

# Tracking of Research Results (TRR) to support R&I Policy Making

Semantic Data Linking from Multiple Heterogeneous Sources

Intelcomp

A COMPETITIVE INTELLIGENCE CLOUD/HPC PLATFORM FOR AI-BASED STI POLICY MAKING (GRANT AGREEMENT NUMBER 101004870)

Opening event  
27 April 2021



# Context



## Tracking of data beyond the duration of the projects for policy making

### Output data:

need to be accurate even when monitoring data are not available (ind. 1-4 + 14)

### Performance of researchers and organizations:

need to be tracked post-implementation (ind. 5-10)

### Insights:

can/could be derived about the impact (ind. 11-13)



## Issue



Because Policy priorities changes



Future data needs are NOT known



New type of evidence need to be produced



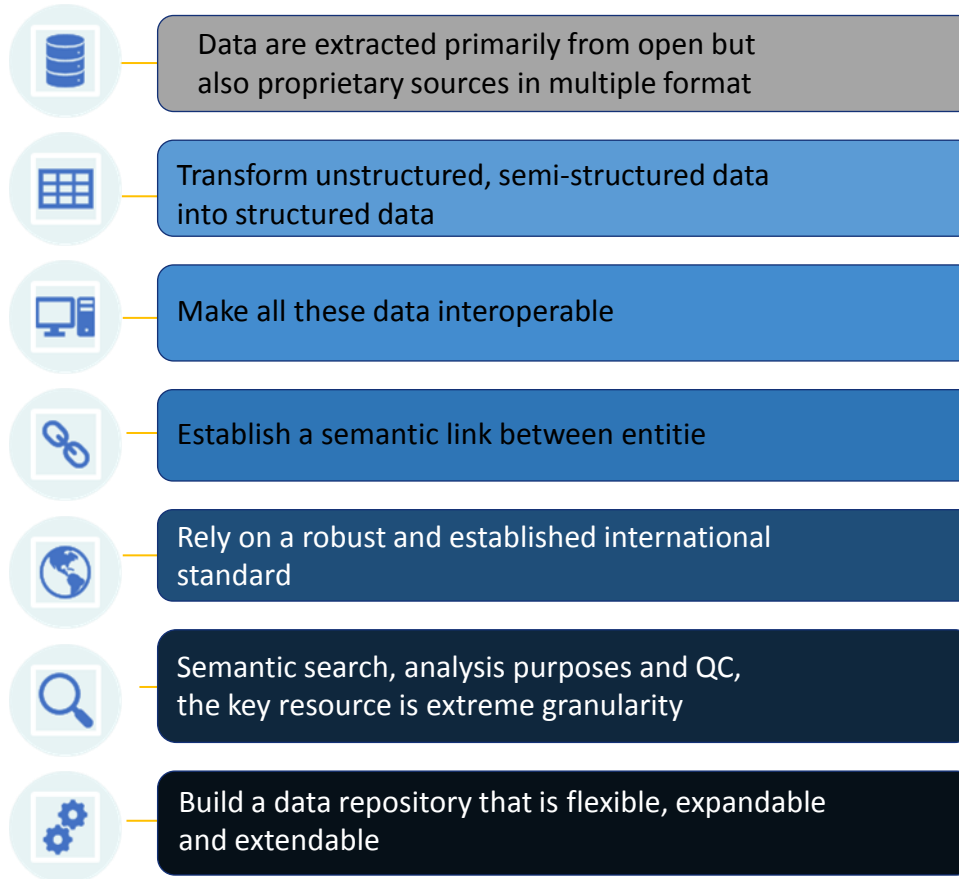
## Solution



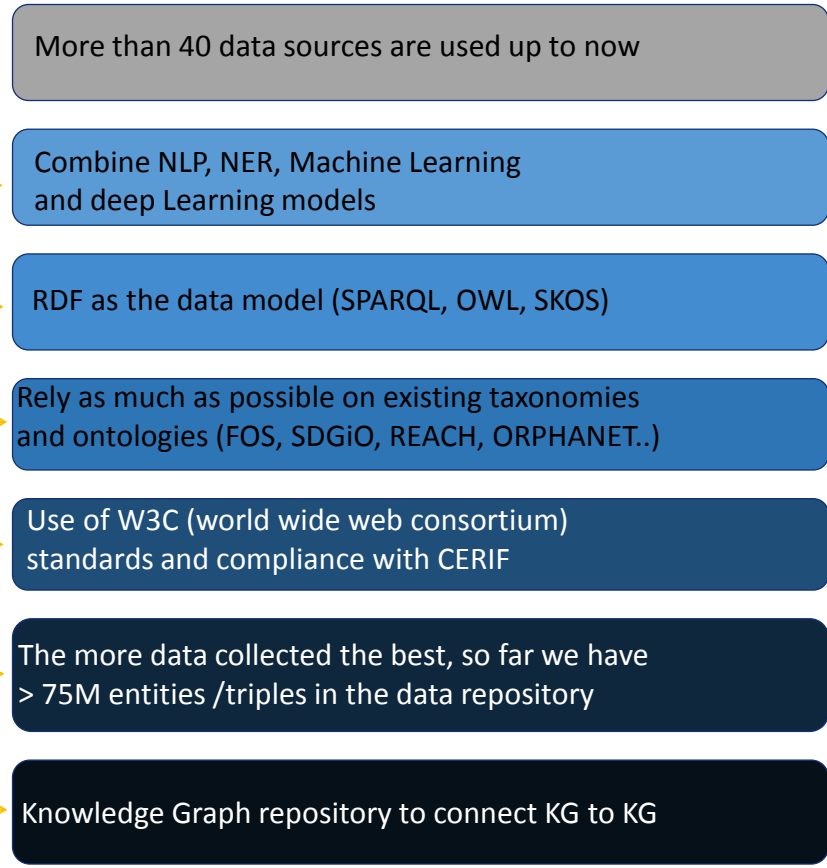
TRR use a bottom up approach on highly disaggregated (to the lowest possible denominator) data that can be later aggregated for the preferred indicator

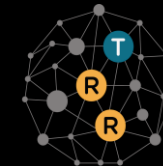
# Methodology

## What is needed?

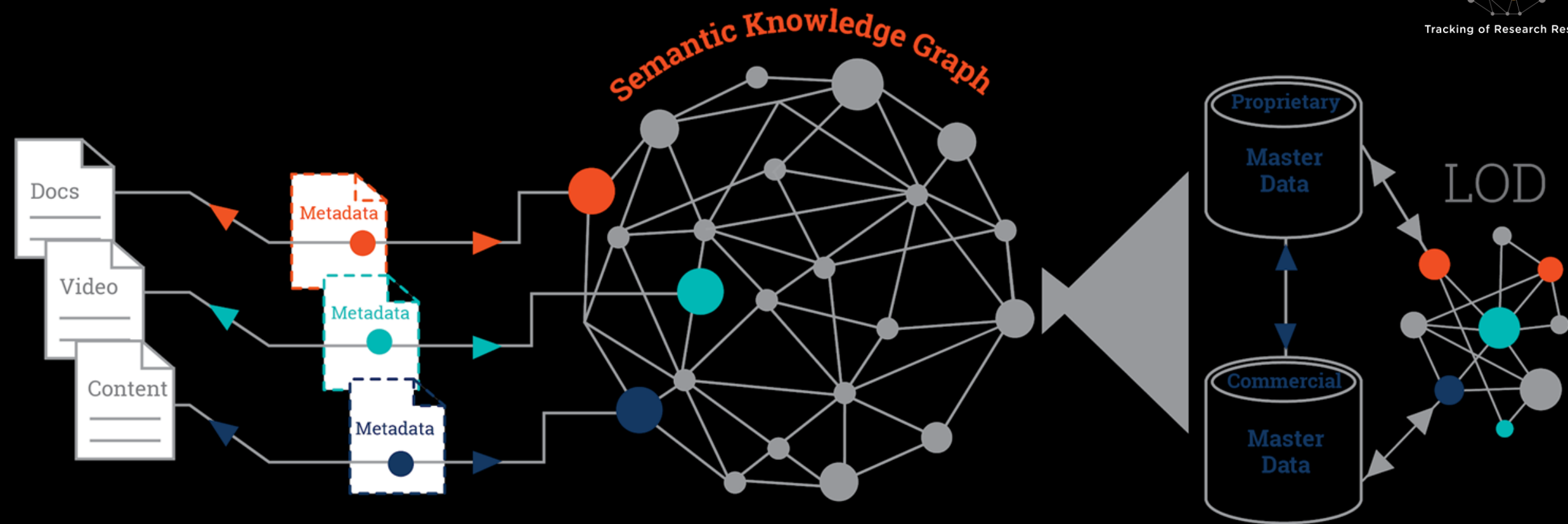


## How id we address it?





Tracking of Research Results



## Build a Knowledge Graph, Integrate Data

Visualization is not considered as an output but an input for output we have charts and tables

The problems of scale are compounded by other challenges such as the breadth of topics covered, their jargon specific to each field and the changes in meanings of phrases over time.

Data Integration

Master Data Management

Information Discovery

Open Data



European  
Commission

+

○

**Ask less,  
ask anything (bar)  
TRR  
philosophy: a  
few key points**

Unique coverage of data sources, with an aim to link them through specific entities

All key entities are tracked: researchers, organisations, projects

Coverage of all key stages of the R&I lifecycle

Tracking FP entities across time, incl. beyond the end of funding -> all output is relevant

Capture quasi-FP innovation sphere

Not just FP data -> better understand & benchmark

First projects to track data to medium- and long-term economic and societal/health impacts

Link previous project activities to events that happened recently

Tracking event/news data -> who, what, where in my vicinity doing what?

