontology Molecular Function
- ChEBI Chemical Entities of Biological Interest
- SO Sequence Ontology
- BTO BRENDA Tissue Ontology
- CL Cell Ontology
- Uberon Uber Anatomy Ontology
- GO:CC Gene Ontology Cellular Component