Digital Management of Rare Diseases

Ségolène Aymé,
Founder of Orphanet
segolene.ayme@icm-institute.org

**Virtual Symposium
Autoimmunity and the Lung**
19 November 2020

Digital management can only benefit RD

Direct difficulties
- Patient are few
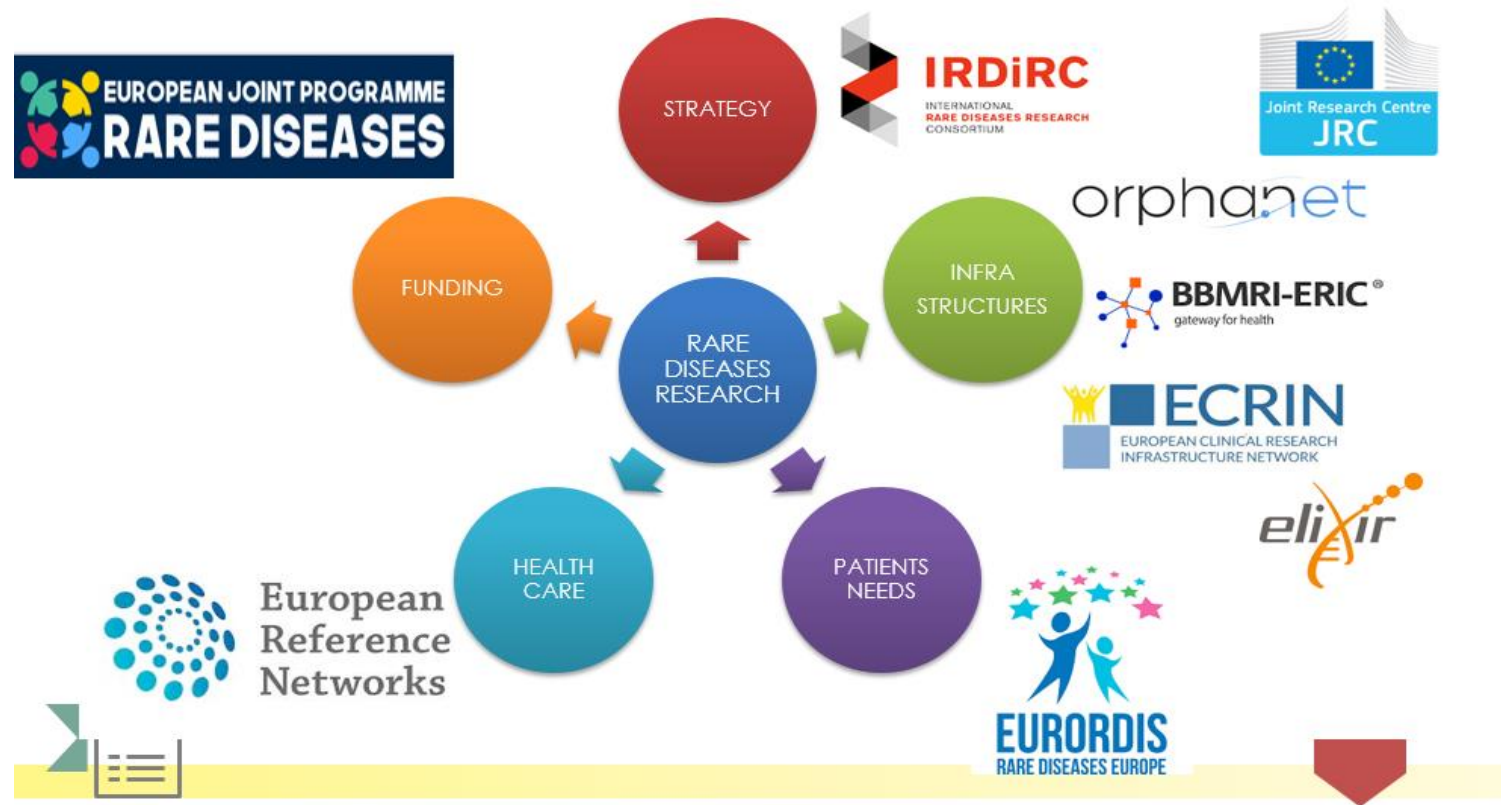- Knowledge is scarce
- Experts are rare
- Small markets

