



**SmartNanoTox**

Smart Tools for Gauging Nano Hazards

Final conference  
24<sup>th</sup> June 2020



**NanoCommons**

Nano-Knowledge Community

# NanoCommons KnowledgeBase: Supporting a lasting legacy from SmartNanoTox data and models



UNIVERSITY OF  
BIRMINGHAM

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2020 Programme (H2020) under grant agreement no. 731032.*

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# NanoCommons KnowledgeBase

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- **Remove barriers** from nanosafety **regulatory and industry** processes
- Develop an **integrated Knowledgebase** to facilitate development and application of regulatory tools such as **grouping & read-across**
- Create an **interconnected community** via a **FAIR data single market**
- Enable **full exploitation of EU-funded research data** & promotion of **data driven innovation** leading to **positive socioeconomic impact**.



**Experimental Workflows  
Design & Implementation**



**Data Processing  
& Analysis**

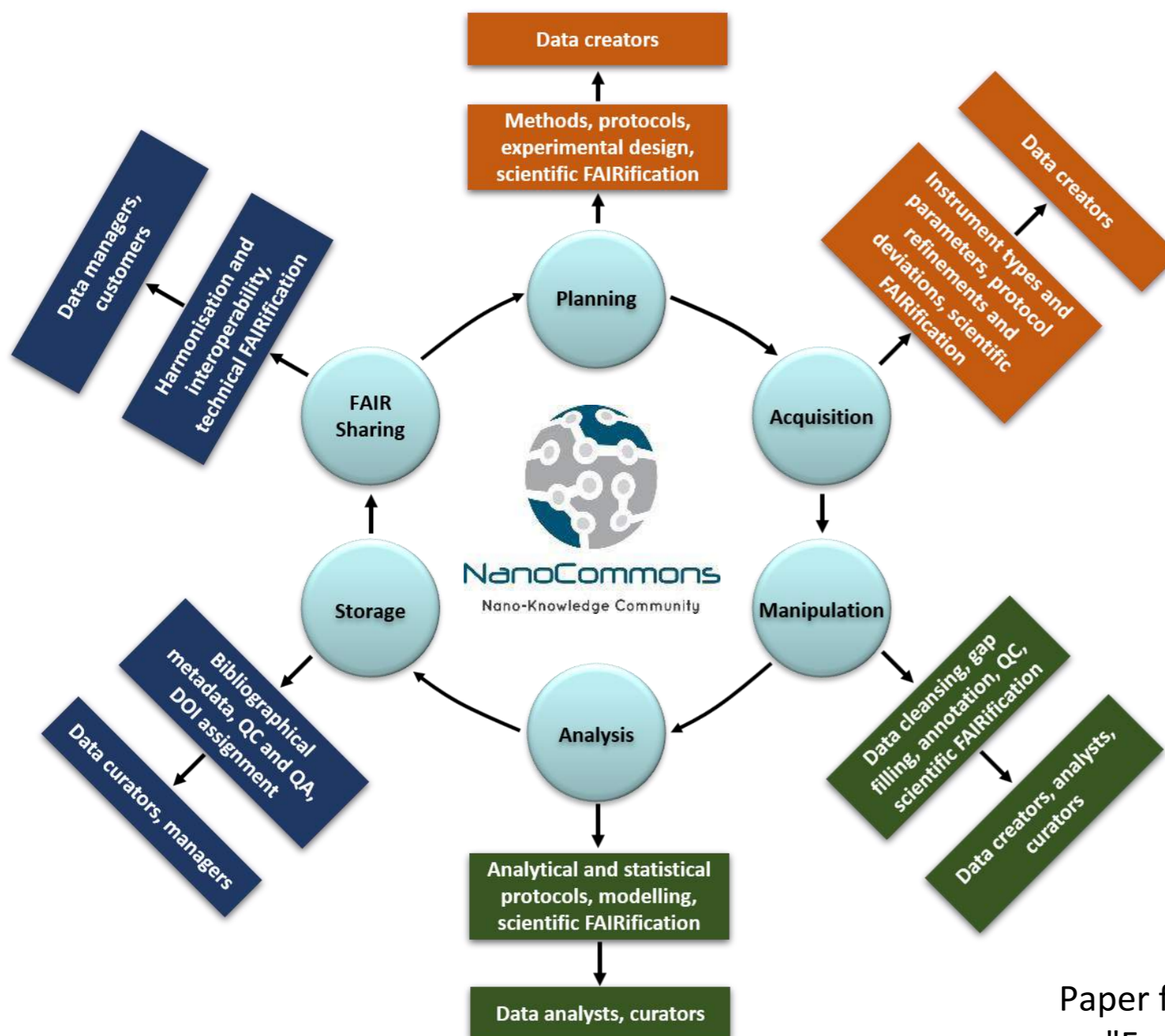


**Data Visualisation  
& Predictive Toxicity**



**Data Storage  
& Online Accessibility**

# Data lifecycle & metadata



Metadata is "data about data."

**Descriptive** metadata – assay type, cell line used, concentrations, calibrations, instrument and software parameters, etc.

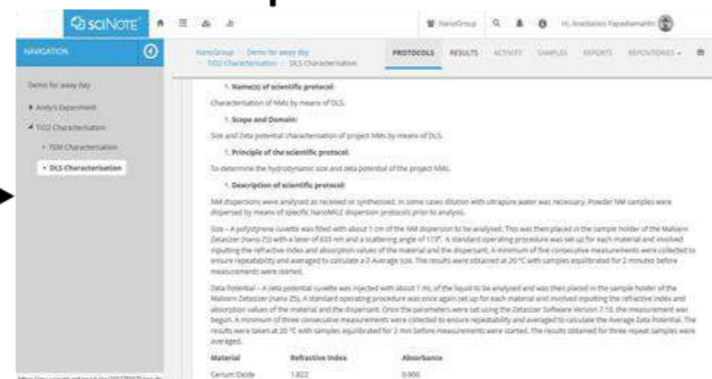
**Technical** metadata – statistical approach, data cleaning / gap filling approach etc.

