



Introduction to the DiseaseMap Project: Step 1

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Diane Lefaudeux, Johann Pellet, Christophe Pison and
Charles Auffray

SBGN10, 16 August 2014

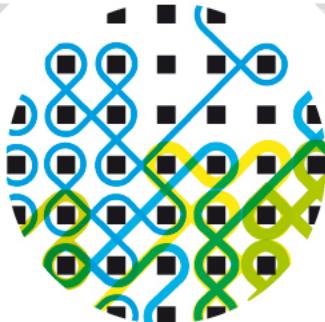
University of Southern California, Los Angeles, California, USA



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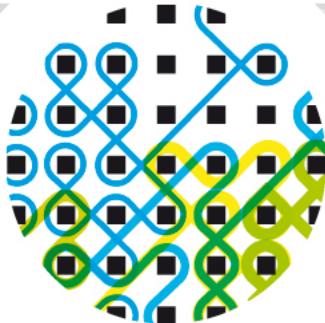


DiseaseMap definition

Background: examples of similar projects

SBGN standard

U-BIOPRED AsthmaMap



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→ DiseaseMap definition

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U-BIOPRED AsthmaMap

What is DiseaseMap?

DiseaseMap is a collection of **computerized comprehensive** metabolic, signaling and gene regulatory pathways relevant to a particular disease.

DiseaseMap is developed as an advanced combination of **well-established approaches** in Systems Biology.

Participation of **domain experts** ensures the highest quality of knowledge representation.

Must-read papers



Fujita KA, Ostaszewski M, Matsuoka Y, Ghosh S, Glaab E, Trefois C, Crespo I, Perumal TM, Jurkowski W, Antony PM, Diederich N, Buttini M, Kodama A, Satagopam VP, Eifes S, Del Sol A, Schneider R, Kitano H, Balling R. **Integrating pathways of Parkinson's disease in a molecular interaction map.** *Mol Neurobiol.* 2014 Feb;49(1):88-102

PMID: 23832570



Molecular Neurobiology
February 2014, Volume 49, Issue 1, pp 88-102,
Open Access

Integrating Pathways of Parkinson's Disease in a Molecular Interaction Map

Kazuhiro A. Fujita, Marek Ostaszewski, Yukiko Matsuoka, Samik Ghosh, Enrico Glaab, Christophe Trefois, Isaac Crespo, Thanneer M. Perumal, Wiktor Jurkowski, Paul M. A. Antony, ... [show all 19](#)

1 Citation

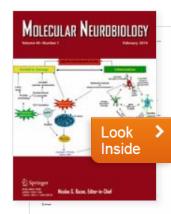
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Abstract

Parkinson's disease (PD) is a major neurodegenerative chronic disease, most likely caused by a complex interplay of genetic and environmental factors. Information on various aspects of PD pathogenesis is rapidly increasing and needs to be efficiently organized, so that the resulting data is available for exploration and analysis. Here we introduce a computationally tractable, comprehensive molecular interaction map of PD. This map integrates pathways implicated in PD pathogenesis such as synaptic and mitochondrial dysfunction, impaired protein degradation, alpha-synuclein pathology and neuroinflammation. We also present bioinformatics tools for the analysis, enrichment and annotation of the map, allowing the research community to open new avenues in PD research. The PD map is accessible at http://minerva.uni.lu/pd_map.

* K. Fujita and M. Ostaszewski contributed equally to this work.



Within this Article

- » Introduction
- » Neurodegeneration in Parkinson's Disease Arises from Dysregulation of Interlinked Molecular Pathways
- » Vulnerability and Preferential Loss of Midbrain Dopaminergic Neurons
- » Synaptic Dysfunction
- » Mitochondrial Dysfunction
- » Failure of Protein Degradation Systems
- » α -Synuclein Misfolding and Pathobiology
- » Neuroinflammation
- » Neuronal Death Through Apoptosis-Related Mechanisms
- » Annotation, Enrichment and Analysis of the PD Map
- » Annotation of the PD Map Using

Le Novère N, Hucka M, Mi H, Moodie S, Schreiber F, Sorokin A, Demir E, Wegner K, Aladjem MI, Wimalaratne SM, Bergman FT, Gauges R, Ghazal P, Kawaji H, Li L, Matsuoka Y, Villéger A, Boyd SE, Calzone L, Courtot M, Dogrusoz U, Freeman TC, Funahashi A, Ghosh S, Jouraku A, Kim S, Kolpakov F, Luna A, Sahle S, Schmidt E, Watterson S, Wu G, Goryanin I, Kell DB, Sander C, Sauro H, Snoep JL, Kohn K, Kitano H. **The Systems Biology Graphical Notation.** *Nat Biotechnol.* 2009 Sep;27(9):864

PMID: 19668183



Journal home > Archive > Computational Biology > Perspective > Full Text

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Perspective

Nature Biotechnology 27, 735 - 741 (2009)
Published online: 7 August 2009 | [Corrected](#) online: 9 September 2009 | doi:10.1038/nbt.1558

There is an [Erratum](#) (September 2009) associated with this Perspective.

The Systems Biology Graphical Notation

Nicolas Le Novère¹, Michael Hucka², Huaiyu Mi³, Stuart Moodie⁴, Falk Schreiber^{5,6}, Anatoly Sorokin⁷, Emek Demir⁸, Katja Wegner⁹, Mirit I Aladjem¹⁰, Sarala M Wimalaratne¹¹, Frank T Bergman¹², Ralph Gauges¹³, Peter Ghazal^{14,15}, Hideya Kawaji¹⁵, Lu Li¹⁶, Yukiko Matsuoka¹⁶, Alice Villéger^{17,18}, Sarah E Boyd¹⁹, Laurence Calzone²⁰, Melanie Courtot²¹, Ugur Dogrusoz²², Tom C Freeman^{14,23}, Akira Funahashi²⁴, Samik Ghosh¹⁶, Akiya Jouraku²⁴, Sohyoung Kim¹⁰, Fedor Kolpakov^{25,26}, Augustin Luna²⁶, Sven Sahle²⁴, Esther Schmidt²⁴, Steven Watterson²², Guanning Wu²⁷, Igor Goryanin⁴, Douglas B Kell^{18,28}, Chris Sander⁸, Herbert Sauro¹², Jacky L Snoep²⁸, Kurt Kohn¹⁰ & Hiroaki Kitano^{16,30,31}

Circuit diagrams and Unified Modeling Language diagrams are just two examples of standard visual languages that help accelerate work by promoting regularity, removing ambiguity and enabling software tool support for communication of complex information. Ironically, despite having one of the highest ratios of graphical to textual information, biology still lacks standard graphical notations. The recent deluge of biological knowledge makes addressing this deficit a pressing concern. Toward this goal, we present the Systems Biology Graphical Notation (SBGN), a visual language developed by a community of biochemists, modelers and computer scientists. SBGN consists of three complementary languages: process diagram, entity relationship diagram and activity flow diagram. Together they enable scientists to