Derived obstacles
- Transnational collaboration is necessary
- Funding is difficult to obtain

Targets for action
- Make the most of data and technologies
- Build Stakeholders's forum
- Develop policies

The European Ecosystem 1997-2020

Achievements contributing to digital management of RD

1- Establishment of National Centres of Expertise

Based on Quality Criteria
- Competence and experience
- Specific human resources
- Structural and equipment resources
- Appropriate organisation

Mission
- Expert care / tele-expertise
- Guidelines / training
- Research / registries

2- Establishment of Networks of National Centres of Expertise

- o Rare Bone Disorders
- o Rare craniofacial anomalies and ENT disorders
- o Rare Congenital Malformations and Rare Intellectual Disability
- o Rare inherited and congenital anomalies
- o Rare Endocrine Conditions
- o Rare Kidney Diseases
- o Rare Neurological Diseases
- o Rare Neuromuscular Diseases
- o Rare and Complex Epilepsies
- o Rare Respiratory Diseases

- o Rare Skin Disorders Rare Eye Diseases
- o Rare Diseases of the Heart
- o Rare Hereditary Metabolic Disorders
- o Rare Hematological Diseases
- o Rare Hepatological Diseases
- o Rare Connective Tissue and Musculoskeletal Diseases
- o Rare Immunodeficiency, Autoinflammatory and Autoimmune Diseases
- o Rare Multisystemic Vascular Diseases
- o Rare Adult Cancers (solid tumors)
- o Paediatric Cancer
- o Genetic Tumour Risk Syndromes

3- Dissemination of Information
www.orpha.net

The portal for rare diseases and orphan drugs

" Rare diseases are **rare, but** rare disease patients are **numerous** "

Access our Services

Inventory, classification and encyclopaedia of rare diseases, with genes involved

Inventory of orphan drugs

Directory of patient organisations

Directory of professionals and institutions

Directory of expert centres
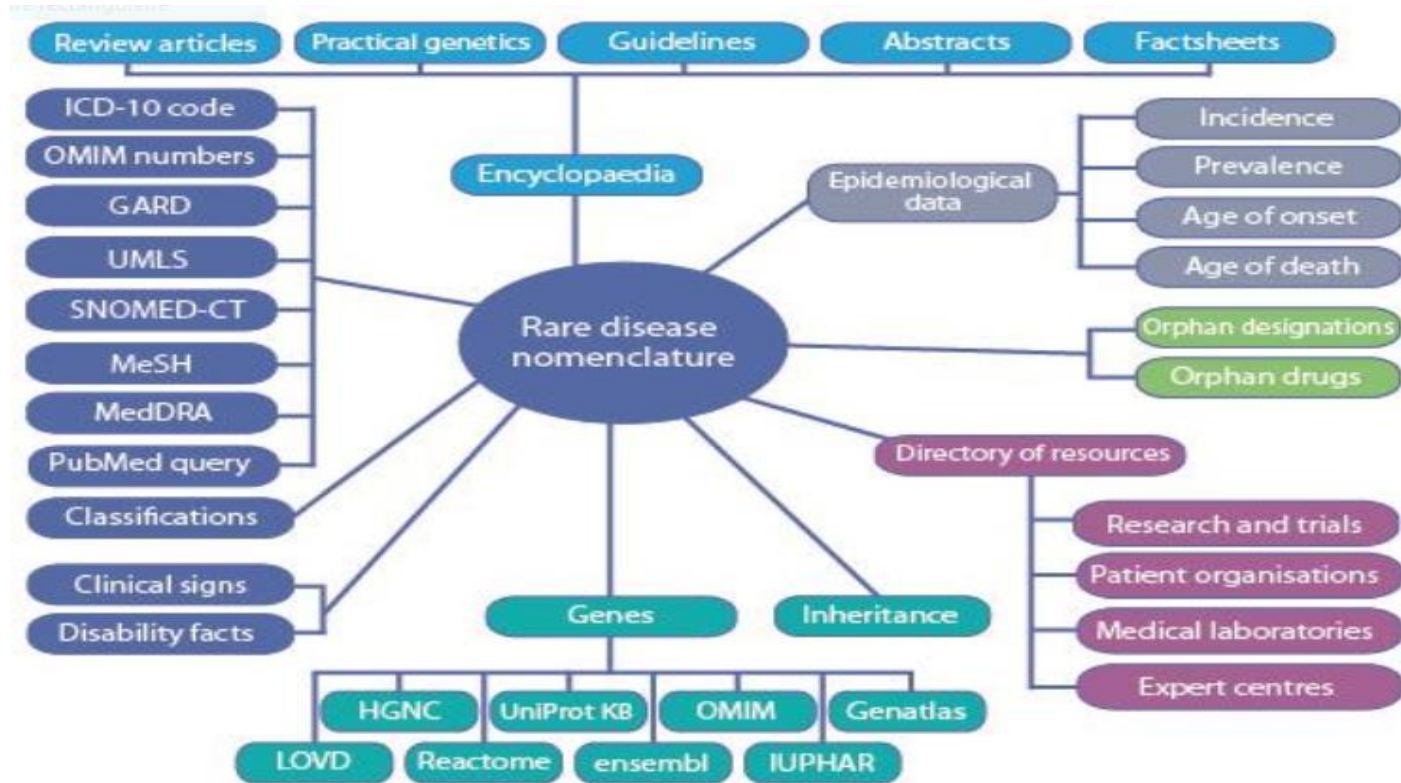
Directory of medical laboratories providing diagnostic tests