New indicators and line of thinking

1. Outputs, products and interventions

2. Collaborations

3. Scientific publications

4. Intellectual property rights

14. Scientific prizes

5. Innovation

6. Dissemination activities

7. Further funding/investment

8. Next destinations

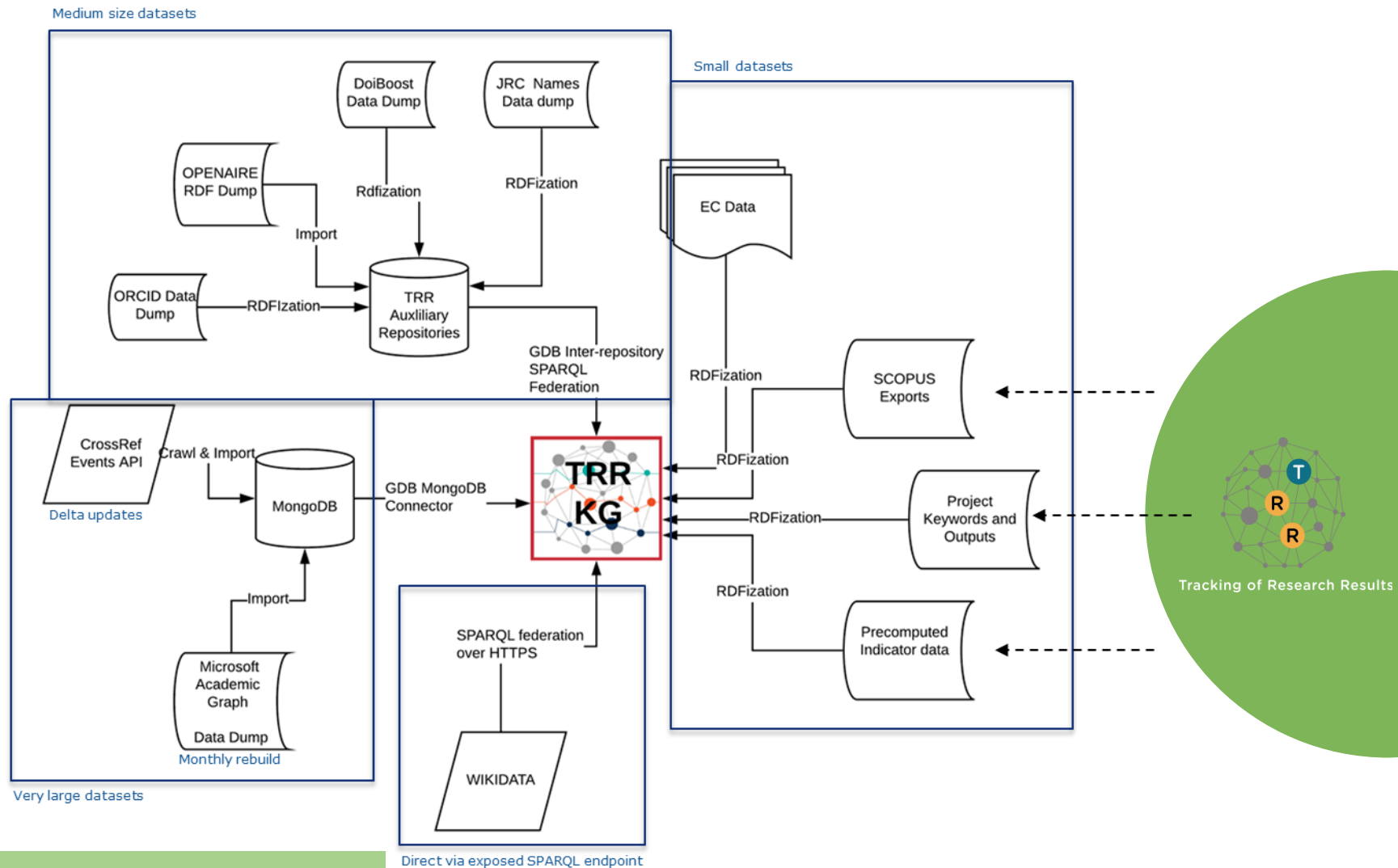
9. Effects on the company /private sector

10. New companies created

**11. Impact on health and welfare/health and environmental impacts**

12. Impacts on creativity, culture & society/social, economic, capability and cultural impact

13. Influence on policy making/political impact





One multi-faceted, interlinked data infrastructure for all use cases

Because the underlying data is harmonised and curated in a Knowledge Graph repository , it is also *flexible and expandable* in how it can be used, and what it can be used for.

R&I: bottom-up and multidisciplinary  
Missions oriented policies will be top-down and multidisciplinary

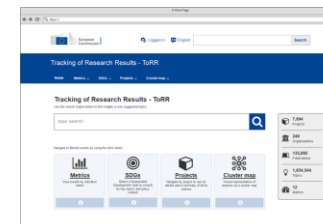


Discover

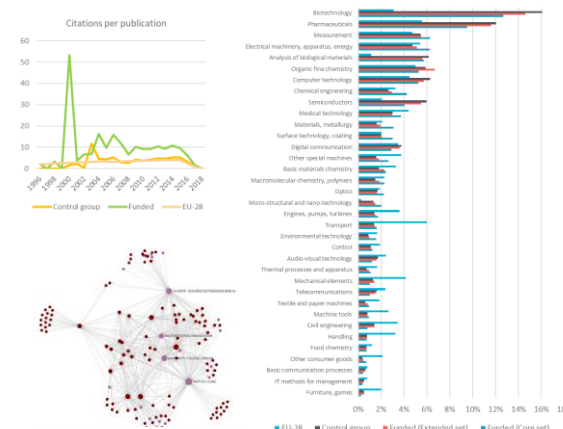
Analyse and Report

Direct Access to Data

« Ask anything » semantic queries



Metrics and Indicators



Bulk downloads

Project ID		META DATA	
Funding Scheme	FP7 HEALTH	Acronym	CRUMBS IN SIGHT
Number of Participants	6	EU Contribution	€ 3.0 mil.
		Participant Organizations	KNAW, AMT, RUMC, MPG, CNRS, USFD, EKUT
Insights extracted from project reports			
200234_mouse: Crlb knockout mice, Crlb Crlb double knock out mice, conditional knockdown mice, Mpg conditional knockout cKO mice, Mpg cKO mice, Crlb / Crlbfl ChaoCrlb mice, conditional Crlb knockout mice, double knockout mice			
200234_vector: pharmaceutical CRB gene therapy vector, Gene therapy vector, CRB Gene Therapy Vector, CRB gene therapy vector, AAV HCRB gene therapy vectors, AAV26 HCRB clinical gene therapy vector, gene therapy vectors and Müller glia progenitor cell therapy, clinical AAV HCRB gene therapy vector, clinical AAV26 HCRB gene therapy vectors			
200234_mutant: Crlb mutants			
200234_serotype: AAV serotype			
200234_platform: baculovirus production platform for the AAV's serotype			
Thematic Key-words / Phrases: Müller-glia-cells, CRB, photoreceptor, cell, retina, protein, gene-therapy, adheren-junction, eye-disease, retinal-degeneration, knock-out-mouse, eye, membrane			
Named Entities / IPR		Additional Attributes	
AAV, AAV1, AAV26, CRB, CRB1, CRB2, CRB3, CRB4, HCRB, HCRB1, HCRB2, HCRB3, Crlb / Crlbfl ChaoCrlb		Biology, Cell-Biology, Anatomy, Genetics, Retina, Molecular-Biology, Retinal-Degeneration	
Fields of Study / Themes		SDG 3 - Good Health and Wellbeing	
Relevant SDGs			





**COLLABORATION:  
A KEY TO UNLOCK  
THE CHALLENGES OF  
RARE DISEASES RESEARCH**

FEBRUARY 2021



**Rare diseases**

A staggering 6000 to 8000 life-threatening, or chronically debilitating, rare diseases that each one affect less than 5 in 10,000 persons. It is estimated that altogether rare diseases affect more than 30 million people in the European Union. Many rare diseases manifest themselves in childhood, resulting in a shortened lifespan and leading to a dependency on care throughout the patients' lives, causing significant suffering to the patients and their families. Patients affected by rare diseases often spend years enduring a "diagnostic odyssey" before receiving the correct diagnosis, if ever.

Most rare diseases lack effective treatments representing an enormous unmet medical need. Rare disease patients often need highly specialised health care and social services resulting in high costs for their families and for society.

Each rare disease affects a small number of people, each with its specificities, leading to scarcity and fragmentation of knowledge and expertise. This is why rare diseases are recognised as a field where European and international collaboration is indispensable to improve diagnosis and find treatments.



**EU funded research on rare diseases**

The EU facilitates the formation of multidisciplinary consortia with participants from universities, research organisations, healthcare providers, SMEs, industry and patient organisations from across Europe and beyond.

Over the past 14 years, the EU has supported this field extensively through its Framework Programmes for Research and Innovation with more than €2.4 billion attributed to over 800 research and innovation projects. Research on rare diseases is supported by FP7 (2007-2013) and continues to be supported in Horizon 2020 (2014-2020) in various ways with the majority of the funds directed towards collaborative research projects (consortia) under the Health theme and the Health-Social Challenge respectively. Furthermore, the European Research Council (ERC), the Marie Skłodowska-Curie Actions and the European research infrastructures programmes including other actions have also supported research into rare diseases.

The majority of these funds, more than €1.8 billion are attributed to over than 320 interdisciplinary, transnational consortia bringing together the complementary expertise needed, which no individual research institution and country could possess alone.

**Research and innovation**



## EU contribution to rare diseases and orphan designations:

### key statistics by disease term



Contact: Sergio Di VIRGILIO, June 2020

### Overview of drug legislation for rare diseases in international jurisdictions

Region/ country	Criteria for defining rare disease, population (%) <sup>8,9</sup>	No. of designated orphan drugs (effective date)	No. of drugs approved <sup>2</sup> (effective date)	Legislation (supervising body) <sup>10</sup>	Elements of drug legislation for rare diseases <sup>9,10</sup>				
					Tax incentives	Fast- tracking of drug evaluation	Marketing exclusivity (yr)	Technical assistance to obtain approval	Other
Australia	≤ 2000 (0.01)	180 (2010) <sup>11</sup>	62 (2010) <sup>11</sup>	Australian Orphan Drugs Program (1997) (Therapeutic Goods Administration)	No	Yes	Yes (5)	Yes	Applications reconsidered every 12 months
European Union	5/10 000 <sup>1</sup> (0.05)	664 (2010) <sup>12</sup>	51 (2010) <sup>12</sup>	Regulation No. 141/2000 (2000) (European Medicines Evaluation Agency)	Yes	Yes	Yes (10)	Yes	Not applicable
Japan	≤ 50 000 (0.04)	167 (2004) <sup>10</sup>	95 (2004) <sup>10</sup>	Orphan Drug Regulation (1993) (Ministry of Health, Labour and Welfare)	Yes	Yes	Yes (10)	Yes	Partial reimbursement of development costs Extended registration validity period
United States	≤ 200 000 (0.07)	2194 (2010) <sup>13</sup>	350 (2010) <sup>13</sup>	Orphan Drug Act (1983) (Food and Drug Administration)	Yes	Yes	Yes (7)	Yes	Not applicable

<sup>8</sup>This may also be defined as the number of orphan drug marketing authorizations.