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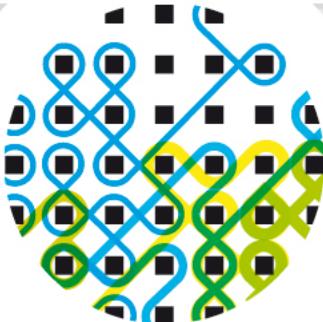
Abstract

Figures & tables

Acknowledgments

Competing financial interests

Box 1



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DiseaseMap definition

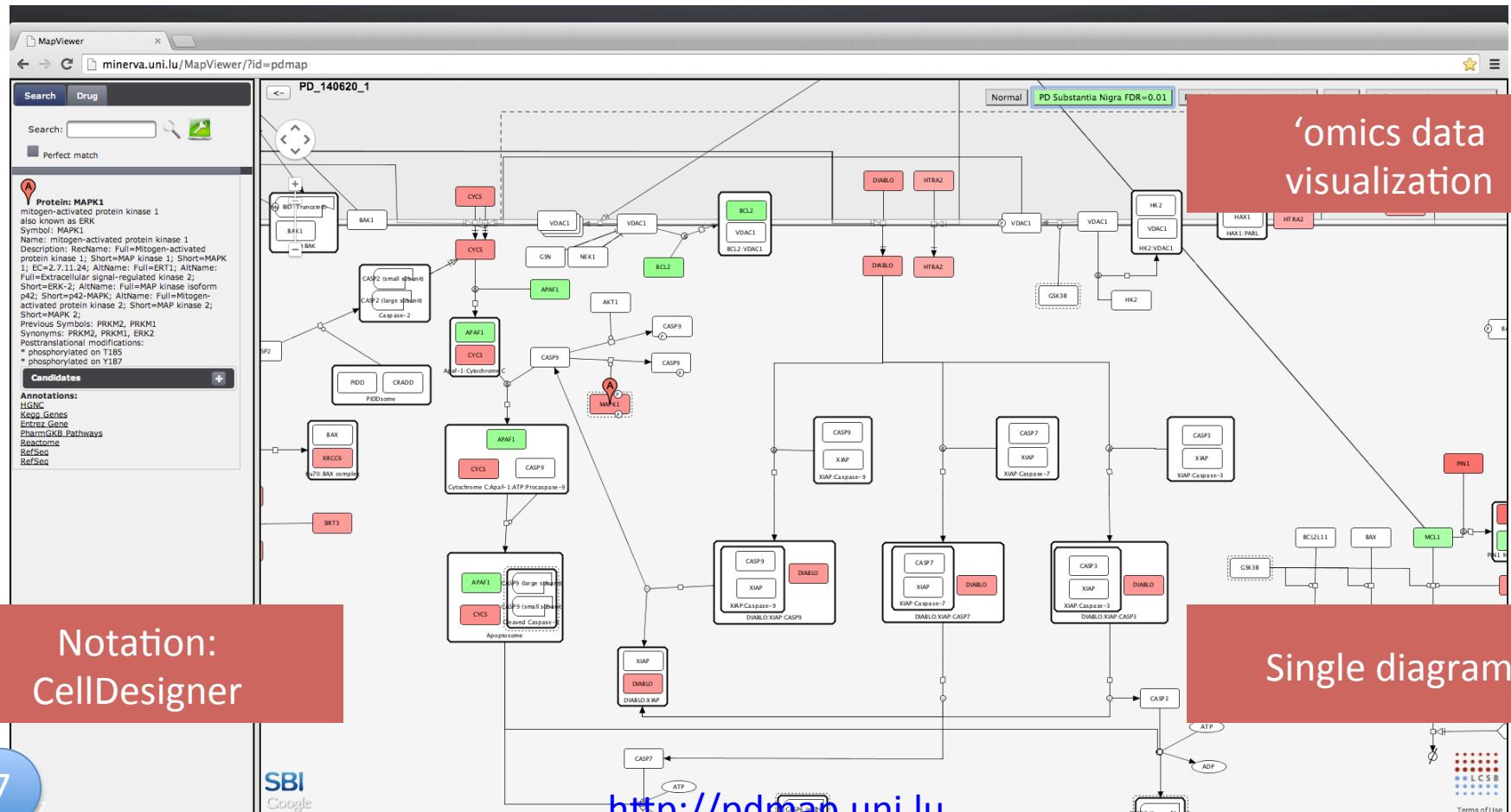
→ **Background: examples of similar projects**

SBGN standard

U-BIOPRED AsthmaMap

Parkinson's disease map

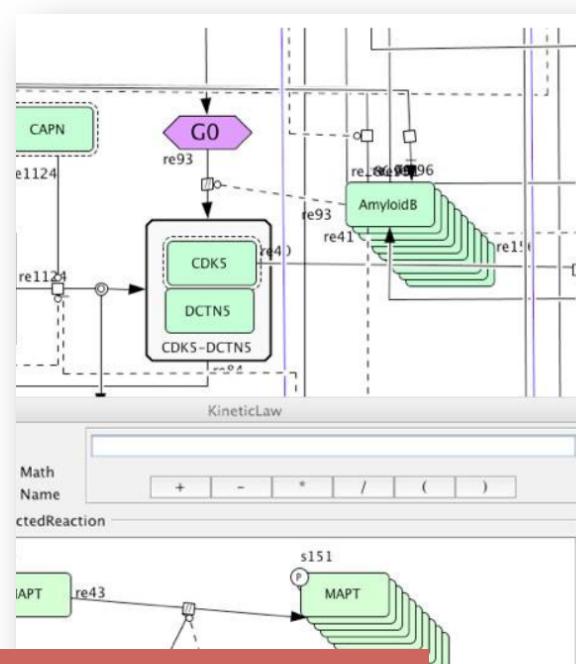
Fujita KA, Ostaszewski M, Matsuoka Y, Ghosh S, Glaab E, Trefois C, Crespo I, Perumal TM, Jurkowski W, Antony PM, Diederich N, Buttini M, Kodama A, Satagopam VP, Eifes S, Del Sol A, Schneider R, Kitano H, Balling R. **Integrating pathways of Parkinson's disease in a molecular interaction map.** *Mol Neurobiol.* 2014