Directory of ongoing research projects, clinical trials, registries and biobanks

Collection of thematic reports: Orphanet Reports Series

ICM

4- Free Access to Data   orphadata.org

5- Nomenclature and Ontology

Opportunities thanks to New Trends
1- Digital Health Hype Cycle
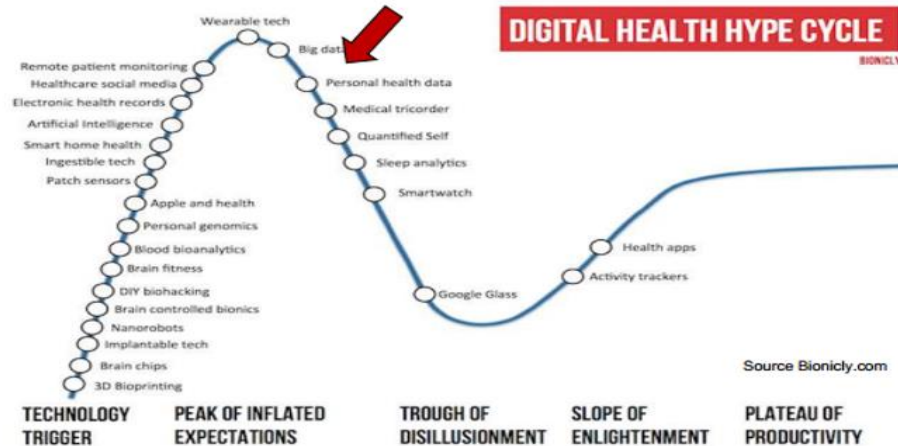
Recognition of the importance of Infrastructures

Common Good concept

- Big investments
- Sustainability
- Precompetitive tools

Specific Funding

- Call for proposals
- Example of IMI calls

Academic recognition

- Articles describing research infrastructures
- Citation of Bioresources in articles
- BRIF BioResource Impact Factor

http://dx.doi.org/10.1186/s12916-015-0284-9.

Opportunities thanks to New Trends

2- Open Science

Open Science Policy

Open Science does not mean Open Bar
As Open as Possible, as Closed as Necessary !

