Orphanet Report Series

Rare Diseases collection

May 2018

List of Research Infrastructures useful to Rare Diseases in Europe

By country of location

www.orpha.net

Inserm

La science pour la santé

From science to health

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of the European Union

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AUSTRIA

BBMRI-ERIC (Biobanking and Biomolecular Resources Research Infrastructure – European Research Infrastructure Consortium)

BBMRI is a distributed research infrastructure and has been on the ESFRI Roadmap since 2006. It is mostly a networking and standardization effort, whose stated mission as an ERIC is to increase efficiency and excellence in European biomedical research in an ethically and legally compliant way, and to promote standard operating procedures and international best practices on a variety of pre-existing national bio-banks. The National nodes are not part of the ERIC. The relation to the central entity is achieved via membership on the Management Board, thus national bio-banks have only an indirect link to the ERIC. This is reflected in the Partner Charter with the national nodes.

http://www.bbmri-eric.eu/

BELGIUM

European Organisation for Research and Treatment of Cancer (EORTC)

The European Organisation for Research and Treatment of Cancer aims to develop, conduct, coordinate, and stimulate translational and clinical research in Europe to improve the management of cancer and related problems by increasing survival but also patient quality of life. The EORTC contributes to the development of new drugs and other innovative approaches in partnership with the pharmaceutical industry. This is accomplished mainly by conducting large, multicenter, prospective, randomized, phase III clinical trials. In this way, the EORTC facilitates the passage of experimental discoveries into state of the art treatments. EORTC Headquarters, a unique pan European clinical research infrastructure, is based in Brussels, Belgium, from where its various activities are coordinated and run.

http://www.eortc.org/

FRANCE

APTEEUS: engaging patients in discovery

APTEEUS is developing personalized treatments for orphan diseases through a process of discovery and innovative drug repurposing process organized around the patient.

http://apteeus.fr/en/

ATLANTIC GENE THERAPIES

ATLANTIC GENE THERAPIE (AGT) is today at the heart of translational research in biotherapy for the treatment of rare genetic diseases. These therapeutic projects can develop effectively thanks to the presence on one site of research teams that are closely associated with different technological platforms. The different actors of AGT have acquired an expertise in translational research that is unique in France. They

focus essentially on translational programs in the fields of neuromuscular disorders (skeletal muscles in particular), the central nervous system and the retina, using vectors derived from AAV, primary cells and also from genetically modified primary cells.

http://www.atlantic-gene-therapies.fr/

European Clinical Research Infrastructures Network (ECRIN)

The European Clinical Research Infrastructures Network is a sustainable, not-for-profit infrastructure supporting multinational clinical research projects in Europe. Multinational clinical research is hampered by the fragmentation of health and legislative systems in Europe. ECRIN provides information, consulting and services to investigators and sponsors in the preparation and in the conduct of multinational clinical studies, for any category of clinical research and in any disease area. This is particularly relevant for investigator- initiated clinical trials and for clinical research on rare diseases where international cooperation is a key success factor. ECRIN is based on the connection of coordinating centres for national networks of clinical research centres and clinical trials units, able to provide support and services to multinational clinical research. Relevant tools for clinical researchers involved in multinational clinical trials are available on the website.

http://www.ecrin.org/

European Research Infrastructure on Highly Pathogenic Agents (ERINHA)

The **ERINHA2** project aims at building a pan-European research infrastructure to reinforce the European coordination and capacities for the study and the surveillance of highly pathogenic micro-organisms. The ERINHA infrastructure provides open access to state-of-the-art BSL-4 facilities for the European scientific community to enhance basic and finalised research activities. The European Research Infrastructure on Highly Pathogenic Agents (ERINHA) promotes the harmonization of biosafety and biosecurity procedures, develops standards for the management of biological resources, diagnosis of group 4 pathogens, and training of BSL4 labs users.

http://www.erinha.eu/

GENETHON

Genethon's mission is to design gene therapy products for rare diseases, and to ensure their pre-clinical and clinical development in order to provide patients with access to these innovative treatments. To meet this challenge, Genethon has acquired the technical and human resources needed to accelerate the medical application of scientific discoveries arising from fundamental research. The translational research programs are supported by a first-rate technological platform and nearly 200 people (researchers, Pharm.Ds, M.Ds, Ph.Ds, engineers and technicians,…) who have joined forces in order to develop these innovative treatments.