**Bibliographic** metadata – who generated the data, publication information, licence information, etc.

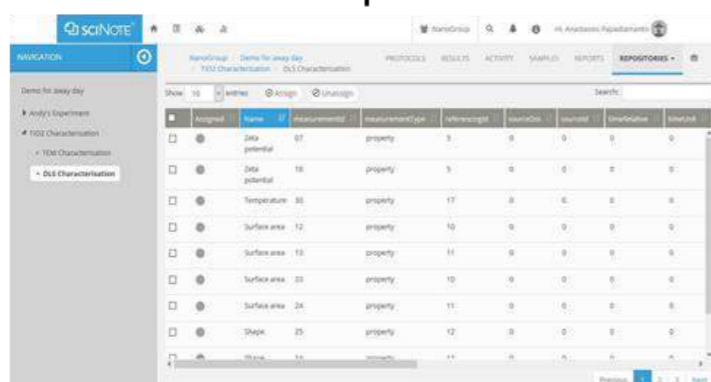
Paper for submission to Nanomaterials special issue  
"From Nanoinformatics to Nanomaterials Risk  
Assessment and Governance"

# Electronic Lab notebooks a key first step

## Experimental design and protocol implementation

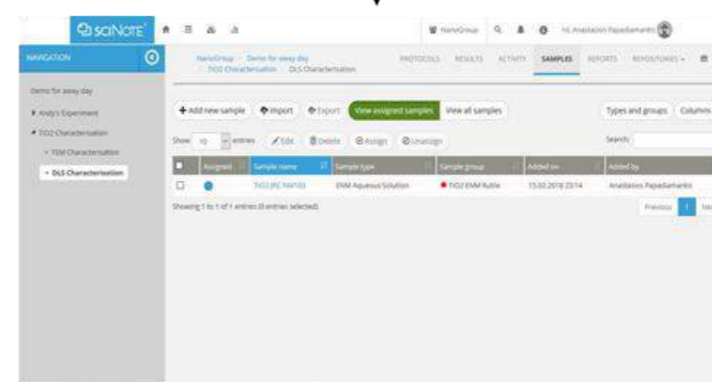


Data curation and annotation and automated extraction



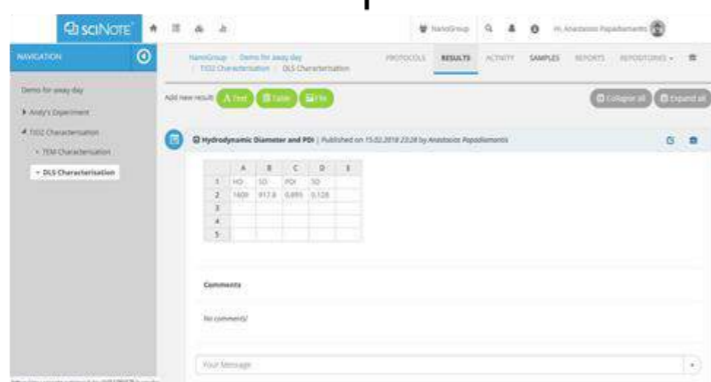
Assigned	Name	Measurement	MeasurementType	Reference	Source	Unit	Value	Uncertainty	Unit
<input type="checkbox"/>	Zeta potential	97	property	9	0	0	0	0	0
<input type="checkbox"/>	Zeta potential	16	property	9	0	0	0	0	0
<input type="checkbox"/>	Temperature	35	property	17	0	0	0	0	0
<input type="checkbox"/>	Surface area	12	property	10	0	0	0	0	0
<input type="checkbox"/>	Surface area	13	property	11	0	0	0	0	0
<input type="checkbox"/>	Surface area	23	property	10	0	0	0	0	0
<input type="checkbox"/>	Surface area	24	property	11	0	0	0	0	0
<input type="checkbox"/>	Shape	25	property	12	0	0	0	0	0
<input type="checkbox"/>	Size	14	property	11	0	0	0	0	0

Samples and endpoints implementation



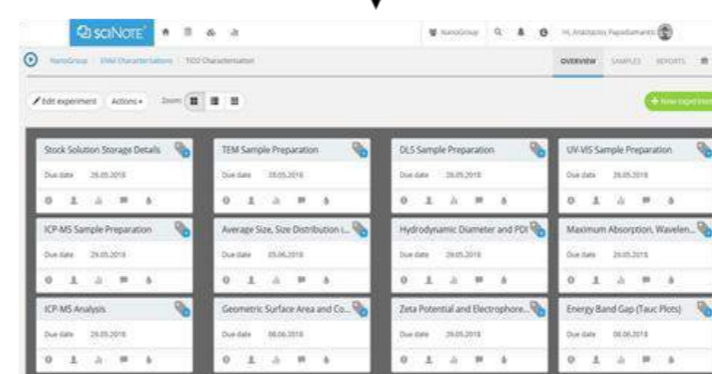
Assigned	Sample name	Sample type	Sample group	Added on	Added by
<input type="checkbox"/>	TEM Sample	EM Aquasol Solution	TEM EM Sample	15.02.2019 23:14	Academics Papadimitriou

Data acquisition



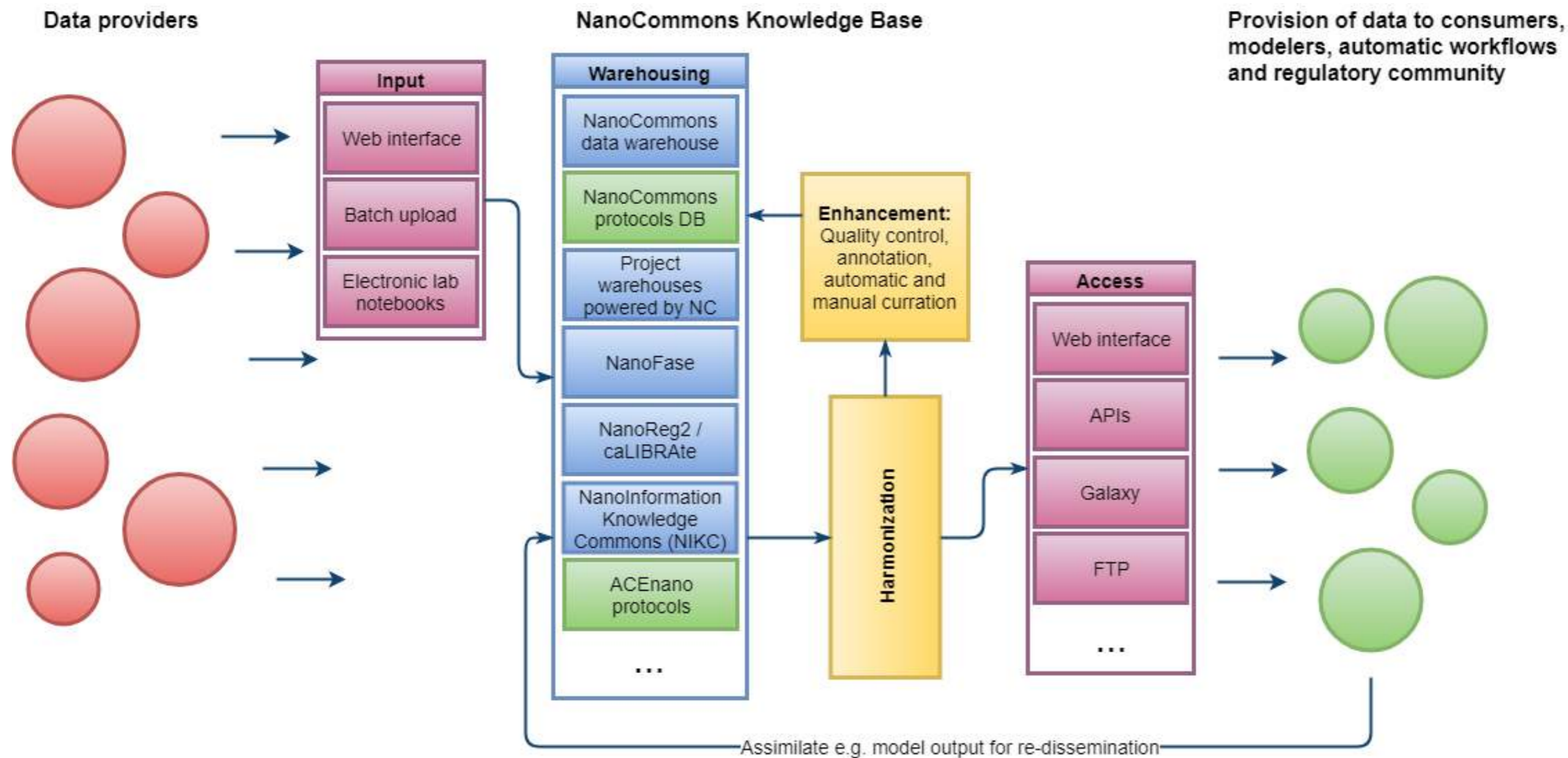
A	B	C	D	E
1	HO	SD	PDI	SD
2	1400	917.8	0.895	0.128
3				
4				
5				