The FAIR principles

Findable
Accessible
Interoperable
Reusable
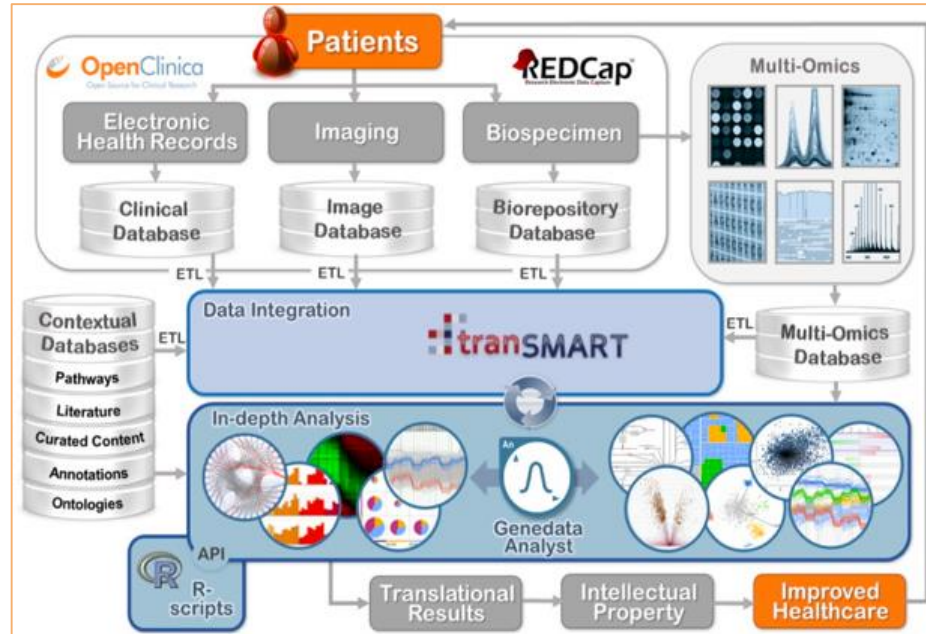
Funding Open Science is not trivial

REVISED **Funding knowledgebases: Towards a sustainable funding model for the UniProt use case [version 2; referees: 3 approved]**

Chiara Gabella, Christine Durinx, Ron Appel

ELIXIR-Switzerland, SIB Swiss Institute of Bioinformatics, Lausanne, 1015, Switzerland

Check for updates

Academic users/Public funding

1. National funding
2. Infrastructure model
3. Institutional support
4. Research project grants
6. User subscription fees
7. Freemium service
8. Razor & blades
9. Public-private consortium
10. Advertising
11. Wiki approach
12. Donations
5. Content licensing

Third party

Commercial users
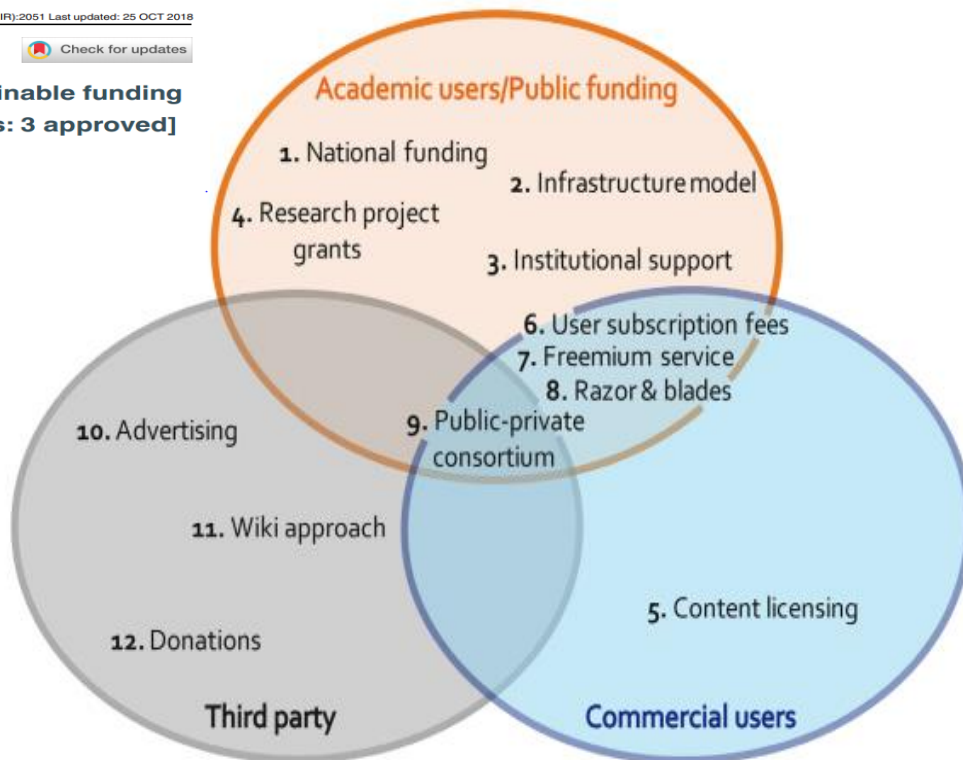
Figure 1. Funding models sources. The 12 considered models are represented depending on the origin of the revenues.