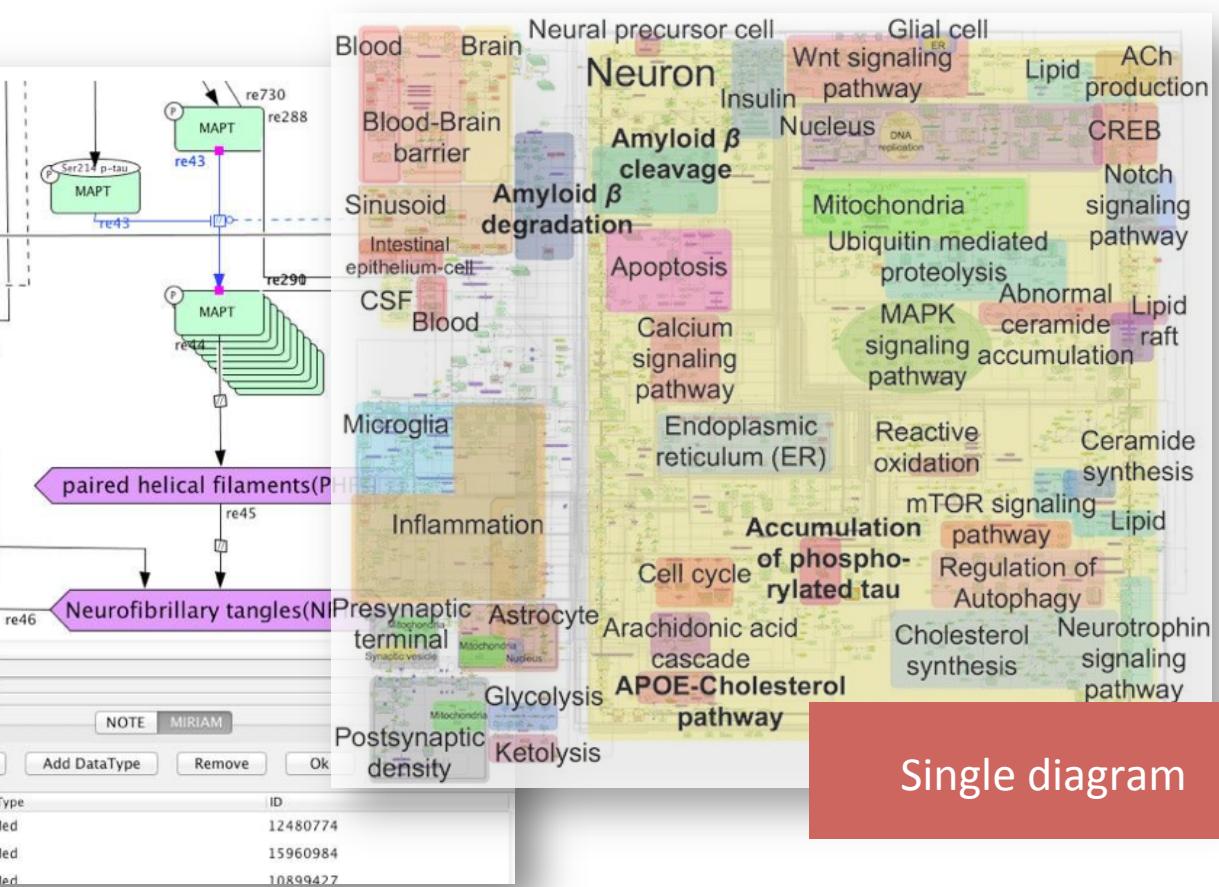
Alzheimer's disease map



SBI The Systems Biology Institute

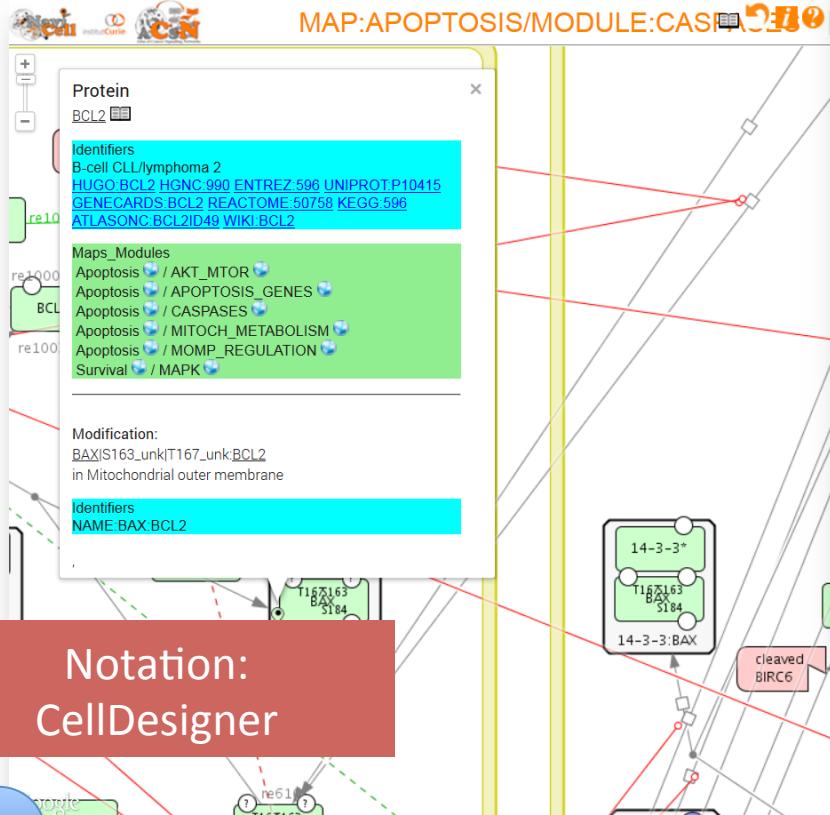
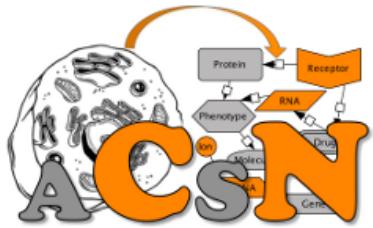