Experimental workflow assignments



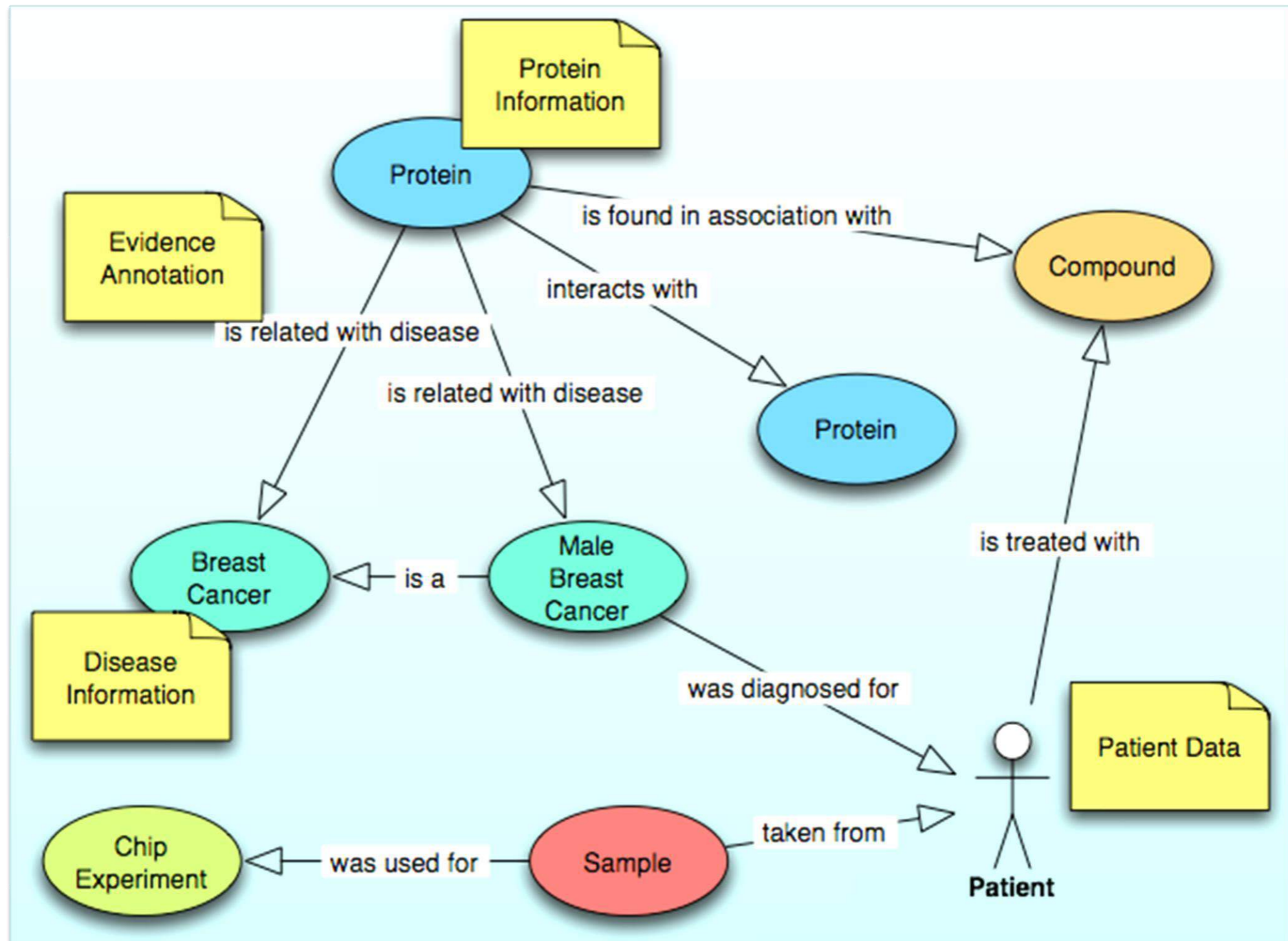
Stock Solution Storage Details	TEM Sample Preparation	DLS Sample Preparation	UV-Vis Sample Preparation
Due date: 28.05.2018	Due date: 28.05.2018	Due date: 28.05.2018	Due date: 28.05.2018
ICP-MS Sample Preparation	Average Size, Size Distribution L...	Hydrodynamic Diameter and PDI	Maximum Absorption, Wavelength
Due date: 28.05.2018	Due date: 05.06.2018	Due date: 28.05.2018	Due date: 28.05.2018
ICP-MS Analysis	Geometric Surface Area and Co...	Zeta Potential and Electrophoresis	Energy Band Gap (Tauc Plots)
Due date: 28.05.2018	Due date: 06.06.2018	Due date: 28.05.2018	Due date: 06.06.2018