Opportunities thanks to New Trends

3- Genomics

Enormous production of data
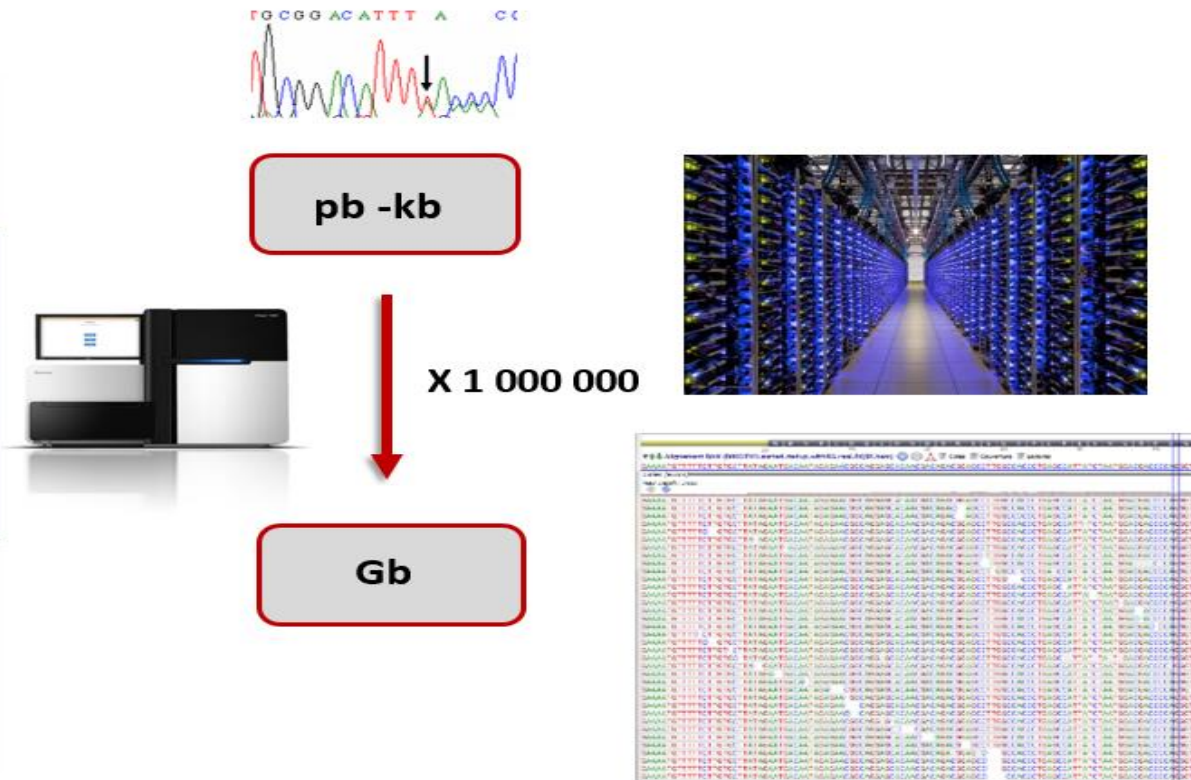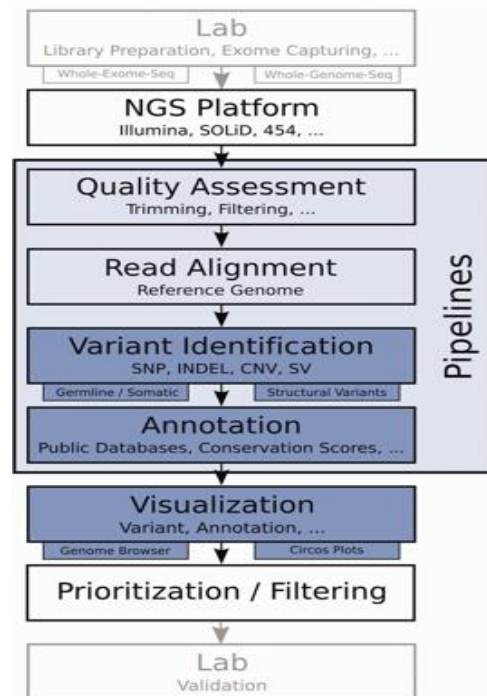
Opportunities thanks to New Trends