<sup>13</sup>Measure of incidence.

# Rare diseases

- Any disease affecting fewer than 5 people in 10,000 in the EU is considered rare. Although this might appear small, it translates into approximately 246,000 people. Most patients suffer from even rarer diseases affecting 1 person in 100,000 or more. Approximately 5,000-8,000 distinct rare diseases affect 6-8% of the EU population i.e. **between 27 and 36 million people.**

Maybe not so rare

# Data Sources

## Structured Thematic databases (Health) :

- Clinical Trials;
- Medicines (orphan drugs and human-medicinal products);
- Health Technology Assessments;
- Clinical Guidelines;
- Cochrane Reviews;
- Database of Abstracts of Reviews of Effects (DARE);
- NHS Economic Evaluation database (NHS EED);
- Chemicals (ECHA)

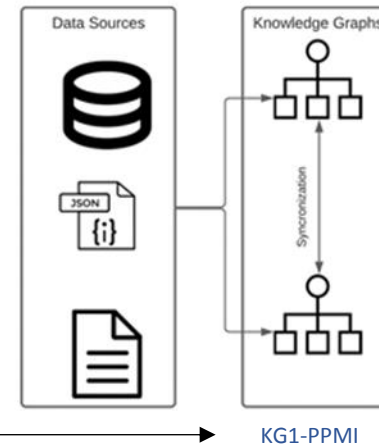
## KG2-ONTOTEXT

- ❖ CORDIS data;
- ❖ OpenAire;
- ❖ Microsoft Academic;
- ❖ Scopus;
- ❖ CrossRef Events;
- ❖ Wikidata;
- ❖ European Media MonitorThrough JRCNames links;
- ❖ Lens.org In the process of integration;
- ❖ Consortium output;

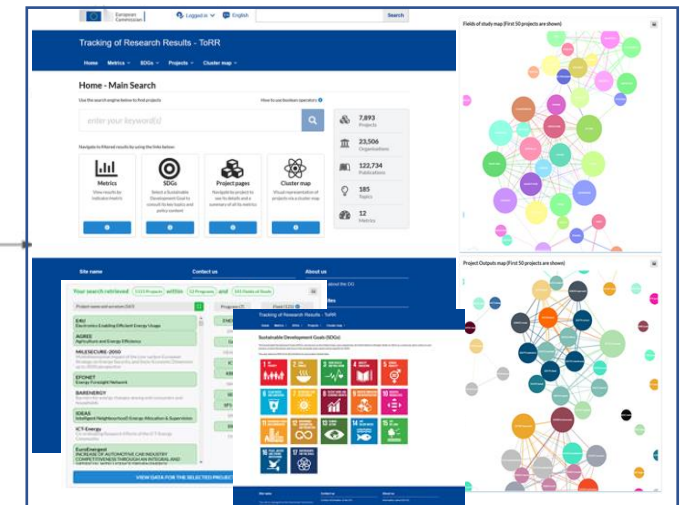
## KG1-PPMI

- CORDA/SESSAM – documents and monitoring data;
- Company website data – additional data on companies and their products;
- MAG – publications, researchers, FOS;
- PATSTAT – patents ;
- EUIPO & TM-Link – Trademarks ;
- Web scraped EC data – policy documents (EU Publications Office; EC; EP repositories);
- Web scraped Media data (based on EMM sources) – media mentions;

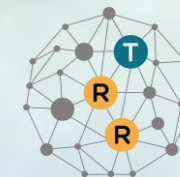
## KG2-ONTOTEXT



## ToRR



# Health Case study



Tracking of Research Results

## Rare Diseases in EU research programmes

Topic clusters and  
FET/KET technology

Interdisciplinarity (field  
of study network)

Cross-cutting  
programmes analysis  
(FP7/H2020/3rd EU  
Health 2014-2020)

Contribution to diseases  
and EMA Orphan  
Designations

EU support to the  
development of EMA  
Orphan Designation in  
FP7 projects

EU support to clinical  
trials addressing Rare  
Diseases

Overview of outputs  
produced in the FP  
projects portfolio

Overview of  
innovations produced  
by participating  
organisations in the  
FP7 projects portfolio

Overview of citations in  
policy documents of  
FP7 projects portfolio

Tracking of research  
results after/beyond  
EU funding

Today Scientific  
breakthroughs linked  
to FP7 projects

What's happening on  
the market?



European  
Commission

# Contribution to diseases & EMA Orphan designations

Top-25 most frequently addressed rare diseases in the analysed set of FP7 rare diseases projects, by number of projects

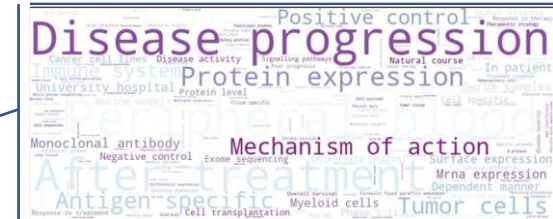
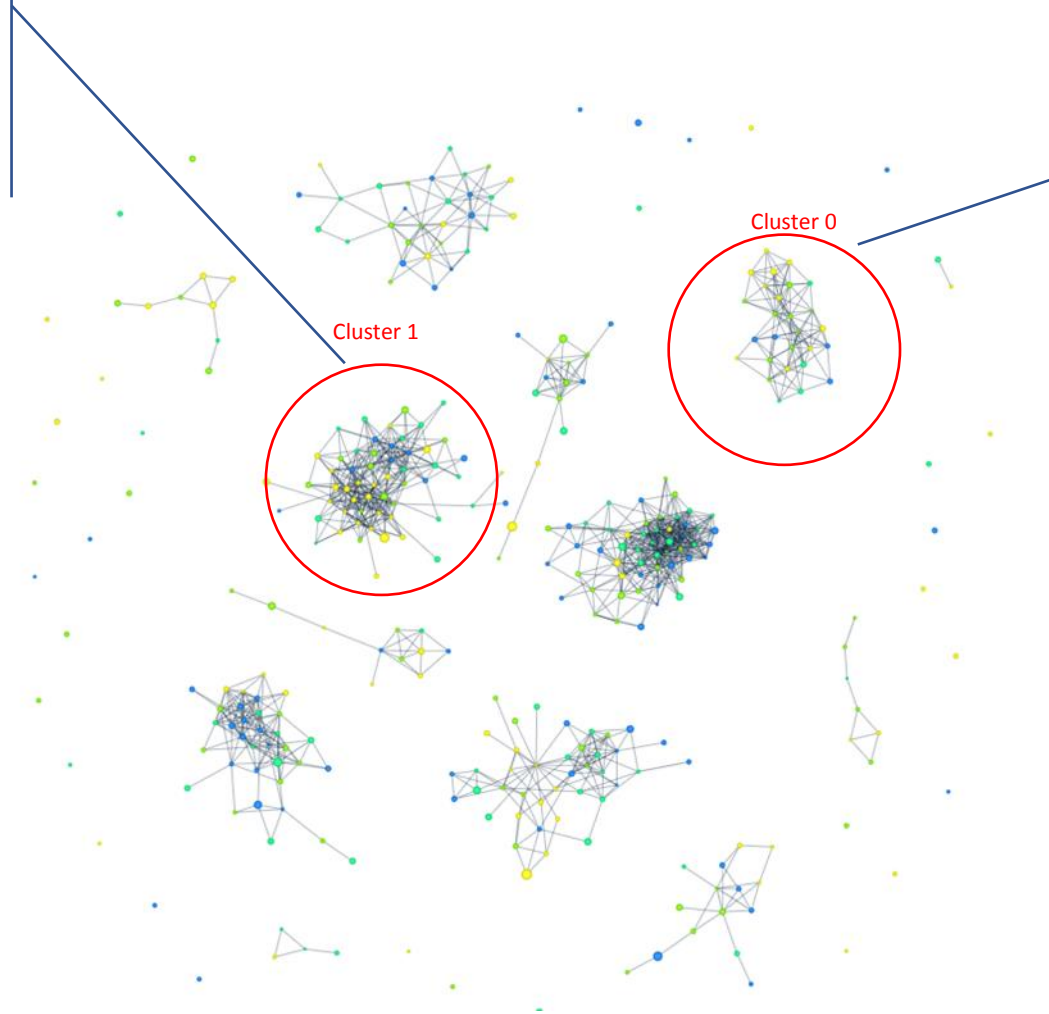
DISEASE	TOTAL EC CONTRIBUTION, EUR MILLION	TOTAL PROJECT COSTS, EUR MILLION	NUMBER OF PROJECTS
malaria	422,7	542,5	139
tuberculosis	436,6	582,5	98
pancreatic cancer	361,2	483,0	57
cystic fibrosis	220,0	290,9	48
glioma	304,8	419,9	37
Pseudomonas aeruginosa	235,0	323,0	33
sepsis	238,7	328,0	32
hepatocellular carcinoma	156,7	209,1	32
leishmaniasis	142,1	191,2	31
avian influenza	97,5	129,1	28
Duchenne muscular dystrophy	216,1	317,2	28
amyotrophic lateral sclerosis	124,6	180,8	25
multiple myeloma	132,2	175,8	25
Becker muscular dystrophy	131,0	176,3	23
severe combined immunodeficiency, adenosine deaminase deficiency, SCID, ADA	153,4	205,8	20
ovarian cancer	109,4	146,0	20
dengue	97,5	134,2	18
hepatocellular carcinoma, pexastimogene devacirepvec	128,6	173,2	18
Hearing loss, acute acoustic trauma, sudden deafness, surgery induced acoustic trauma	67,8	91,4	16
retinitis pigmentosa	36,2	46,5	16
non-small cell lung cancer anaplastic lymphoma kinase (ALK)-positive, NSCLC	103,0	162,2	16
small cell lung cancer	75,5	108,8	14
graft-versus-host disease	125,3	168,1	14
pre-eclampsia	57,7	75,2	14

Top-25 most frequently addressed EMA orphan designations in FP7 projects, by number of projects