# NanoCommons KB Architecture concept

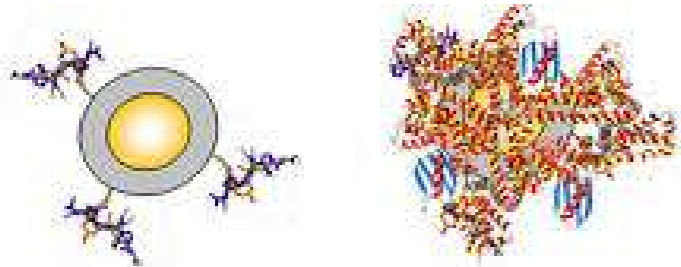


# Knowledge management - handling complexity

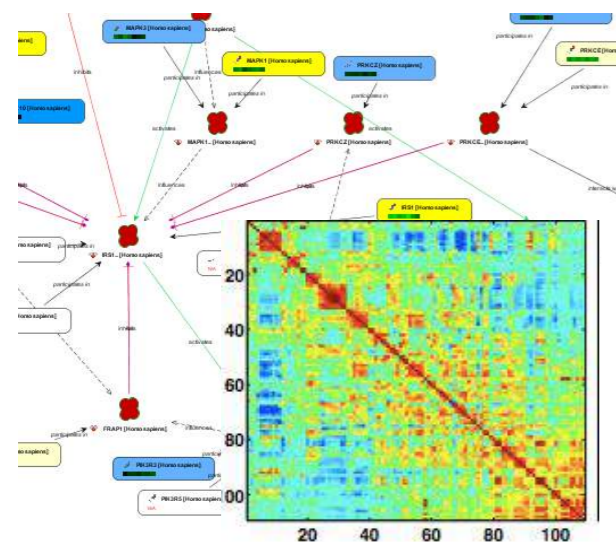
## Semantic Model



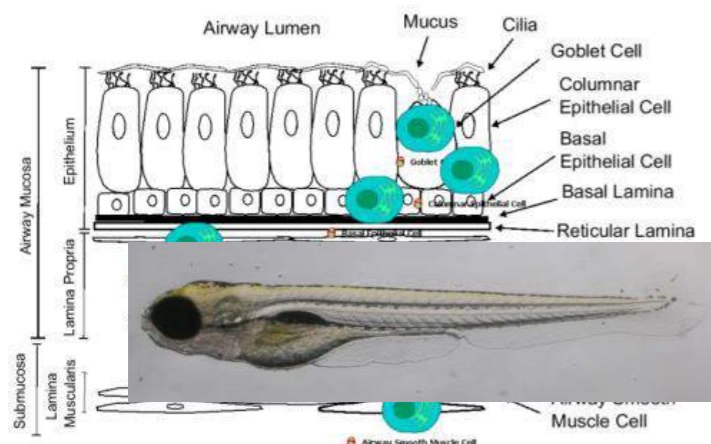
# Coupling data and applications



## Particle characterisation

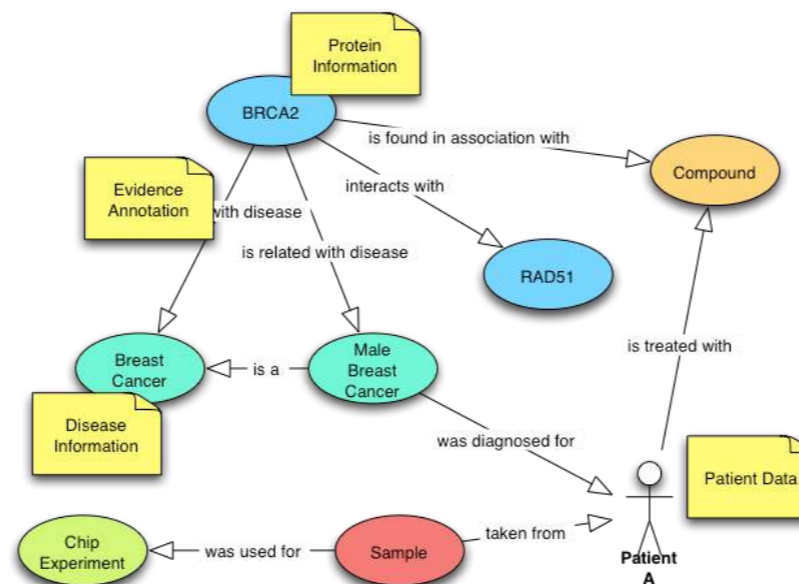


## Molecular "omics" data and prior knowledge

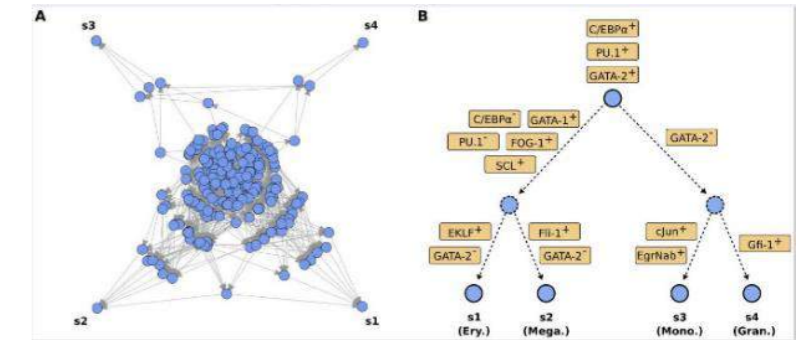