3- Artificial Intelligence
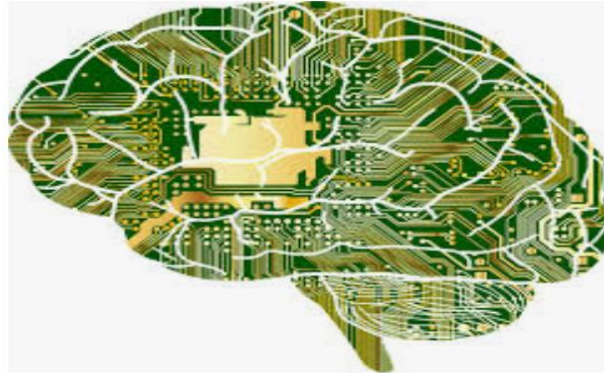
1st opportunity: Clinical Decision Support Systems

Goal → Diagnosis to be considered   Rare diagnosis to be considered

Target → All healthcare professionals   Experts in tertiary centers

DB content → Common + rare disorders   Rare diseases only

Vocabulary → Controled   Free-text

Tools →

IBM Watson Isabel Health Ada Health BabylonHealth WebMD ………	Symptomia PubMed Google

Mendelian
Possum
LDDB
FindZebra
Phenomizer
Decipher
MatchMaker exchange
Phenotips
PhenoDB

……..

Sources of Data used by CDSS

- Data from Publications
  - Scientific articles – Half open
  - Abstracts - open

- Data from Open public infrastructure
  - Orphanet
  - OMIM
  - ClinVar

- Real World Data from organized private sources
  - Electronic health records
  - Registries, cohorts

- Real World Data from unorganized sources
  - Internet
  - Social media

Faviez et al. Orphanet J of Rare Diseases 2020

Recommendations

- ✓ Use standardized metrics to facilitate evaluation and comparison

- ✓ Validate the findings on external datasets and real patient cases

- ✓ Use standardized terminologies to enhance interoperability – HPO

- ✓ Combine expert and data knowledge to enhance explicability

- ✓ Provide robust methods dealing with the imbalance and data volume issues

- ✓ Make training sets accessible

2nd opportunity: Generation of new Knowledge

- Data from primary sources
  - Omics data
  - Imaging data
  - Ex vivo data
  - Clinical data from EHR
  - Telesurveillance data

- Methods
  - Deep Phenotyping
  - Supervised or unsupervised methods

- Challenges from rarity
  - Lack of large datasets to train algorithms
  - Need for harmonization of heterogeneous data
  - Few data standards / Common data elements
  - Stratification of diseases by their underlying mechanism

IA used in the field of RD

- **Data from primary sources**

    - Omics data
    - Imaging data
    - Ex vivo data
    - Clinical data from EHR
    - Telesurveillance

- **Methods**
    - Deep Phenotyping
    - Transfer Learning

- **Challenges from rarity**
    - Lack of large datasets to train algorithms
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Concluding Thoughts

Remaining challenges

- Digital data readiness is insufficient in most countries /heterogeneous solutions

- Social/Psychological/cultural challenges rather than technical

- Shortage of data experts / data managers / data analysts

- Legal obligations security / privacy: Pseudonymization

- Still archaic system of rewards for data management teams

- Short funding cycles of infrastructures not fit for purpose

- ? Right level of multilateral cooperation, given political tensions and general competition

Personal view

- Establish networks of controlled-access data that can be searched

- Specialized shared data collections with patient organisations
  - Common Data Elements
  - Ontologies, Metadata
  - Standard tools (eHR, Xnat, Omero…)
  - Governance requiring some investment from hosting institutions

- No central DB, but a federated network of data providers

- Open data as much as possible

- Maximize collaborations

The ecosystem matters
Is it in place for your Rare Diseases ?

No excuse not to deliver now