ORPHAN DESIGNATION	RELATED DISEASES	NUMBER OF PROJECTS
Ciprofloxacin	cystic fibrosis	18
Artesunate	malaria	16
Dexamethasone	multiple myeloma	14
everolimus	gastric cancer, renal-cell carcinoma, tuberous sclerosis	9
Nitric oxide	cystic fibrosis	8
Sirolimus	beta thalassaemia intermedia, chronic non-infectious uveitis, sickle cell disease	8
Ribavirin	Crimean Congo haemorrhagic fever, Lassa fever	7
Complement factor H	haemolytic uraemic syndrome	7
Doxorubicin	hepatoblastoma	6
Mercaptopurine	acute lymphoblastic leukaemia	5
Itraconazole	invasive aspergillosis	5
6-mercaptopurine monohydrate	acute lymphoblastic leukaemia, B-cell acute lymphoblastic leukaemia	5
Glucagon	congenital hyperinsulinism	4
mifamurtide	hepatocellular carcinoma	4
Vorinostat	multiple myeloma	3
blinatumomab	acute lymphoblastic leukaemia, B-cell acute lymphoblastic leukaemia	3
Gastrin 17C diphtheria toxoid conjugate	pancreatic cancer	3
Givinostat	Becker muscular dystrophy, Duchenne muscular dystrophy	3
Chelidonium radix special liquid extract	pancreatic cancer	3
Deferiprone	sickle cell disease	2
Recombinant human minibody against complement component C5 fused with RGD-motif	ischaemia injury associated with solid organ transplantation, reperfusion injury associated with solid organ transplantation	2
Panobinostat	Hodgkin lymphoma, multiple myeloma	2
Avian polyclonal IgY antibody against Pseudomonas aeruginosa	cystic fibrosis	2
Sapacitabine	acute myeloid leukaemia, myelodysplastic syndromes	2
Adeno-associated viral vector	acute intermittent porphyria	2



Bottom-up methodology that not only cuts across programmes,  
But clusters them to reveal new dimensions



cluster	fos_top30 per cluster	projects
1	University hospital, Peripheral blood, Disease progression, After treatment, Mrna expression, Positive control, Expression data, Mechanism of action, In patient, Expression analysis, Sample collection, Operating procedures, Protein expression, Clinical study, Cell transplantation, Immune system, Animal studies, Plasma samples, Inflammatory response, Signalling pathways, Exome sequencing, Cell based, Cell activation, Protein level, Genetic variants, Tumor cells, Clinical grade, Serum samples, Data management, Functional studies	BIOSHARE-EU, INTREALL, EUROSARC, BESTCILIA, RD-CONNECT, InSPiRe, METFIZZ, EEC, ASTERIX, AHEAD III, PERFORM, CHRONIOUS, ESI-TBVI, TBSUGENT, ENCE-CF-LAM-LTX, EUCO-NET, LOULLA&PHILLA, SAGHE, TB PAN-NET, ENRIECO, EPIWORK, CHICOS, TRANSEURO, DALI, CHANCES, NIDIAG, EUROMEDICAT, THE HIP TRIAL, IMPACTT, EUROAGENTEST2, COHEMI, PHARMAS, COACH, TIRCON, E-PREDICE, TAIN, INTERPREGGEN, CONTRAST, NANOMAL, DEVELOPAKURE, MEUSIX, IMPROVED, AfriCoLeish, SKIP-NMD, DSD-LIFE, DESSCIPHER, CHILD-EU, ODAK, COSMIC, ASPRE, PHAGOBURN, PANCARELIFE, NEOVANC, EUGENMED, CULPRIT-SHOCK, LENA, FEMNAT-CD, DESIRE, SYMPATH

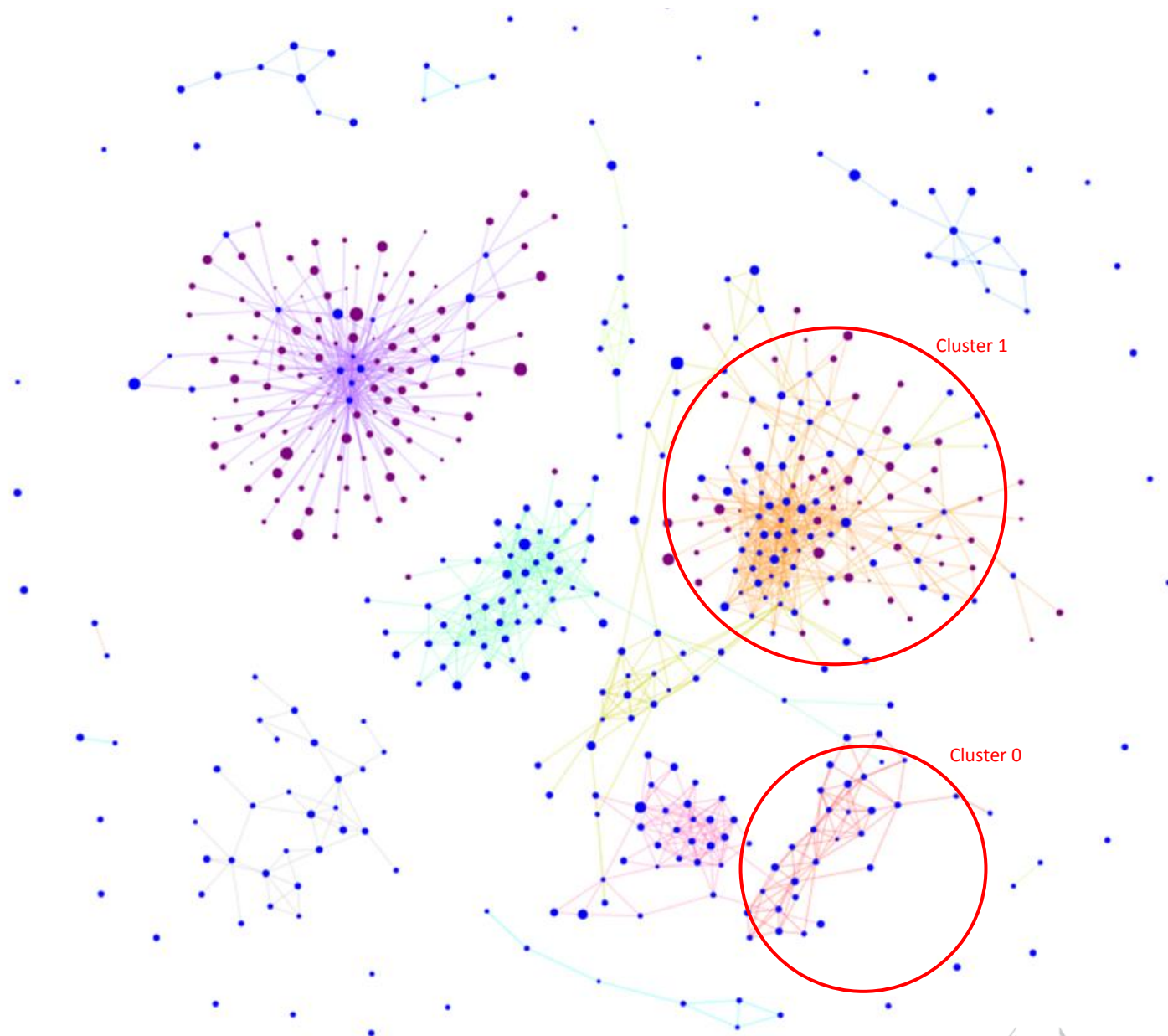
cluster	fos_top30 per cluster	projects
0	World health, Health organization, Health sector, Health services, Health professionals, Health related, Climate change, Disease control, Human health, Primary care, Policy development, Country level, Public policy, Socio economic impact, Health problems, Resource allocation, Disaster risk reduction, Science policy, Millennium Development Goals, Priority setting, Pharmaceutical industry, Early detection, Community level, Research evidence, Public awareness, Research policy, Emergency situations, Emergency planning, Sub saharan, Burden of disease	CUREHLH, EUNEFRON, LEUKOTREAT, FIGHT-MG, PEMPHIGUS, HOMITB, ADAMANT, EURIPFNET, STAR-T REK, OPTISTEM, NIMBL, EPC-TM-NET, CURELUNG, CANCERALIA, LUNGTARGET, INTRICATE, CELL-PID, IMMOMEC, OPTATIO, OVER-MYR, OCTIPS, REGENER-AR, TRIAD, PathCO, TUMADOR, IACT, CAM-PAC

348 FP7 Rare diseases related projects in 10 clusters with prevalence scoring for FET and KET topics

# Comparison to other programmes

FP7 Cooperation  
Programme  
RTD

EU Health  
2014-2020  
Programme  
CHAFEA



Indicators for portfolio\_rare\_diseases\_RTD\_FP7 (Call)

Input

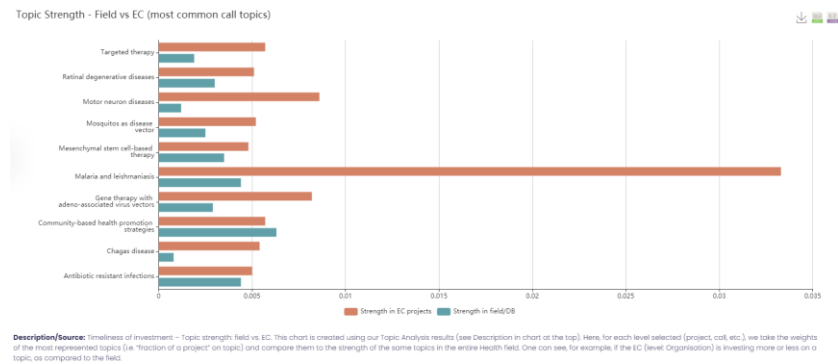
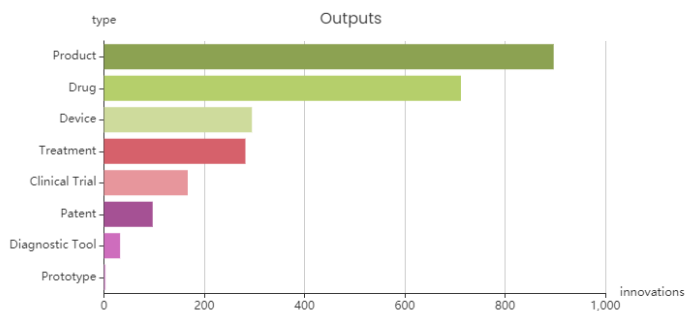
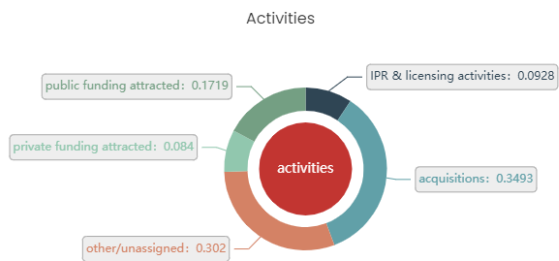
Throughput/Output