## Classical Toxicology

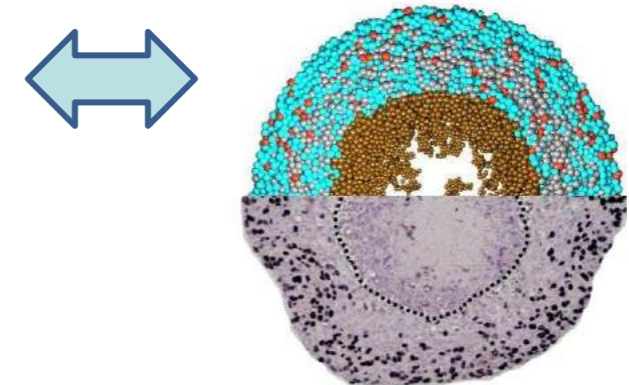
## Knowledge management Semantic Model



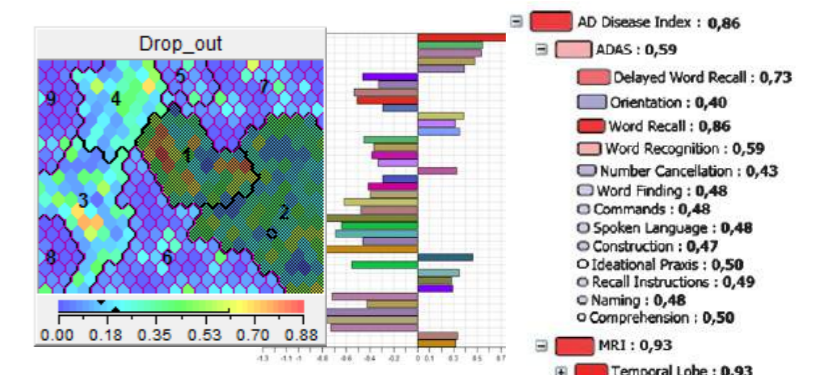
## Network inference and data analysis



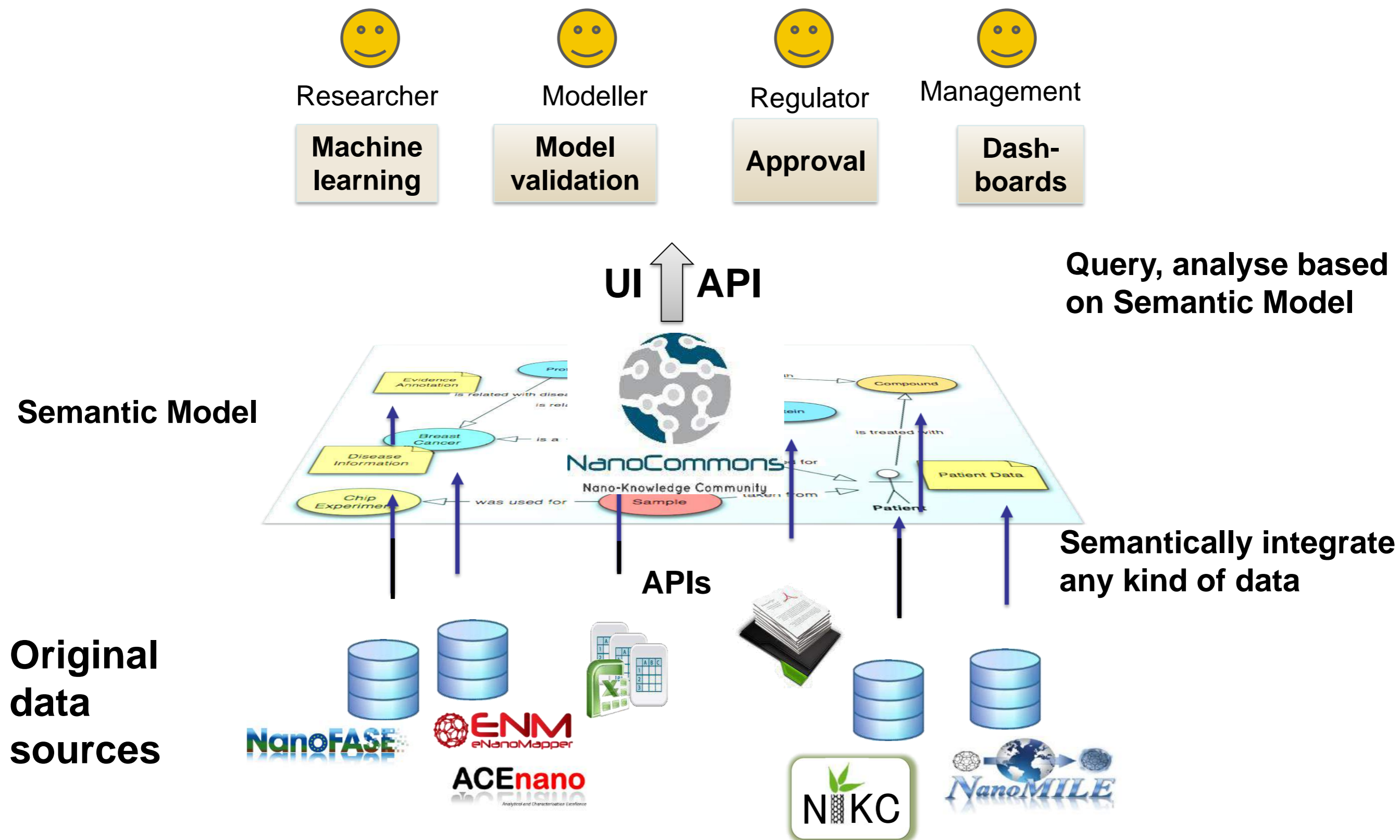
## Computational Simulation



## Biomarker profile



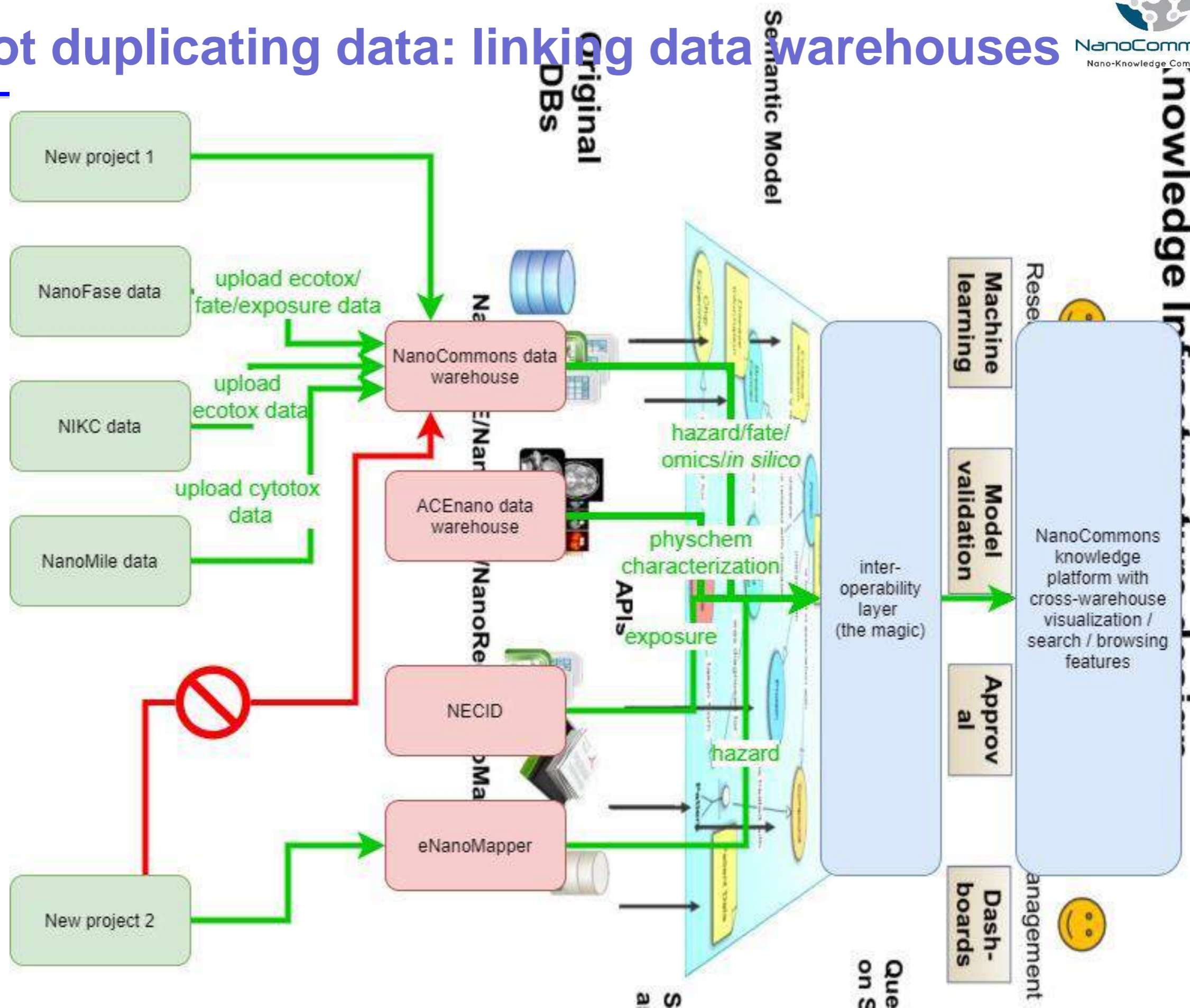
# Semantic Model for integration and interoperability