Notation:
CellDesigner

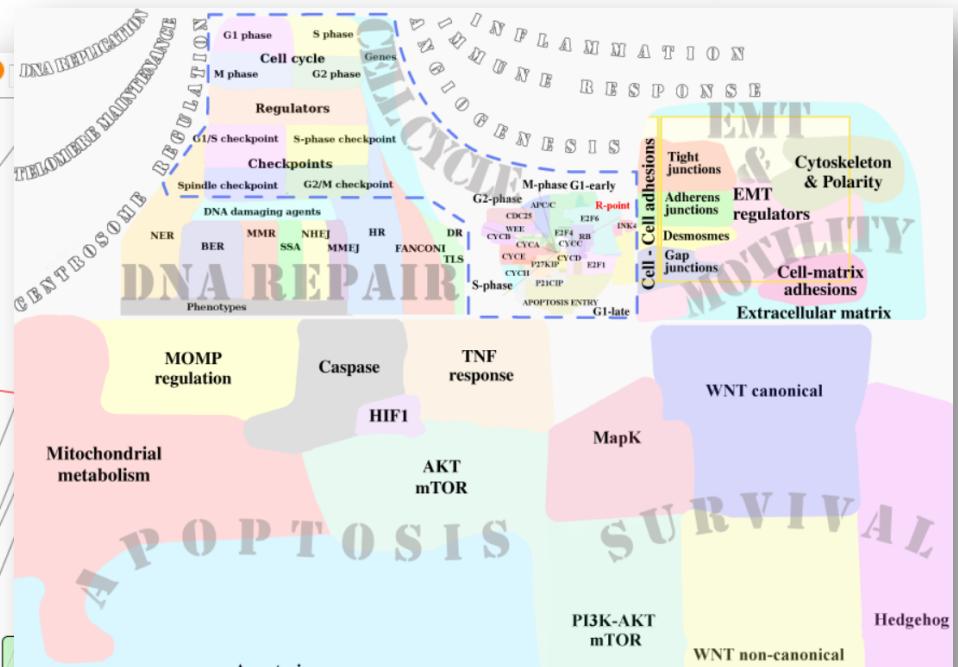


Single diagram

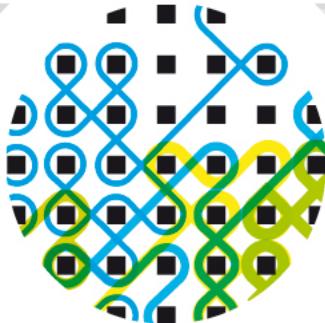
The Atlas of Cancer Signaling Networks



<https://acsn.curie.fr/>



A collection of maps + outlines/navigation



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DiseaseMap definition

Background: examples of
similar projects

→ **SBGN standard**

U-BIOPRED AsthmaMap

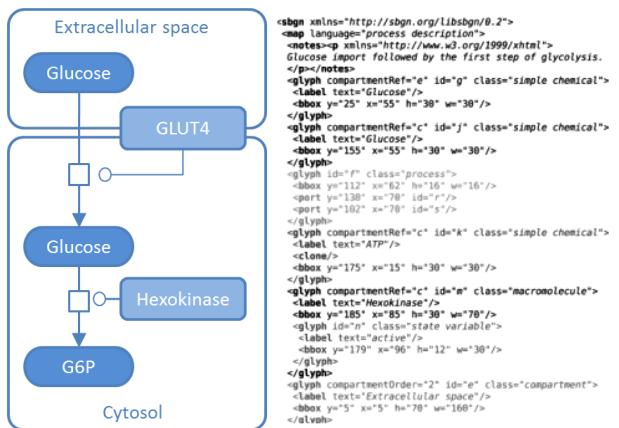
The standard language

Systems Biology Graphical Notation (SBGN), the recently immerged state-of-the-art graphical standard, ensures unambiguous and consistent knowledge representation.

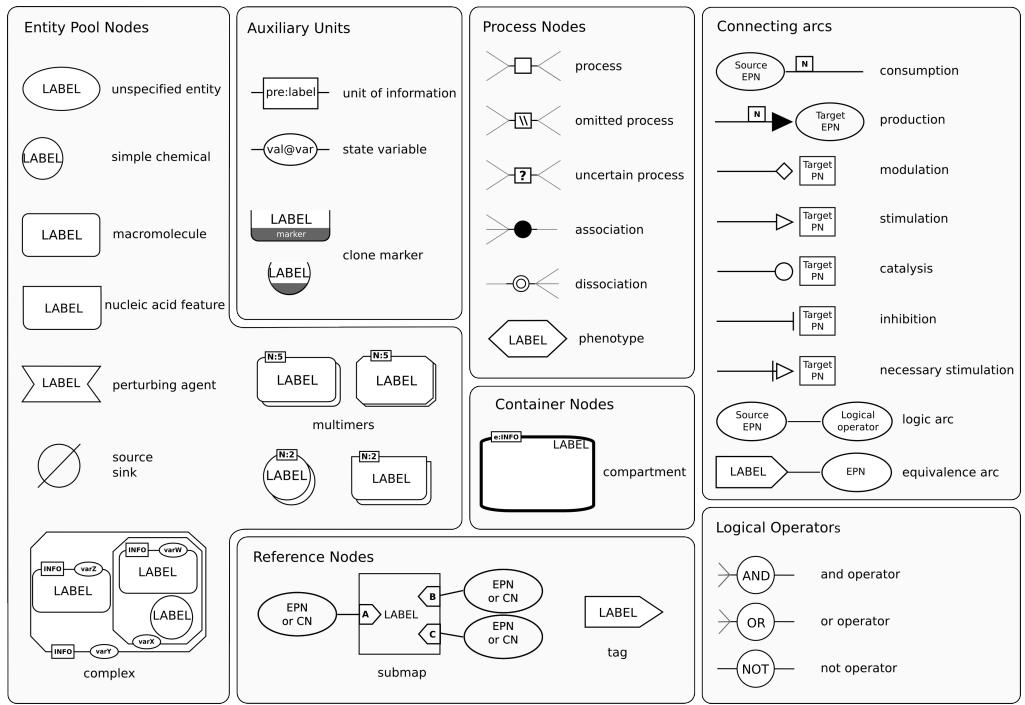
The diagrams have to be **human-readable**

The diagrams have to be **machine-readable**

SBGN can do both



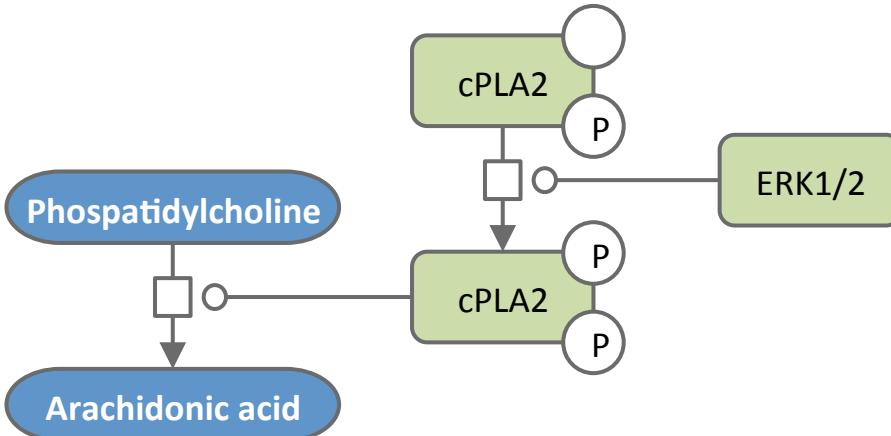
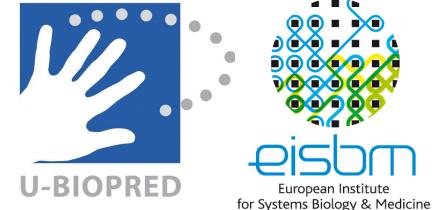
SBGN Process Description language