Academic Impact

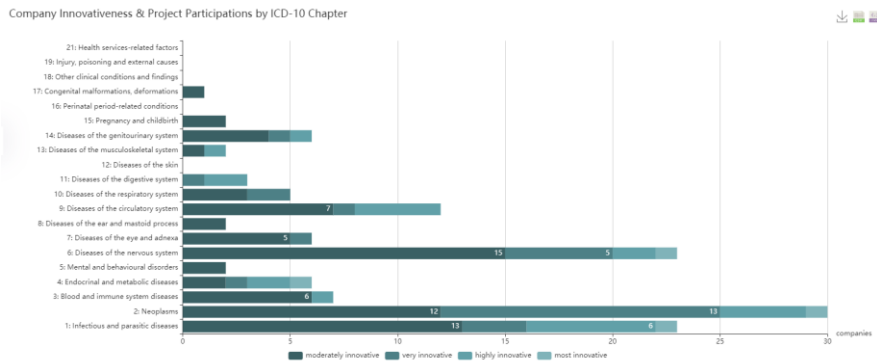
Economic Impact

Societal Impact

Innovations by Participant Companies



**Description/Source:** Innovations by participant companies. For each project, we take the participants that are private-for-profit organizations (companies) and extract their current innovation activities and outputs from their websites. One can examine, how innovative prior project participants are today. For calls, programmes, organisations and the entire Health field, we aggregate the data from all corresponding projects. For topics and categories, we aggregate the data from all projects that are at least 30% on that topic or category. Each company is counted exactly once.



**Description/Source:** Company innovativeness and project participations by ICD class. We have classified each project to one or more ICD-10 chapters (<https://icd.who.int/browse10/2019/en>). Each chapter matched, receives all the private-for-profit participants (companies) of a project. The total length of the bars represents the number of companies involved in projects in that ICD chapter. Each bar is split into segments of companies of a particular innovativeness level. A company's innovativeness rank (among other participants) is determined by analysing the text on its website. For calls, programmes, organisations and the entire Health field, we aggregate the data from all corresponding projects. In this chart, companies can be double-counted.



**Description/Source:** Clinical trials linked to projects per ICD-10 chapter. We have classified each project to one or more ICD-10 chapters (<https://icd.who.int/browse10/2019/en>). Each chapter matched, receives all the clinical trials linked to a project. For calls, programmes, organisations and the entire Health field, we aggregate the data from all corresponding projects. Clinical trials are linked to a project using a set of criteria (match in substance, participants, timeline, etc.). On the left, we list our findings for a general match ('looser' set of criteria) and on the right, for a narrow (tight) match to projects.



# Looking at outcome and impact of Rare Diseases Research Projects

## EMA rare diseases and orphan designations analysis

Total number of EMA rare diseases and orphan designations analysed: 671 diseases

Total number of FP7 projects contributing to EMA orphan designations: 765 projects addressing 209 diseases (i.e. 31% of the 671 analysed rare diseases were found to be addressed by FP7 projects)

Total EU contribution allocated to the identified projects: EUR 3.36 billion

## EU support to the development of EMA orphan designations

Estimated number of EMA orphan designations addressed in FP7 projects: 61 designations

## EU support to clinical trials addressing rare diseases

Identified number of clinical trials linked to the analysed FP7 rare diseases projects :

104 clinical trials using 50 medicines/active substances

## Overview of outputs produced in the analyzed portfolio of FP7 projects

Total number of researchers linked to the projects analysed: 34,225 researchers

Total number of publications produced: 25,838 publications

Total number of patents produced: 236 patents

Total number of innovation outputs produced: 8,139 outputs

## Overview of citations of FP research in policy documents for the analysed portfolio of FP7 projects

Total number of FP7 publications cited in EC and EP documents:

107 publications cited 206 times in 84 EP and EC policy documents

## Overview of innovations produced by the participating firms in the analysed portfolio of FP7 projects

Total number of firms that participated in the projects analysed: 1060 firms

Total number of innovation announcements identified: 9605 innovation announcements, including 1427 announcements linked to new products/innovations on the market

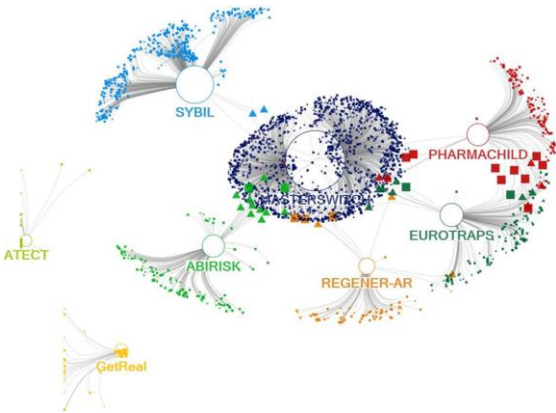
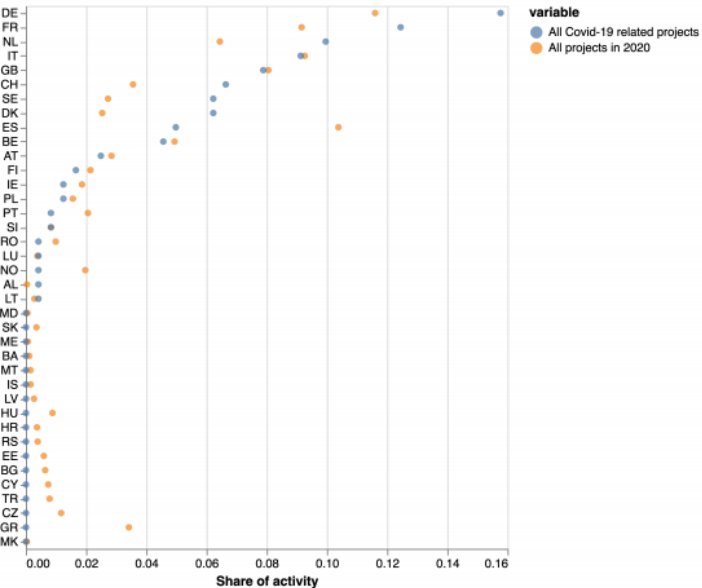
Total number of announcements of additional funding attracted: 107 announcements

Of which: 55 announcements identified as public funding and 21 announcements identified as private funding

# The COVID-19 Story

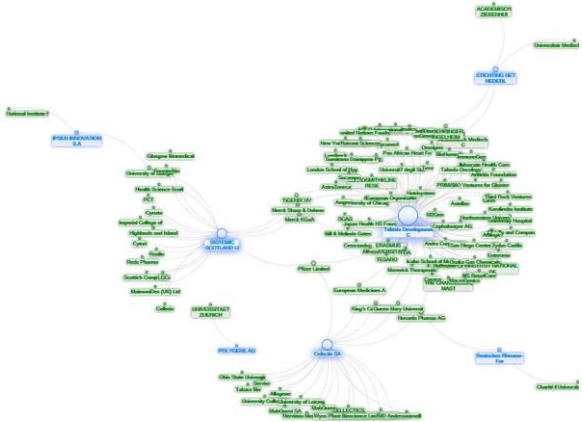
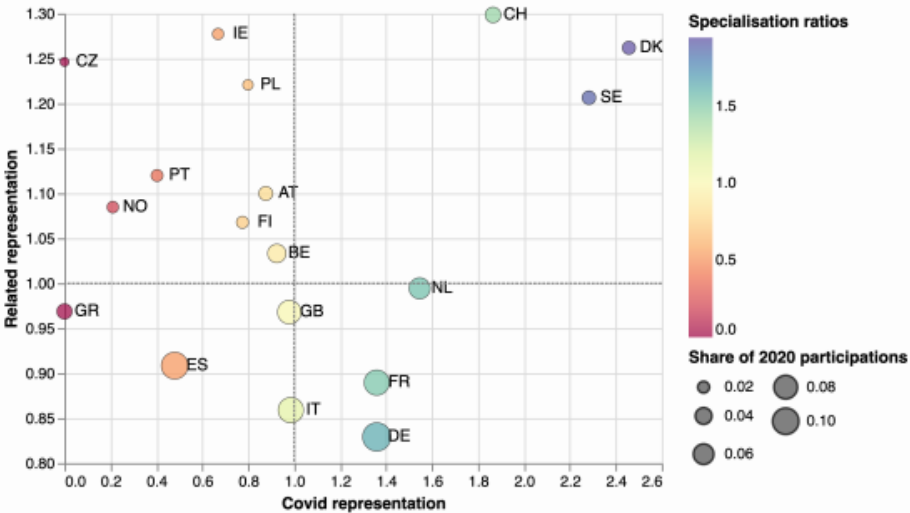
## Tocilizumab

An immunosuppressive drug, mainly for the treatment of rheumatoid arthritis but today evaluated in patients admitted to hospital with COVID-19 (RECOVERY)



Gatekeepers

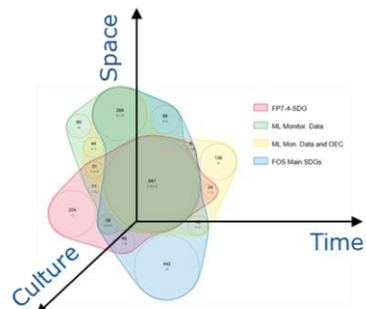
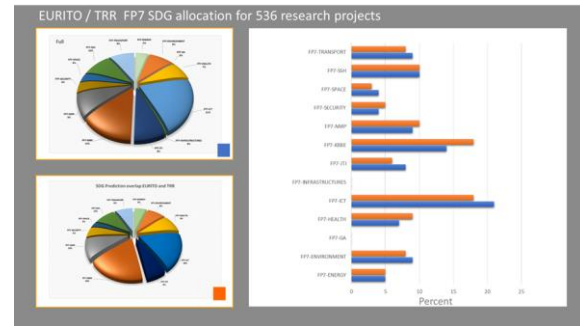
COLLABORATION NETWORKS OF RESEARCHERS LINKED TO PROJECTS RELATED TO TOCILIZUMAB