NanoCommons  
Nano-Knowledge Community

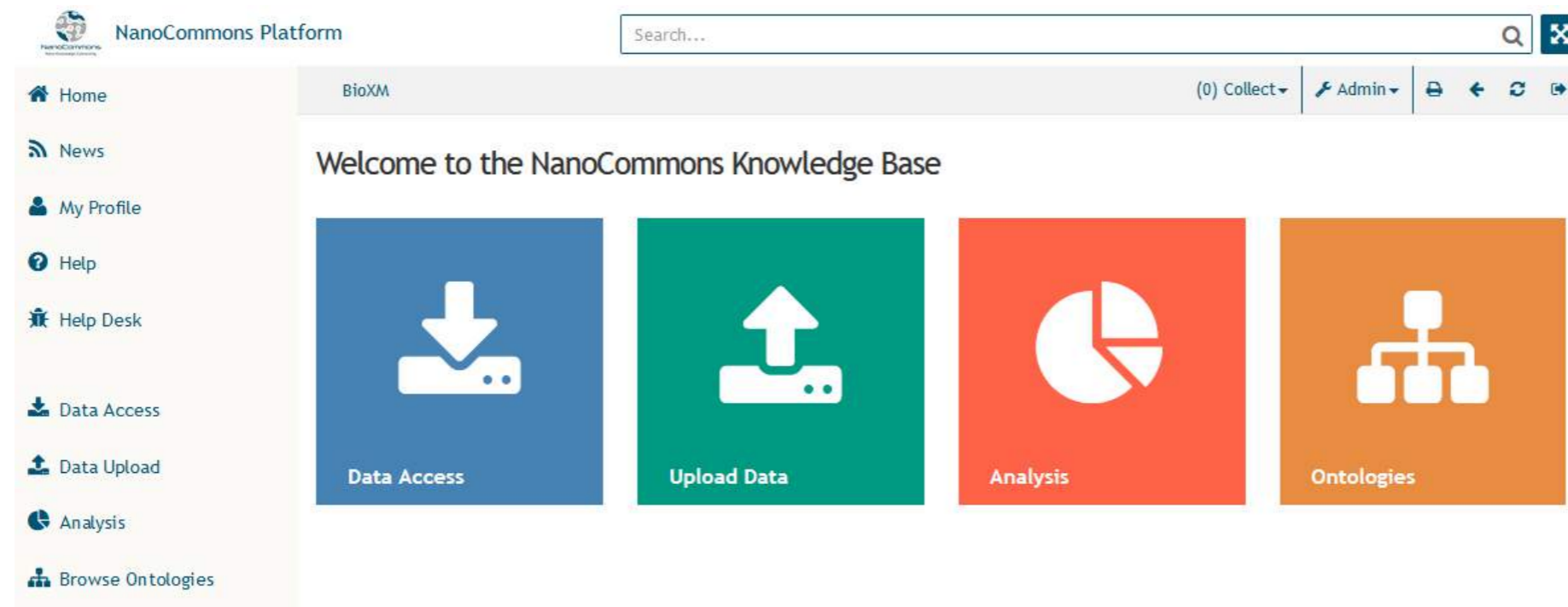
# Not duplicating data: linking data warehouses



# NanoCommons Knowledge Base - Content



<https://ssl.biomax.de/nanocommons>



~500 Particles, Phys-Chem Characterisations, Protocols, Toxicology Experiments, Omics, Mesocosm from NanoMILE/NanoFASE (NanoMILE data freely available, NanoFASE data embargoed 2 years (DTA available))

In-silico descriptors, Corona predictions, groupings, alerts from NanoCommons / NanoSolveIT

Literature mined datasets (>250 studies) relating to > 350 particles

Expanding rapidly via ongoing TA projects.....

# Services - Data Sustainability beyond Archives

## Archive:

- Data store
- Metadata (Description)



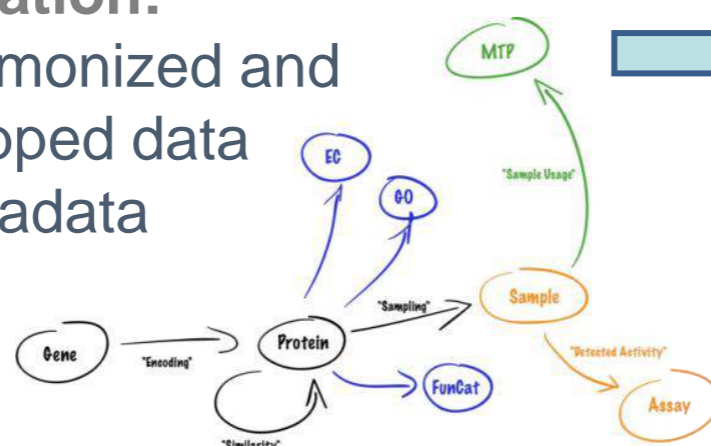
## Functions:

- Browse
- Search
- Retrieve
- Analyse



## Semantic integration:

- Harmonized and mapped data
- Metadata



## Functions:

- Navigate along connections
- Combine molecular, phenotype and environmental Information
- Visualize



## Enrichment with e.g. Biological knowledge or Environmental Data

- Genomes
- Pathways
- Protein-protein-interactions
- Transcription factor network
- Water/Soil chemistry (pH, ionic strength, NOM)
- Co-pollutants
- Species distributions / sensitivities
- Long range trends / future predictions

# Data sustainability – beyond archives

## Archive:

- Data store
- Metadata (Description)