http://www.genethon.fr/

I-STEM

Created in 2005 through collaboration between Inserm – Institut National Health and Medical Research – and AFM-Telethon – French Association against Myopathies – I-Stem is the largest French laboratory research and development dedicated to human pluripotent stem cells, embryonic origin or obtained by reprogramming gene. I-Stem is part of the Biotherapy Institute for Rare Diseases, which includes so far the four centers of research and development funded directly by the AFM Telethon. The

specific vocation of I-Stem is to explore all the therapeutic potential of human pluripotent stem cells for applications in patients affected by rare diseases of genetic origin. In this context, two major areas of research are developed. The first one is cell therapy, which aims to replace lost or diseased cells to other cells with the same characteristics, produced in the laboratory from pluripotent stem cells. The second area is pharmacology based on automated screening of large libraries of compounds with therapeutic potential, following modeling of molecular mechanisms associated with diseases, as revealed by the study of pluripotent stem cells from affected donors. I-Stem teams are currently working on a dozen genetic diseases that affect different organs. The Institute also hosts every year many researchers interested in other diseases and provides training and technology support.

http://www.istem.eu/

Orphanet

Orphanet is a unique resource, gathering and improving knowledge on rare diseases so as to improve the diagnosis, care and treatment of patients with rare diseases. Orphanet aims to provide high-quality information on rare diseases, and ensure equal access to knowledge for all stakeholders. Orphanet maintains the Orphanet rare disease nomenclature (ORPHAnumber), essential in improving the visibility of rare diseases in health and research information systems. Orphanet offers a range of freely accessible services: An inventory of rare diseases and a classification of diseases elaborated using existing published expert classifications; a encyclopaedia of rare diseases in English and French, progressively translated into German, Italian, Spanish and Portuguese; an inventory of orphan drugs at all stages of development; a directory of expert resources, providing information on expert clinics, medical laboratories, ongoing research projects, clinical trials, registries, biobanks and patient organizations in the field of rare diseases, in each of the 41 countries in Orphanet's consortium which is managed by the INSERM in Paris. Orphanet produces ORDO, the Orphanet Rare Diseases Ontology. Orphanet and ORDO are IRDIRC recognized recources. The Orphanet dataset is freely available for research purpose at www.orphadata.org http://www.orpha.net

OrphanDev

OrphanDev is an academic platform specialized in supporting researchers, clinicians and the health industry actors in the development of drugs for rare diseases. This multidisciplinary team supports all projects from private or public sector, throughout the crucial stages of drug development. It provides its scientific and regulatory expertise in Orphan Designation and Protocol Assistance Applications; its logistical and methodological support for clinical trials in rare diseases with a specificity in the patient's recruitment strategy; and its experience in national and European calls for projects. This set of services and tools allows the acceleration of the development of therapies for rare diseases.

http://www.orphan-dev.org/

PHENOMIN: French National Infrastructure for Mouse Phenogenomics

The French National Infrastructure for Mouse Phenogenomics constitutes a unique distributed resource for the creation, the care, the phenotyping, the distribution and archiving of animal models for academics and private corporations.

http://www.phenomin.fr/

High-throughput sequencing for the identification of mutations

High-throughput sequencing for the identification of mutations is a platform settled at Genoscope. In 2011 five other national public and private high-throughput sequencing platforms have joined this action, leading to the rise of a network of six platforms of high expertise and capacity. The network aims at meeting the growing needs of the scientific community to use this new technology for the identification of genes involved in human diseases, with a particular focus on monogenic diseases. The goal of the open call for proposals is to support research projects aimed at identifying – by the use of high throughput exome sequencing and/or region specific sequencing - genes involved in rare diseases whose molecular basis remains unknown.
http://www.cns.fr/spip/High-throughput-sequencing-and.html

Platform of Integrative Chemical Biology of Strasbourg (PCBIS)

The Platform of Integrative Chemical Biology of Strasbourg (PCBIS) gives access to High Throughput Screening (HTS), chemical libraries and target libraries to academic and private laboratories. The platform evaluates the ADME properties of active molecules.

http://www.pcbis.fr/

RADICO / French National Programme on Rare Disease Cohorts (RAre Disease COhorts)

RaDiCo (Rare Disease Cohorts) is financed by the Ministry of Research until December 2019 in the amount of 10,072,118 € in the context of the 'Cohorts' program of *Investissements d'Avenir* (Investments for the Future) managed by the National Research Agency (ANR). The program is designed to equip France with major epidemiological instruments enabling enhanced elucidation of health determinants, optimization of medical practices and optimization of public health policies related to patients with rare disease. The principal objective of RaDiCo is prospective collection, in the field of rare diseases (RD), of extensive phenotype data with a view to clinical and epidemiological research in liaison with translational and basic research. The data may be diverse: anatomical (medical imaging), biochemical, molecular, etc.