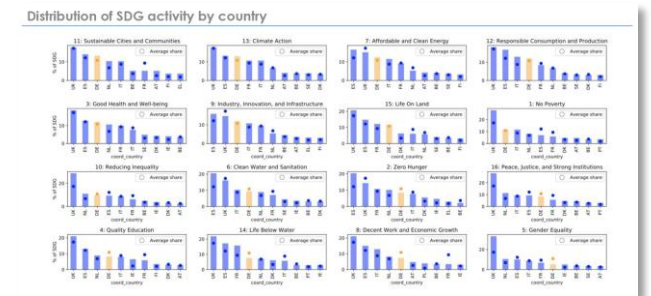
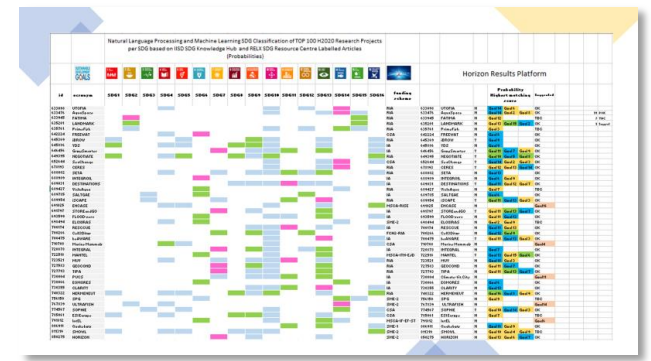
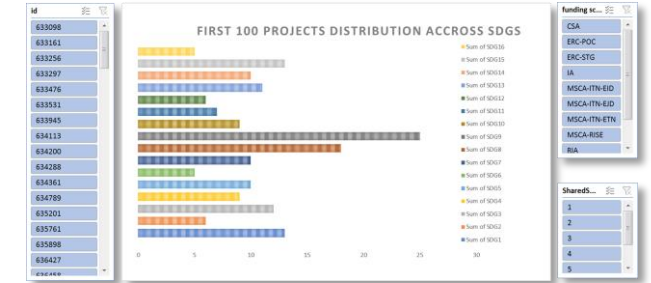
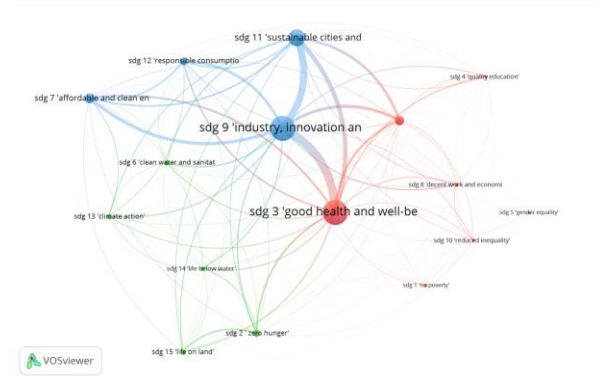
COLLABORATION NETWORKS OF COMPANIES INVOLVED IN PROJECTS ADDRESSING TOCILIZUMAB

# The SDGs Story

- 1. FP74SDG**  
Sustainable Development Goal(s) assigned to the projects by FP7-4-SD project (<https://www.fp7-4-sdg.eu/>)  
manually assigned by experts, reference data for the validation of the different predictions
- 2. ML Monitoring Data Main SDGs**  
Main Sustainable Development Goal(s) assigned by TRR using Natural Language Processing and Machine Learning;  
Models were trained using the Deliverables and Monitoring Data for FP7 Projects;
- 3. ML Monitoring Data SDGs Full Dist.**  
Full probability distribution for all 17 SDGs from the Natural Language Processing /Machine Learning approach;
- 4. ML Monitoring Data & OECD Main SDGs**  
Main Sustainable Development Goal(s) assigned by TRR using Natural Language Processing and Machine Learning;  
Models were trained using the Deliverables and Monitoring Data for FP7 Projects and OECD documents from SDG Path Finder (<https://sdg.pathfinder.org/>);
- 5. ML Monitoring Data & OECD SDGs Full Dist.**  
Full probability distribution for all 17 SDGs from the Natural Language Processing /Machine Learning approach;
- 6. FOS Main SDGs**  
Main Sustainable Development Goal(s) assigned by TRR using the keyword mapping between Microsoft Academic Fields of Study (FOS) and SDGs;
- 7. FOS SDGs Full Dist**  
Full probability distribution for all 17 SDGs from the keyword mapping between Microsoft Academic Fields of Study (FOS) and SDGs;

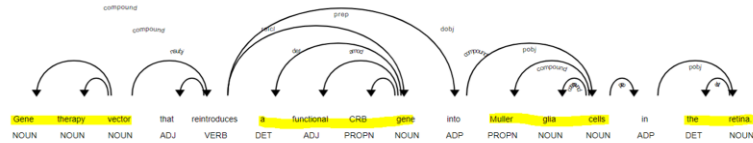


## Mapping of links between SDGs based on FP7 project data





## NOUN CHUNKS



## EXTRACTED INSIGHTS

PROJECT ID	OUTPUT ID	OUTPUT NAMES FOUND IN THE REPORT	PROPER NOUNS/IPR
200234 (Crumbs in Sight)	200234_vector	<p>pharmaceutical CRB gene therapy vector</p> <p><b>Gene therapy vector -&gt; object mentioned in the sentence above</b></p> <p><b>CRB1 Gene Therapy Vector -&gt; most frequently mentioned term</b></p> <p>CRB gene therapy vector</p> <p>most suitable CRB gene therapy vector</p> <p>AAV hCRB1 gene therapy vectors</p> <p>AAV2/6 hCRB1 clinical gene therapy vector production</p> <p>gene therapy vectors and Müller glia progenitor cell therapy</p> <p>clinical AAV hCRB1 gene therapy vector</p> <p>suitable AAV hCRB1 gene therapy vector</p> <p>AAV hCRB1 gene therapy vector</p> <p>AAV hCRB1 gene therapy vectors</p> <p>clinical AAV2/6 hCRB1 gene therapy vectors</p>	<p>CRB</p> <p>CRB1</p> <p>AAV</p> <p>hCRB1</p> <p>AAV2/6</p> <p>AAV6</p> <p>Crb1/Crb2</p> <p>UniQure</p> <p>AAV-based</p>

## AUGMENTED Project Portfolio

META DATA			
Project ID	200234	Acronym	CRUMBS IN SIGHT
Funding Scheme	FP7 HEALTH	EU Contribution	€ 3.0 mil.
Number of Participants	6	Participant Organizations	KNAW, AMT, RUMC, MPG, CNRS, USFD, EKUT

Project Outputs	200234_ <b>mouse</b> : Crb2 knockout mice, Crb1 Crb2 double knock out mice, conditional knockdown mice, Mpp3 conditional knockout cKO mice, Mpp3 cKO mice, Crb1 / Crb2F/ Chx10Cre/ mice, conditional Crb2 knockout mice, double knockout mice
	200234_ <b>vector</b> : pharmaceutical CRB gene therapy vector, Gene therapy vector, CRB1 Gene Therapy Vector, CRB gene therapy vector, AAV hCRB1 gene therapy vectors, AAV2/6 hCRB1 clinical gene therapy vector, gene therapy vectors and Müller glia progenitor cell therapy, clinical AAV hCRB1 gene therapy vector, clinical AAV2/6 hCRB1 gene therapy vectors
	200234_ <b>mutant</b> : Crb1 mutants
	200234_ <b>serotype</b> : AAV serotype
	200234_ <b>platform</b> : baculovirus production platform for the AAV1 serotype

<b>Thematic Keywords / Phrases</b>	Müller-glia-cells, CRB, photoreceptor, cell, retina, protein, gene-therapy, adheren-junction, eye-disease, retinal-degeneration, knock-out-mouse, eye, membrane
<b>Named Entities / IPR</b>	AAV, AAV1, AAV2/6, CRB, CRB1, CRB2, CRB2F, hCRB, hCRB1, Mpp3, Crb1 / Crb2F/ Chx10Cre
<b>Additional Attributes</b>	
<b>Fields of Study / Themes</b>	Biology, Cell-Biology, Anatomy, Genetics, Retina, Molecular-Biology, Retinal-Degeneration
<b>Relevant SDGs</b>	SDG 3 – Good Health and Wellbeing

	Researcher
Name, Surname:	Jan Wijnholds
Affiliation: Name and PIC	KNAW (999518362)
Link to profile:	<a href="https://academic.microsoft.com/author/2008286538">https://academic.microsoft.com/author/2008286538</a>
Project:	CRUMBS IN SIGHT (200234);
Affiliated to beneficiary PIC?	Yes
Number of publications	15
Mentions in deliverables	236 mentions, of which 55 mentions in text Mentioned in the DoW
Author and project FOS	<u>Author FOS</u> : biology; retina; retinal; retinitis pigmentosa; CRB1; anatomy; molecular biology; cell biology; retinal degeneration  <u>Project FOS</u> : Photoreceptor cell , Retinal degeneration , CRB1 , Gene therapy of the human retina , Outer nuclear layer