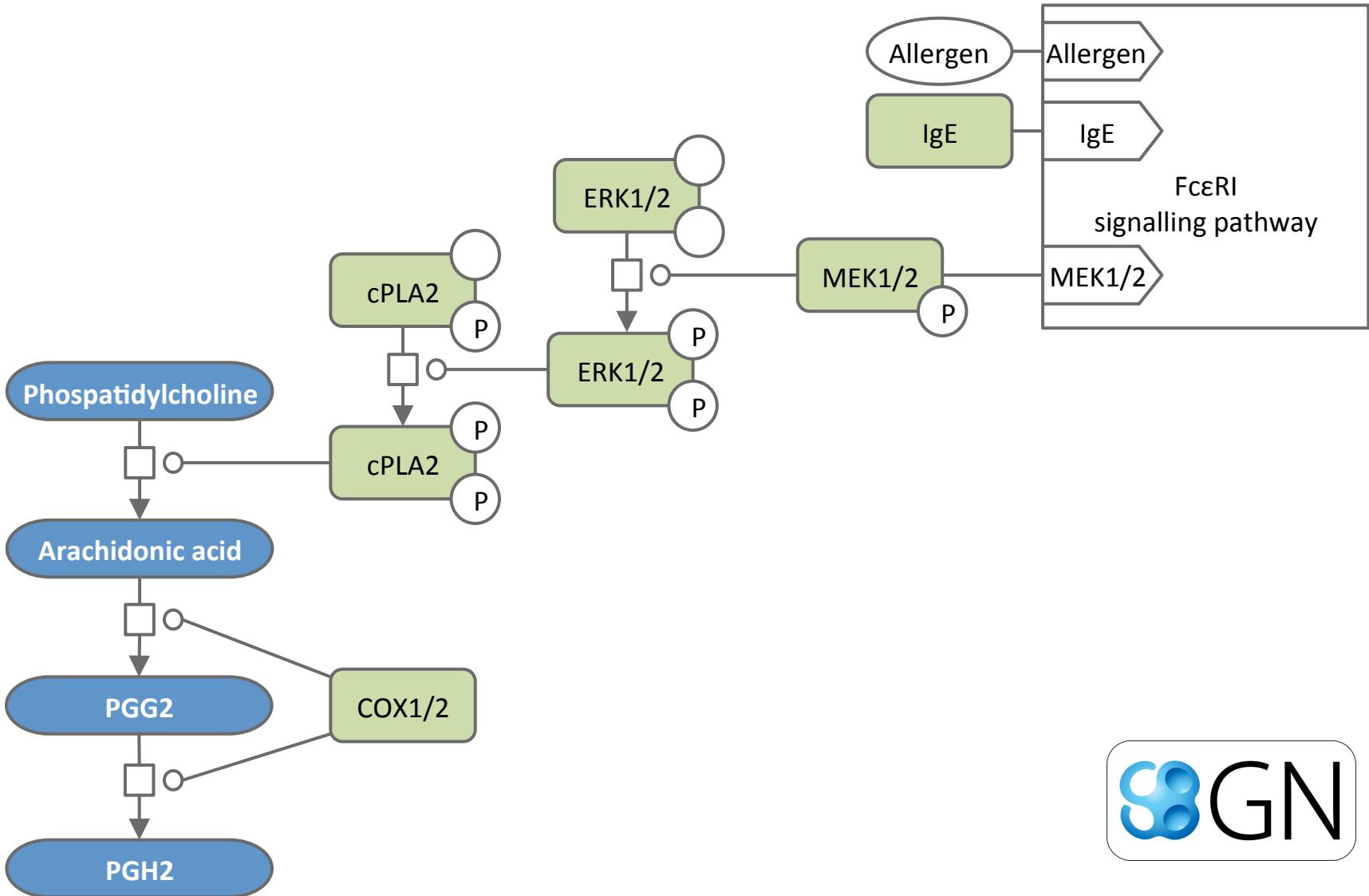
Important features:

- Developed by a **community** of biochemists, modelers and computer scientists;
- Enables representing diverse biological objects and their interactions using **minimal number of symbols**.

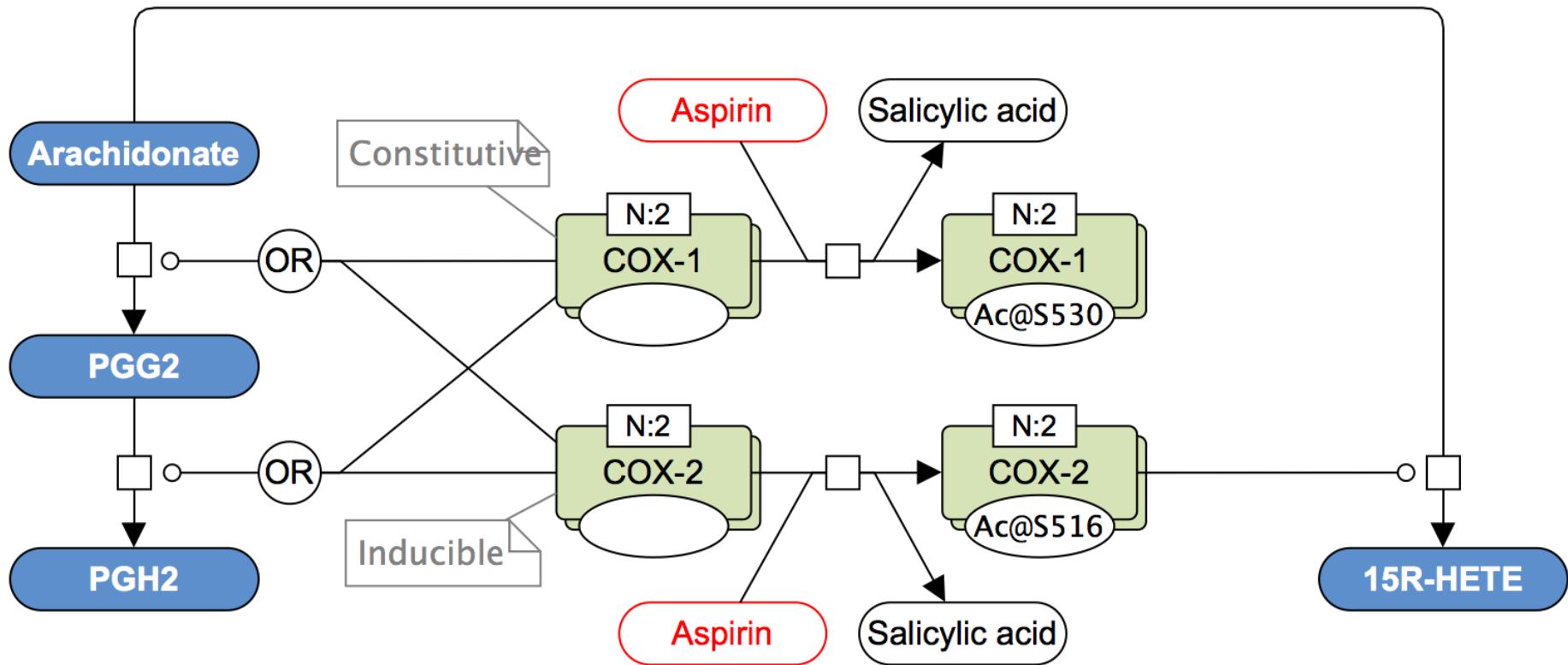
An example of SBGN diagram: cPLA2 activation