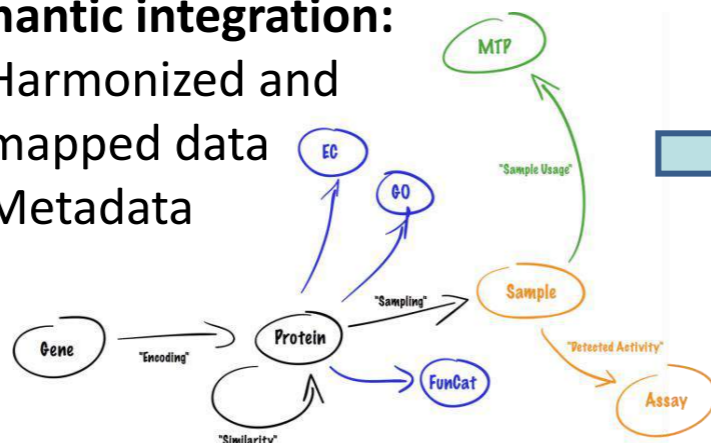
## Functions:

- Browse
- Search
- Retrieve
- Analyse



## Semantic integration:

- Harmonized and mapped data
- Metadata



## Functions:

- Navigate along connections
- Combine molecular, phenotype and environmental Information
- Visualize

## Example NanoMILE/NanoFASE knowledge base content:

- |   |  |
|---|--|
| <ul style="list-style-type: none"> <li>• Genomes</li> <li>• Pathways</li> <li>• Protein-protein-interactions</li> <li>• Transcription factor network</li> </ul> | <ul style="list-style-type: none"> <li>• Particles</li> <li>• Orders/procurement</li> <li>• Material safety sheets</li> <li>• Ecotoxicological data</li> <li>• 'Omics</li> </ul> |
|---|--|



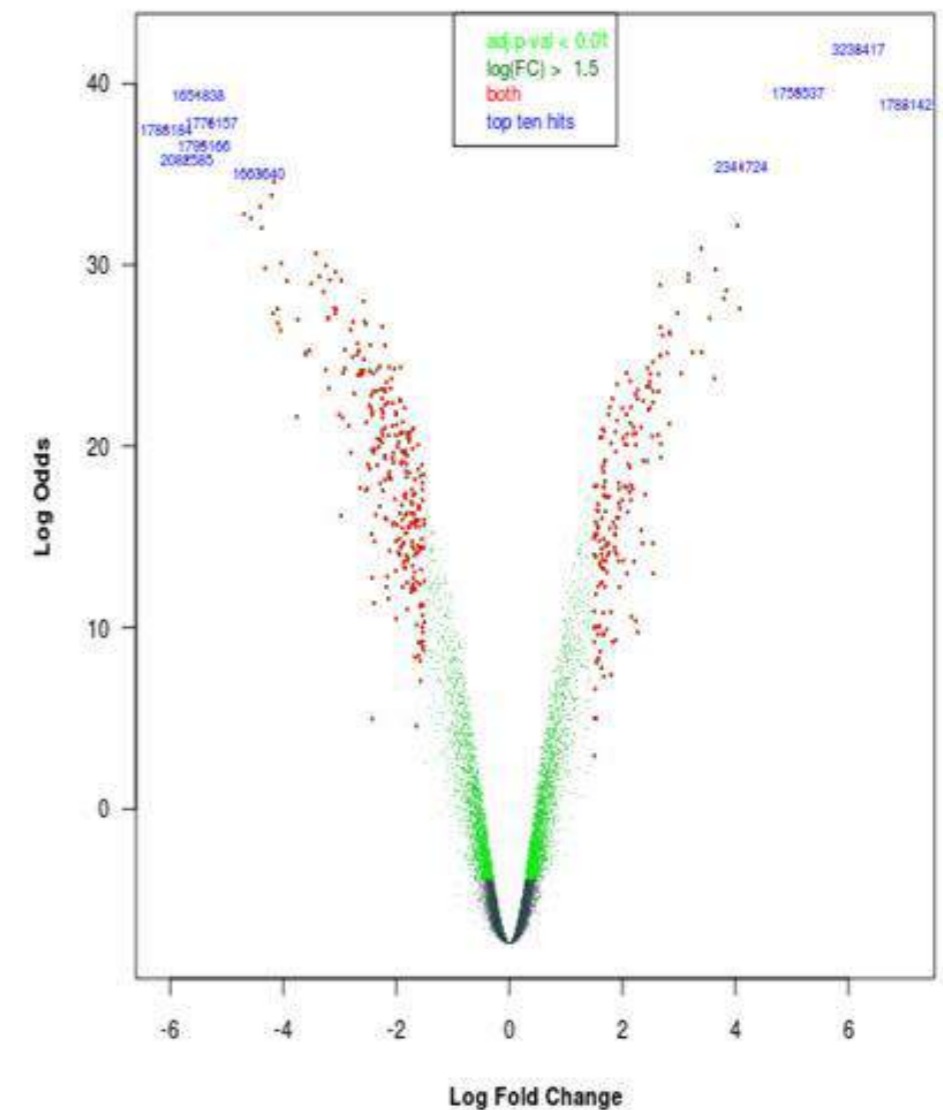
# Integrated Services – Differential Expression analysis

## Analysis RNA-Seq Differential Expression

Analysis RNA-Seq Differential Expression

LIMIT	2.2.1 Limit 50	x	✓
PVAL	2.3.1 p-value 0.05	x	✓
LogFC	2.4.1 Foldchange 1.5	x	✓
Adjust	2.5.1 Adjust p-value for multiple testing by Benjamini Hochberg	x	✓
Cutoff	10		
Group1	A549_AgNO3_01hrs_3Rep A549_AgNO3_01hrs_1Rep	A549_AgNO3_01hrs_4Rep A549_AgNO3_01hrs_2Rep	x ✓
Group2	A549_AgNO3_06hrs_1Rep A549_AgNO3_06hrs_3Rep	A549_AgNO3_06hrs_2Rep A549_AgNO3_06hrs_4Rep	x ✓
Group3	A549_AgNO3_24hrs_1Rep A549_AgNO3_24hrs_3Rep	A549_AgNO3_24hrs_2Rep A549_AgNO3_24hrs_4Rep	x ✓

Volcanoplot for contrasts: Group1-Group4



# Integrated Services – Corona model

## Corona Analysis Overview

[+ New Analysis Run](#)

[Task Manager](#)

Per page: **25** Results: 4





















Filter results by:

 Analysis ID 

 Apply

[+ Add Filter](#)

Show/Hide  Sort by 

					Analysis Results	
Analysis ID	NanoParticle ID	Protein ID	Analysis Start	Started by User	Heatmap	Mapping
 Analysis-0000000098	 NP00477	 Q9GU57	19.02.2020 13:49:22	 martinz		1IXT_gold_12_16.map
 Analysis-0000000102	 NP00728	 P04264	21.02.2020 18:17:13	 dm_admin		6E2J_tio2_anatase_25_12.map
 Analysis-0000000107	 NP00478	 Q16696	24.02.2020 09:46:18	 martinz		3T3S_sio2_amorphous_12_-8.map
 Analysis-0000000202	 NP00477	 Q9AHD4	28.02.2020 10:20:48	 martinz		3QY8_gold_12_16.map