project_id	output_id	output_forms	output_fos_matched_w/names
			['crb1':2, 'progressive retinal degeneration':1, 'optical coherence tomography':1, 'leber congenital amaurosis':1, 'toulidine blue staining':1, 'cross-sectional imaging':1, 'vascular alterations':1, 'retinitis pigmentosa':1, 'functional analysis':1, 'retinal lamination':1, 'adherens junctions':1, 'retinal function':1, 'double knockout':1, 'spectral domain':1, 'knockout mouse':1, 'cross breeding':1, 'cell division':1, 'mouse strain':1, 'early onset':1];
200234	200234_mouse	['Crb1-Crb2 double knock-out mice', 'Mps3 conditional knockout cKO mice']	['molecular evolution':9, 'work package':3, 'multidisciplinary approach':1, 'degenerative disease':1, 'production strategy':1, 'recombinant virus':1, 'lpl deficiency':1, 'clinical grade':1, 'cell specific':1, 'start codon':1, 'viral gene':1, 'high titer':1, 'phase i/ii':1, 'ex vivo':1, 'crb1':1];
200234	200234_serotype	['AAV serotype']	['muller glia':21, 'work package':11, 'crb1':7, 'retinal degeneration':5, 'adeno-associated virus':4, 'molecular evolution':4, 'retinal pigment epithelium':3, 'retinitis pigmentosa':3, 'photoreceptor cell':3, 'progenitor cell':3, 'leber congenital amaurosis':2, 'transmembrane protein':2, 'cell transplantation':2, 'therapeutic strategy':2, 'single application':2, 'double knockout':2, 'polarized cell':2, 'clinical grade':2, 'high homology':2, 'stem cell':2, 'membrane-associated guanylate kinase':1, 'ophthalmological experiment':1, 'technology implementation':1, 'drosophila melanogaster':1, 'pharmaceutical industry':1, 'manufacturing services':1, 'functional importance':1, 'intracellular domain':1, 'membrane associated':1, 'heterogeneous group':1, 'future application':1, 'post translational':1, 'rod photoreceptors':1];
200234	200234_vector	['AAV2/6 hCRB1 gene therapy vectors', 'gene therapy vectors and Müller glia progenitor cell therapy', 'AAV2/6 hCRB1 clinical gene therapy vector production', 'AAV hCRB1 gene therapy vectors', 'CRB1 gene therapy vectors generated in WPS', 'final CRB gene therapy vector', 'AAV hCRB1 gene therapy vector']	['gene silencing':1, 'gene transfer':1, 'cell polarity':1, 'visual system':1, 'cell adhesion':1, 'model system':1, 'visual field':1, 'cell therapy':1, 'viral vector':1, 'fund raising':1, 'viral gene':1, 'phase i/ii':1];



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ABOUT US



## Restoring Mueller glia cells – photoreceptor interactions with Crumbs

Fast Start

Results in Brief

Reporting

Results

### Objective

Mutations in the Crumbs homologue 1 (CRB1) gene cause photoreceptor degeneration resulting in progressive retinitis pigmentosa (RP) or later congenital aneurals (CA). Cells that currently are unsuitable blinding diseases. CRB1 is localized in Mueller glia cells at a subapical domain adjacent to adherens junctions between Mueller glia cells and photoreceptors. Disruption of CRB1 results in loss of adhesion between Mueller glia cells and photoreceptors. Mutations result in loss of CRB1 and other retinal neurons with loss of vision or blindness. The aim of this project is to restore CRB1 and other retinal neurons with loss of vision or blindness. We will analyze the molecular and physiological functions of CRB1. Its family member CRB3, and CRB2 and MUPP1, and CRB1 and MUPP1. We will also assess what role these molecules play in the interaction between Mueller glia cells and photoreceptors and subsequent retinal degeneration in retinas lacking both CRB1 and CRB3, or lacking the CRB1-interacting protein PALF1. To further understand the role of these proteins in neural-glia interactions in general, we will also assess what role these molecules play during development. We will develop a mouse carrying the impaired interaction between glial cells and photoreceptors, we will explore the efficacy of Mueller glia progenitor cell transplantation in mouse retinas. In collaboration with a small enterprise we will also deliver clinical grade adeno-associated virus (AAV) gene therapy vectors to transfer and express human CRB1 specifically in Mueller glia cells of the retina. At the end of the project we will develop a demonstration project using these vectors in clinical phase I/II tests.

### Fields of science

[natural sciences](#) • [biological sciences](#) • [biochemistry](#) • [Neurosciences](#) • [genetics](#)

#### Project information

**CRUMBS IN SIGHT**  
Grant agreement ID: 202234  
[Project website](#)

Status  
Closed project

Start date  
1 April 2008

End date  
31 May 2012

Funded under  
FP7 HEALTH

Overall budget  
€ 3 980 245,32



**EU contribution**  
**€ 2 999 900**

Coordinated by  
KONINKLIJKE NEDERLANDSE AKADEMIE VAN WETENSCHAPPEN - RINWI

Netherlands

HOME COMPANY TECHNOLOGY TARGETED DISEASES PIPELINE NEWS CONTACT



# HORAMA

GENE THERAPY DEDICATED TO RARE OPHTHALMOLOGY PATHOLOGIES

Accueil > press > HORAMA Signs Exclusive License Agreement with Leiden University Medical Center Targeting CRB1 Gene Mutations to Treat Inherited Retinal Dystrophies

< >

## HORAMA Signs Exclusive License Agreement with Leiden University Medical Center Targeting CRB1 Gene Mutations to Treat Inherited Retinal Dystrophies

*Further expansion of HORAMA gene therapy portfolio to treat Inherited Retinal Dystrophies to lead to second clinical program by 2023*

Paris (France) and Leiden (Netherlands), March 18, 2020 – HORAMA SA, a French biotechnology company focusing on gene therapy for the treatment of rare genetic diseases in ophthalmology, announced today an exclusive licensing agreement with the Leiden University Medical Center (LUMC) for global rights to a gene therapy program to treat the Inherited Retinal Dystrophies.

to this agreement with the LUMC, a leading academic institution with highly r  
ne therapy such as Jan Wijnholds, to expand our leadership in gene therapy

"Our studies in the last 20 years resulted in the development of a platform for candidate gene therapy medicines for children

euro "Series B" financing round

### Press release

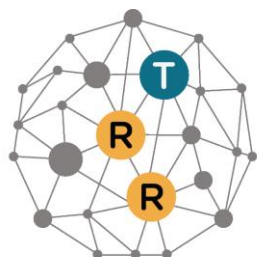
Horama Adds Significant Biopharma Industry and Cell and Gene Therapy Experience to Executive Team

HORAMA appoints life sciences veteran Benedit Timmerman as new Chairman

HORAMA Signs Exclusive License Agreement with Leiden University Medical Center Targeting CRB1 Gene Mutations to Treat Inherited Retinal Dystrophies

HORAMA Strengthens its Management

REITER



Tracking of Research Results



# Broader context

## THANKS

Wider context: DG RTD has launched several big data projects lately

- Tracking of research results in FP7
- H2020 grants (Data4Impact, EURITO, KNOWMAK, REITER, RISE, etc.)
- Big data pilots contributing to the EIS

Key properties of Big Data:

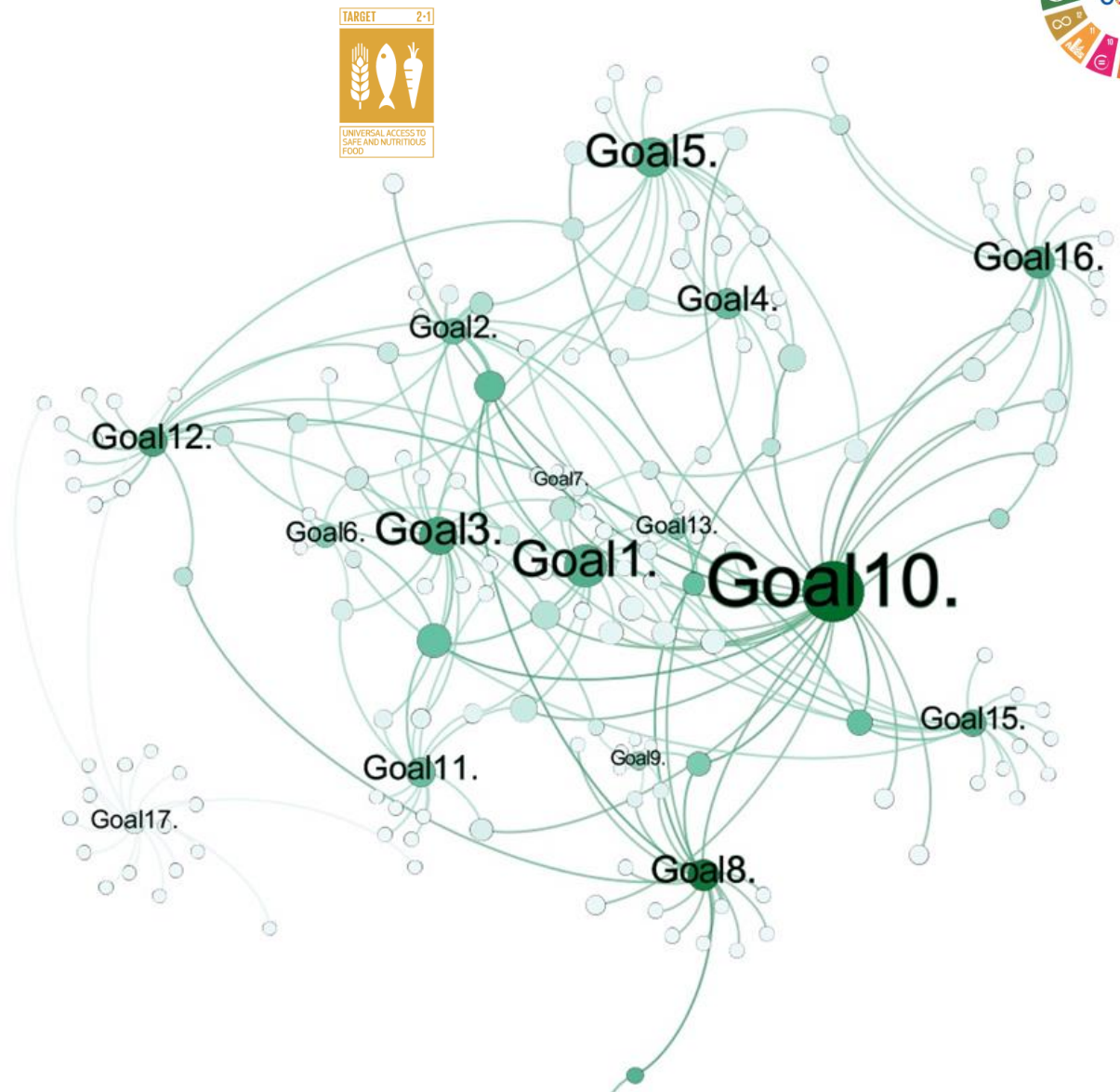
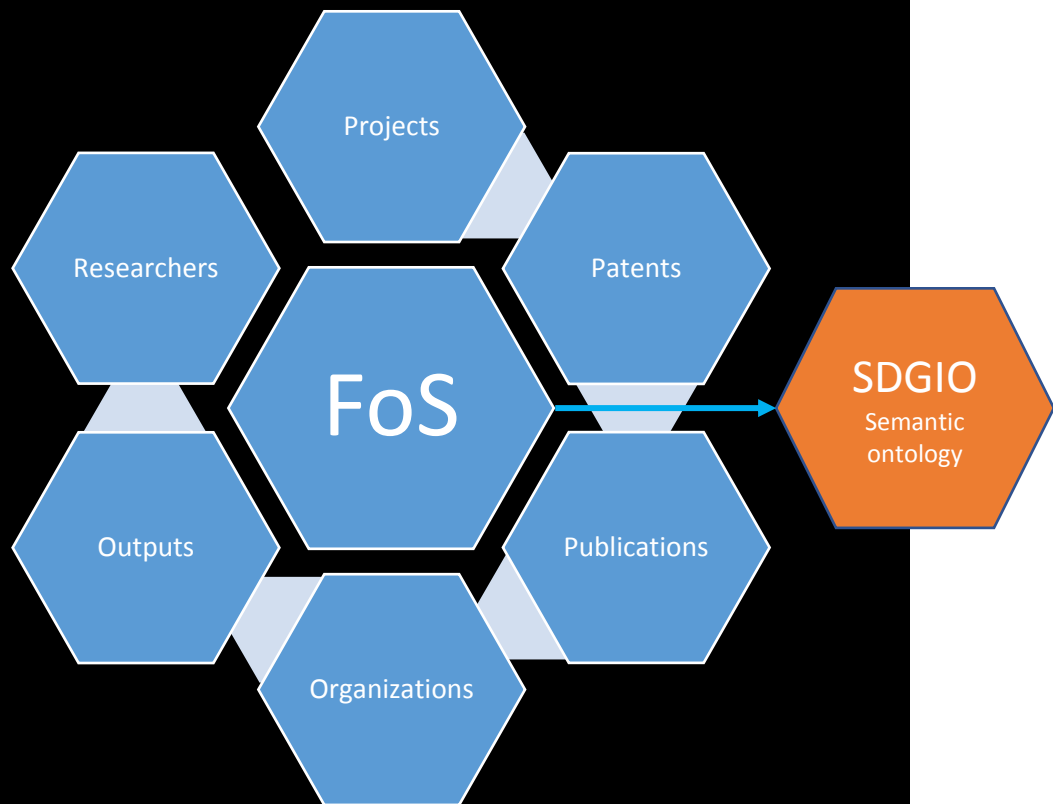
- Volume, i.e., no sampling is generally applied
- Variety, i.e., structured and unstructured data from various sources, in different formats
- Velocity, i.e., real-time/rapid data
- Veracity, i.e., variations in data quality, cleaning, processing, etc.