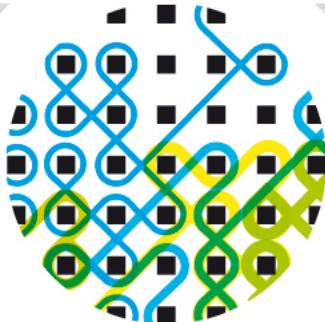


An example of SBGN diagram: cPLA2 activation



An example of SBGN diagram: COX1 and COX2 regulation by aspirin





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SBGN standard

→ **U-BIOPRED AsthmaMap**

What is AsthmaMap?

AsthmaMap is a collection of **comprehensive** metabolic, signaling and gene regulatory **pathways** relevant to severe asthma.

AsthmaMap is being developed as a part of U-BIOPRED project (**Unbiased BIO**markers in **PRED**iction of respiratory disease outcomes).

AsthmaMap is a test-case for eTRIKS platform (**european TRanslational Information and Knowledge Management Services**).

Brief introduction to U-BIOPRED and eTRIKS



U-BIOPRED

Unbiased **BIO**markers in **PRED**iction of respiratory disease outcomes

The U-BIOPRED project aims to speed up the development of better treatments for patients with severe asthma.

Funded by IMI (€20.7m).

U-BIOPRED is actively supported by eTRIKS.



eTRIKS

<http://www.etriks.org/>

european **TR**anslational **I**nformation and **K**nowledge **M**anagement **S**ervices

Funded by IMI (€23.7m).

eTRIKS is based on the tranSMART platform.



tranSMART Foundation

<http://www.transmartfoundation.org/>

The tranSMART Foundation is a global non-profit organisation. tranSMART knowledge management platform enables sharing and analysis of heterogeneous data. The initial version was developed by Johnson & Johnson and Recombinant Data Corporation.



Innovative Medicines Initiative

<http://www.imi.europa.eu/>

Europe's largest public-private initiative aiming to speed up the development of better and safer medicines for patients.

Objectives

AsthmaMap is a collection of pathways important for understanding different phenotypes of severe asthma.

Objectives:

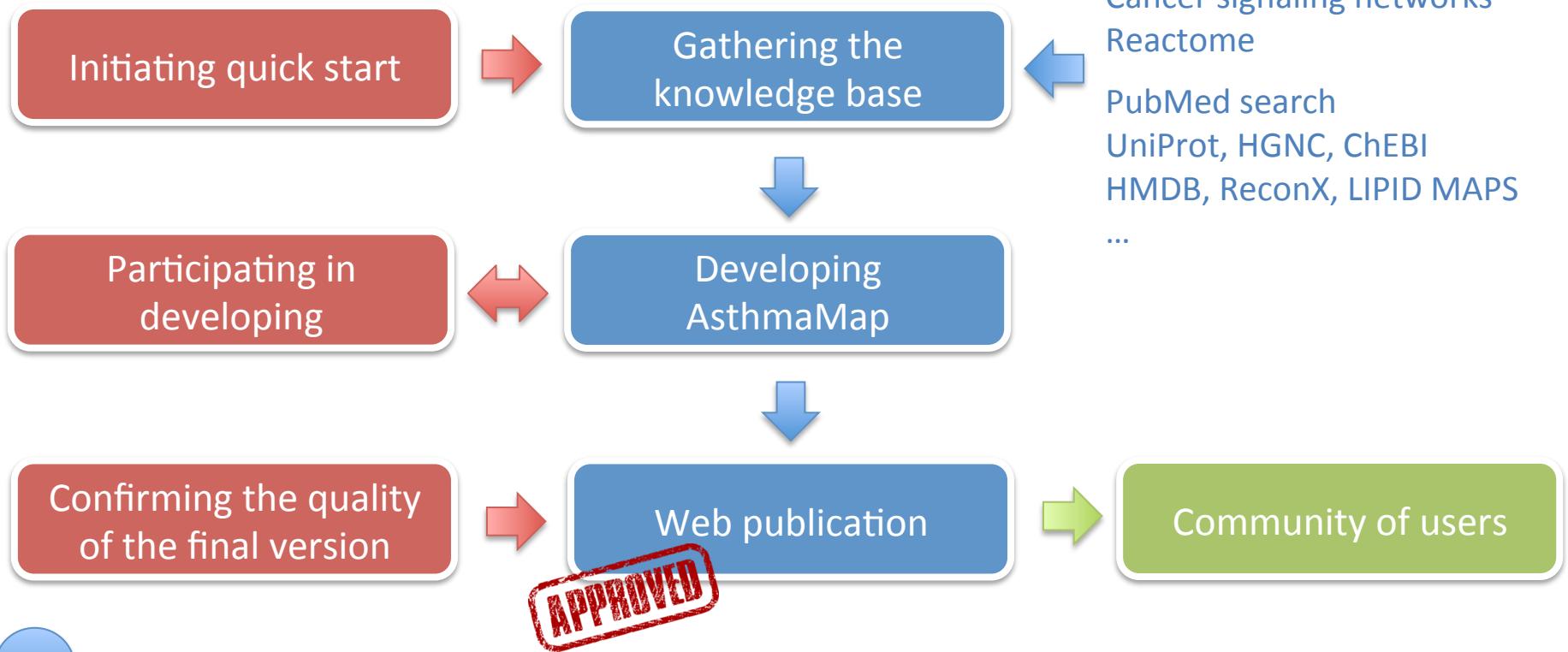
1. Making sense of U-BIOPRED fingerprints and handprints
2. Supporting design of validation experiments
3. Test case for eTRIKS platform

One of the most important features of the project is involvement of the domain experts in the development of AsthmaMap.