# Integrated Services – Corona model

Select Input for **Analysis-0000000046**

## Nanoparticle

Add Remove

## Protein

Add Remove

Cancel Analysis

Confirm Input for **Analysis-0000000046**

## NanoParticles Input

1 NanoParticle selected: NP00809  
Selected number of NanoParticles OK

## Protein Input

2 Proteins selected: P06276  
Q9BV73  
Please select exactly one Protein

Adjust Input

Add Objects

Results: 15 Per page: 25

Names

au

▼ Search

➕ Add

☐ Selected items: 0

Show/Hide ▼

Sort by ▼

	Particle ID	NanoFASE name	Designator	Names
<div><div><div>+</div><div></div></div><div><input type="checkbox"/></div></div>	NP00812	Au carboxylic acid-functionalized (JRC)		Au carboxylic acid-functionalized (JRC)
<div><div><div>+</div><div></div></div><div><input type="checkbox"/></div></div>	NP00811	Au amino-functionalized (JRC)		Au amino-functionalized (JRC)
<div><div><div>+</div><div></div></div><div><input type="checkbox"/></div></div>	NP00810	Au amino-functionalized (JRC)		Au amino-functionalized (JRC)
<div><div><div>+</div><div></div></div><div><input type="checkbox"/></div></div>	NP00809	Au pristine		Au pristine
<div><div><div>+</div><div></div></div><div><input type="checkbox"/></div></div>	NP00741			Au50-UoB;Au50-UoB Citrate capped
<div><div><div>+</div><div></div></div><div><input type="checkbox"/></div></div>	NP00740			Au20-UoB;Au20-UoB Citrate capped
<div><div><div>+</div><div></div></div><div><input type="checkbox"/></div></div>	NP00739			BBIAu80;BBIAu80-Citrate
<div><div><div>+</div><div></div></div><div><input type="checkbox"/></div></div>	NP00738			BBIAu60;BBIAu60-Citrate
<div><div><div>+</div><div></div></div><div><input type="checkbox"/></div></div>	NP00737			BBIAu20;BBIAu20-Citrate
<div><div><div>+</div><div></div></div><div><input type="checkbox"/></div></div>	NP00709	Aust-Ag2S	Aust-Ag2S	Aust-Ag2S
<div><div><div>+</div><div></div></div><div><input type="checkbox"/></div></div>	NP00480			Au_PEG-COOH;IO166E Gold 12 nm PEG-COOH
<div><div><div>+</div><div></div></div><div><input type="checkbox"/></div></div>	NP00479			Au_PEG-OMe;IO166D Gold 12 nm PEG-OMe
<div><div><div>+</div><div></div></div><div><input type="checkbox"/></div></div>	NP00478			Au_PEG-OH/PEG-OMe(50:50)


Add

Close

Add Close

# Integrated Services – Corona model


## Nanoparticle NP00477

NanoParticle	 <a href="#">NP00477</a>
Names	Au_PEG-OH; IO166B Gold 12 nm PEG-OH
Description	

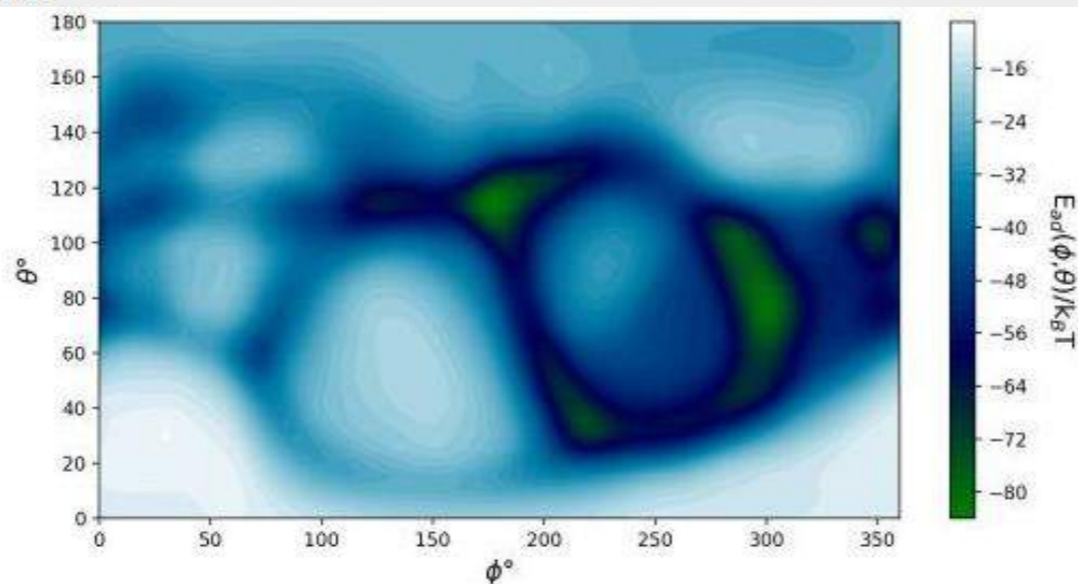
## Protein Q9GU57


Protein	 <a href="#">Q9GU57</a>
ProteinName	Conotoxin Gm9.1


## PDB Structure 1IXT

PDB ID	<a href="#">1IXT</a> 
Description	structure of a novel p-superfamily spasmodic conotoxin reveals an inhibitory cystine knot motif

## Size & Zeta Potential



Mapping:  [1IXT\\_gold\\_12\\_16.map](#)

LogFile:  [Analysis-0000000098.log](#)

# Next steps in supporting SmartNanoTox

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TA project already underway for SmartNanoTox Experimental data

TA **in development** for computational data and models:

1. Missing a lot of the ontology terms needed for modelling:



**Wiki** to define the terms (with nanoinformatics project experts / EMMC)

**On the fly** annotation using agreed terms (while they are being formalized into ontologies, e.g. ENM)

2. Developing tool for harmonization of MODA templates:



Questionnaire format with drop-down menus (as already done for SOPs)

3. Inputting the computational materials / data into KnowledgeBase

Preserving the



**SmartNanoTox**  
Smart Tools for Gauging Nano Hazards

legacy through open &  
FAIR data

# Acknowledgements & Thanks

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**Edelweiss  
Connect**



**Biomax**  
INFORMATICS



**LEiTAT**  
Technological Center



## Knowledge Base with FAIR data

- Metadata fully searchable (including Ontologies e.g. NCBI Taxon, GO, eNMP)
- API based data access (Jaqpot)
- Generation of ontological descriptors for data
- Data upload & download in a format suitable for modelling
- Tool integration (Expression analysis, Modelling)