Non-intrusiveness → Big Data is a byproduct of digital interaction and communication

Key objective: make Big Data small!



# Data linking through TRR Ontology-based text classification



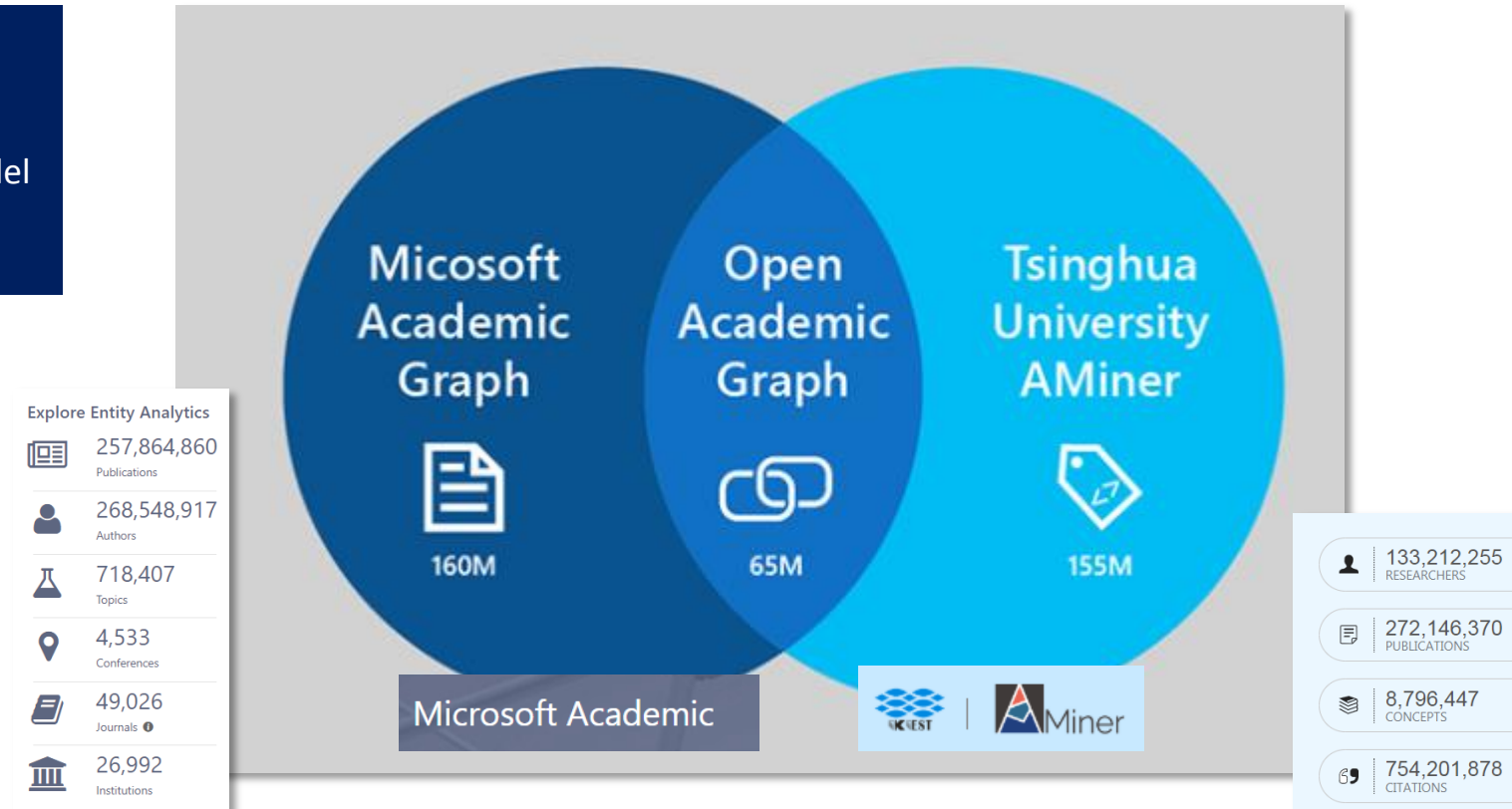


# TRR Ontology-based text classification framework

## Linking publications to specific field of study (FOS)

### Open Academic Graph (billion-scale OAG)

- Open
- 6-level hierarchy
- Extreme granularity
- Lower complexity model to assign text to one or several themes



>700 million entities and > 2 billion relationships

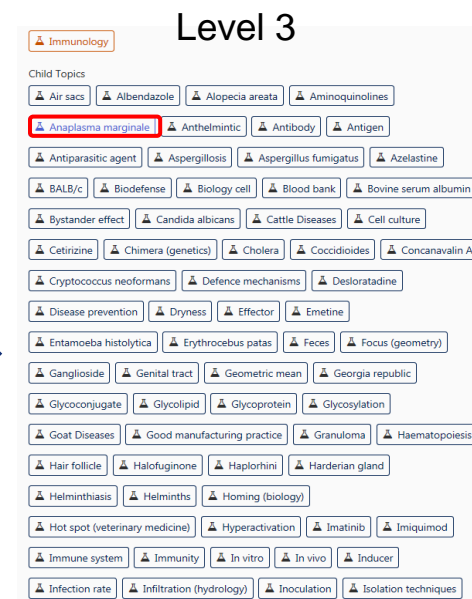
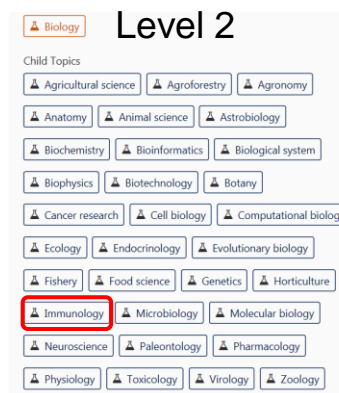
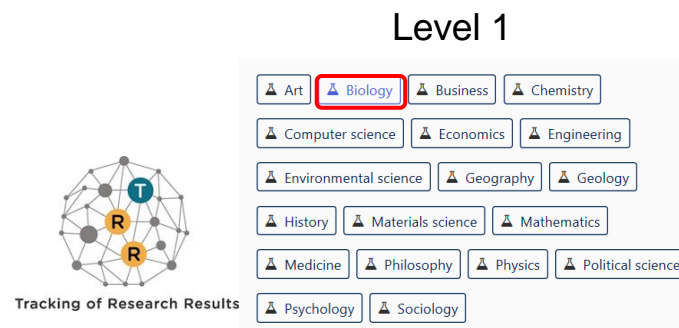


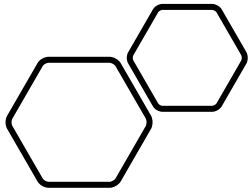
# Microsoft Academic (MAG)Field Of Study (FOS)

- Microsoft Academic Graph [709K Fields of Study](#) concepts semi-automatically constructed with ID and hierarchy
- 6 levels
  - Level 1 entirely manually constructed
  - Level 2 curated manually
  - Levels 3-6 : 100% automatically using hierarchical clustering
- Constructed from Wikipedia so quasi total mapping to Wikidata
  - In the process of importing MAG FOS in Wikidata ([wdt:P6366](#))
  - Soon possibility to use any other thesaurus mapped to wikidata, through the FOS to retrieve/categorize publications/projects.
- Simple Hierarchy modeled by TRR in SKOS

is a free and open knowledge base that can be read and edited by both humans and machines.

SKOS Simple Knowledge Organization System Reference W3C Recommendation. It may be used on its own, or in combination with formal knowledge representation languages such as the Web Ontology language (OWL).





## Estimating distance between texts using topic ontology

- >200M publications = 709K FoS in the hierarchical MAG ontology
- > 200K topics are linked to Wikipedia articles and WikiData