The Editors Committee

AsthmaMap
Editors Committee
(domain experts)

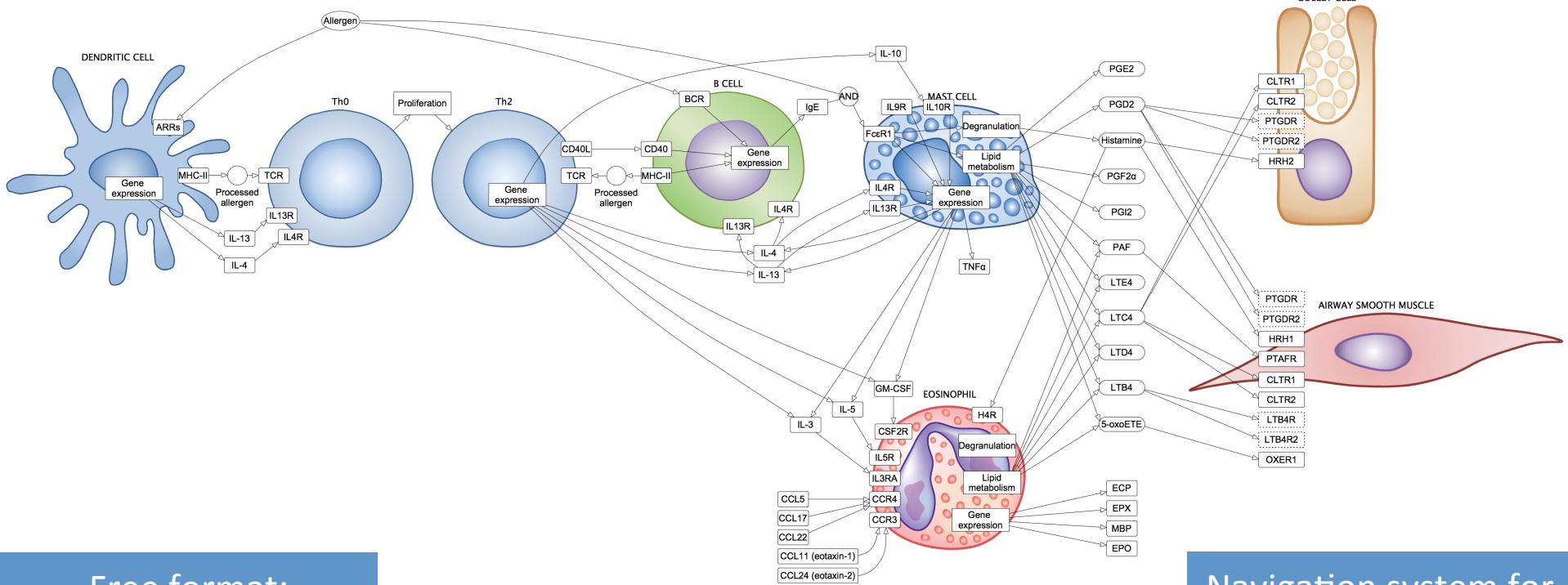
AsthmaMap
Computational Biology
working group



Consensus asthma overview diagram: step back



Building consensus
among participants

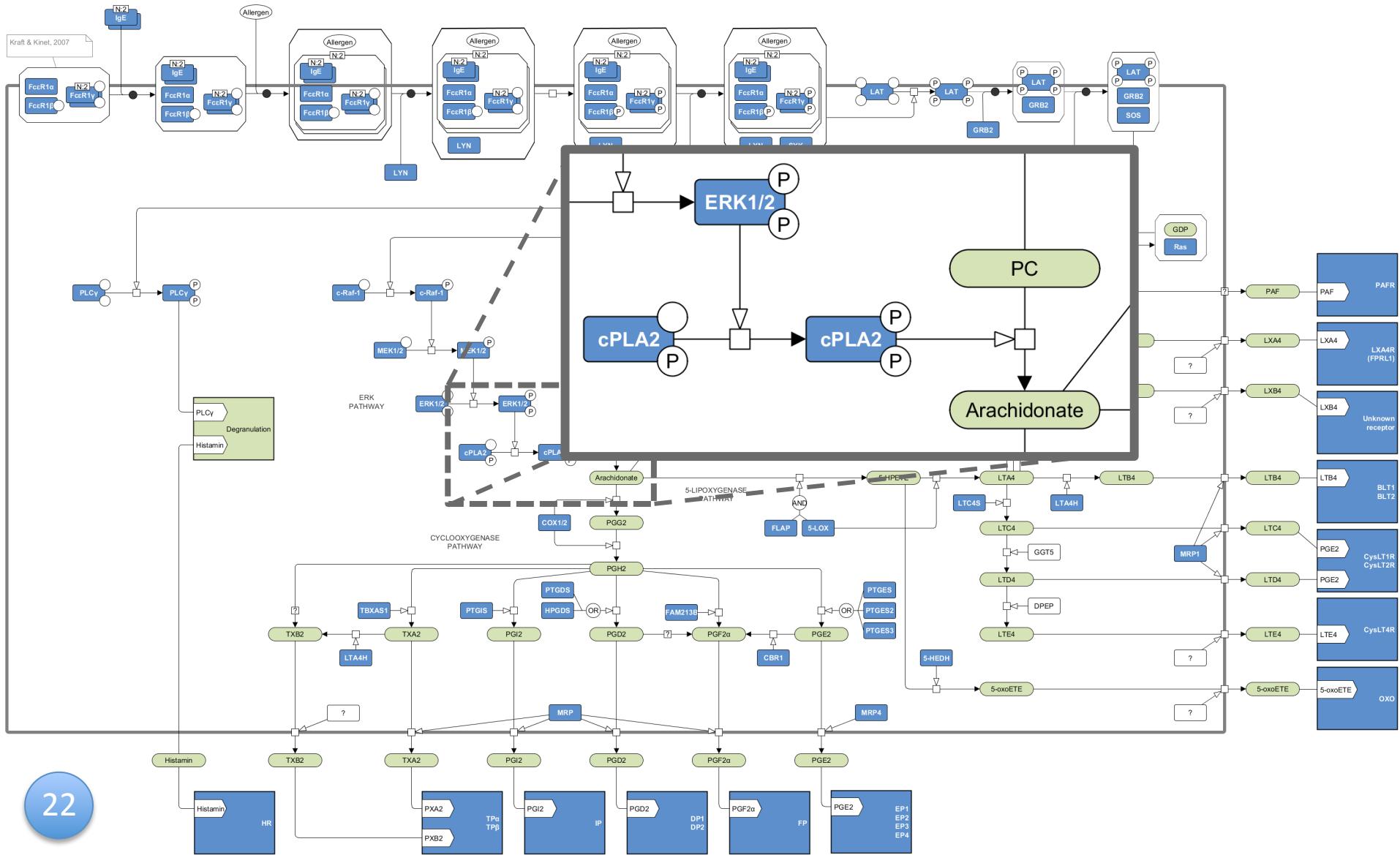


Identifying priority
pathways

Free format:
to be adopted for AF

Navigation system for
detailed diagrams

Easy-to-read unambiguous detailed diagrams



Three level of details

A bird's-eye view in SBGN Activity Flow (modified?)

Outlines in SBGN Activity Flow

Detailed diagrams in SBGN Process Description

Tranlation from SBGNML to LSCB MapViewer

Currently used

Developing diagrams in
yEd Graph Editor



Re-drawing in
CellDesigner



.xml

Uploading to LCSB
MapViewer



Uploading and
visualizing 'omics data

Translator:
CellDesinger
xml file
to LCSB
MapViewer

Proposed

Developing outlines in
yEd Graph Editor



Developing PD and AF
diagrams in SBGN-ED



.sbgn

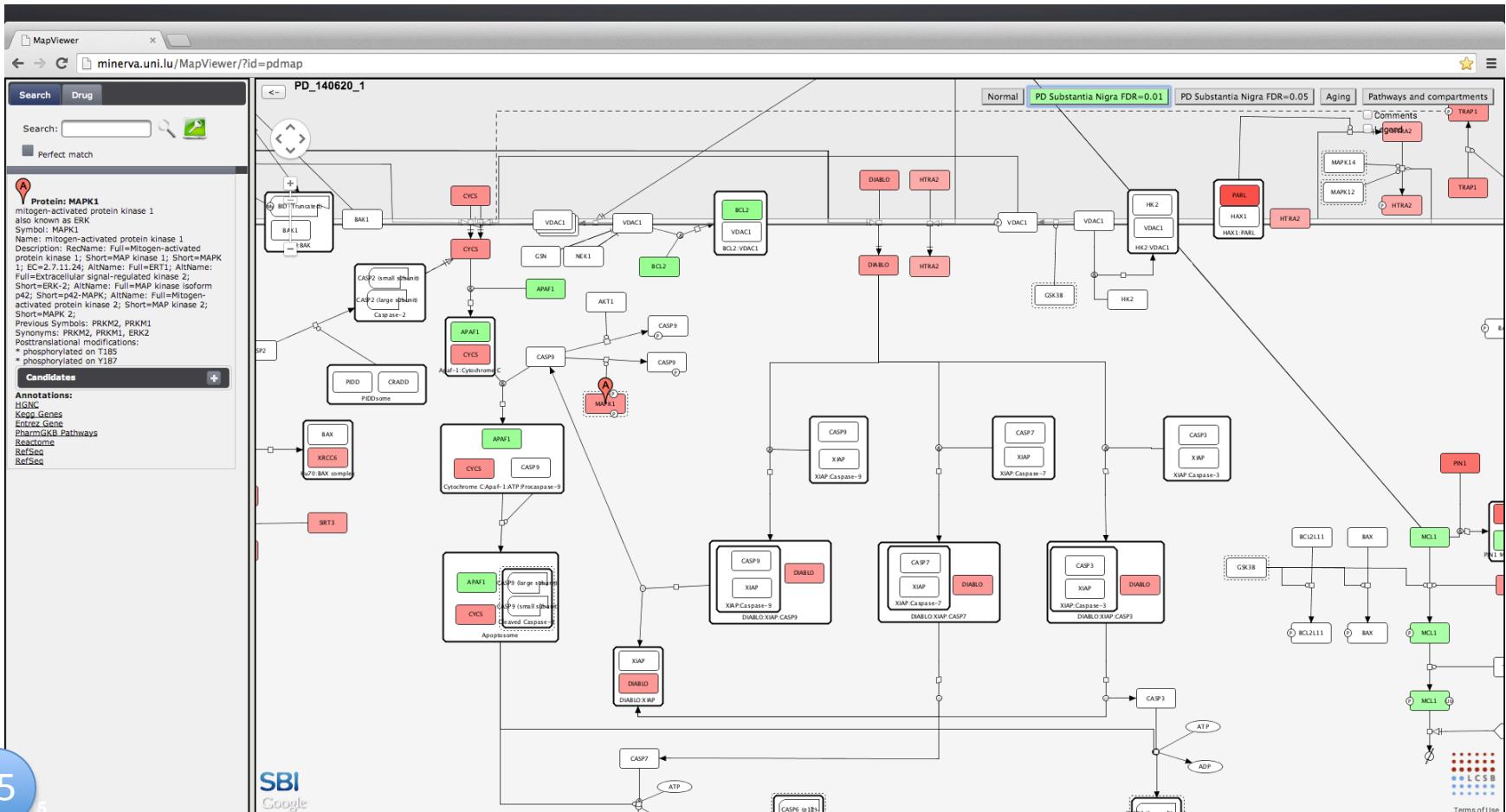
Uploading to LCSB
MapViewer



Uploading and
visualizing 'omics data

Translator:
SBGN-ML file
to LCSB
MapViewer

Parkinson's disease map



DiseaseMap: future development

Extending to maps for other respiratory diseases.

Extending to maps for other allergic/inflammatory diseases.

Collaboration with other similar efforts: Parkinson's disease map, Alzheimer's disease map, the Atlas of Cancer Signaling Networks, ...

Keeping it a highly collaborative and accessible project: sharing sub-maps and data, involving more groups that would be willing to contribute because of their interest.



Acknowledgments

Parkinson's disease map group, LCSB, Luxembourg

Marek OSTASZEWSKI
Piotr GAWRON
Stephan GEBEL
Reinhard SCHNEIDER



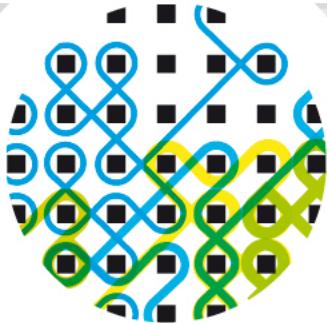
U-BIOPRED AsthmaMap Editors Committee

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Ian ADCOCK (Imperial College London)
Kian Fan CHUNG (Imperial College London)
Richard KNOWLES (U-BIOPRED)



The SBGN community





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Thank you

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