http://radico.fr/

BIOTHERAPIES INSTITUTE

The Biotherapies Institute unites the knowledge and expertise of four laboratories, initiated and supported by the AFM-Telethon, world leaders of biotherapies for rare diseases. The objective is to accelerate the development of treatments against rare diseases. The mission of the Biotherapies Institute is to unite the skills, expertise and resources, strengthen the complementarity of resources and better coordinate cross-functional projects, especially clinical development. 650 researchers, engineers and experts in project management, clinical development, regulatory affairs, technology transfer and 25 000 m2 of laboratory space in Paris, Evry and Nantes: the Biotherapies Institute is a unique and exceptional force for translational research, from fundamental to making treatments available for patients.

http://www.institut-biotherapies.fr/

GERMANY

ChemBioNet: resource network supporting academic chemical biology research

The ChemBioNet was initiated by biologists and chemists from academia who realized the need for interdisciplinary open access platforms to support research projects for systematic usage of small molecules to explore biological systems. This initiative wants to provide chemists with bioprofiles for their unique synthetic molecules and biologists developing unique assay systems, with access to high throughput technologies to identify compounds useful for dosage dependent, temporally or locally controlled interference with biological functions. In summary a novel discipline termed Chemical Biology.

http://www.chembionet.info

Care and Trial Site Registry for neuromuscular and neurodegenerative diseases (CTSR)

The aim of the Care and Trial Site Registry (CTSR) is to help the pharmaceutical industry and clinical investigators select trial sites as well as to help to identify potential partners for upcoming research projects.

The **CTSR** provides information relevant

- to clinical studies (such as personnel, facilities and patient population)
- to the assessment as centres of expertise according to the EUCERD criteria

https://ctsr.uniklinik-freiburg.de

EUMINAfab

EUMINAfab is a European Research Infrastructure offering open access to state of the art of multimaterial micro and nanotechnologies. By combining scientific expertise with technological capabilities, EUMINAfab provides innovative and efficient solutions in the area of micro and nanofabrication of functional structures and devices out of a knowledge-based multimaterials' repertoire.

http://www.euminafab.eu

EU-OPENSCREEN

EU-OPENSCREEN, the European infrastructure of open screening platforms for chemical biology provides access to bioactive small molecules. A large collection of diverse compounds, representing the chemical knowledge in Europe, is available for many fields of the life sciences, e.g. human and veterinary medicine, systems biology, biotechnology, agriculture, nutrition. It also offers access to services in all of chemical biology: high-throughput screening, chemical synthesis for hit-optimisation, bio-profiling and in vivo studies, a central database, and training.

http://www.eu-openscreen.de/

Euro-BioImaging

The European Research Infrastructure for Imaging Technologies in Biological and Biomedical Sciences (Euro-BioImaging, EuBI or EuBI ERIC) provides open physical user access to a broad range of state-of-the-art technologies in biological and biomedical imaging for life scientists. In addition, EuBI will offer image data support and training for infrastructure users and providers. The EuBI consists of a set of 29 geographically distributed Node Candidates (specialised imaging facilities) that can grant access to scientists from all European countries and beyond. Currently, researchers can apply to use some of 36 imaging technologies offered through Euro-BioImaging.

http://www.eurobioimaging.eu

European Sequencing and Genotyping Infrastructure (ESGI)

ESGI, the European Sequencing and Genotyping Infrastructure, aims at the integration of world class high-throughput sequencing and genotyping facilities. The project in particular provides access to sequencing and genotyping technologies as well as data analysis methodologies to the scientific community, for a broad range of genetic and systems biology studies using well-phenotyped samples, for example those derived from standardized European biobanks and animal facilities.
http://www.esgi-infrastructure.eu/

Infrafrontier

Infrafrontier, the European infrastructure for phenotyping and archiving of model mammalian genomes provide the facilities and resources for the phenotyping of medically relevant mouse models, and for the archiving and dissemination of those models. Mice indeed constitute a model system to understand the molecular basis of health and disease in humans, due in particular to the high (> 95 %) similarity of genes with humans.

https://www.infrafrontier.eu/

ITALY

Interdepartmental Centre for Stem Cells and Regenerative Medicine (CIDSTEM)

The Interdepartmental Centre for Stem Cells and Regenerative Medicine aims to provide patients with effective therapeutic solutions for severe diseases for which regenerative medicine is either the only or the best therapeutic chance, through ethical and scientific excellence. The GMP facility is devoted to the preparation of epithelial grafts, destined to clinical application in cell therapy and gene therapy and to the development of phase I/II clinical trials based on different types of ATMP, also on external commission.

http://www.cidstem.unimore.it/en/home.htm

THE NETHERLANDS

EATRIS

EATRIS aims to provide access to a top-academic high-end infrastructure and related academic services for research, translational research expertise and large patient cohorts. EATRIS is expected to facilitate the efficient translation of novel biomedical targets into the development of innovative preventive, diagnostic and therapeutic products, including their early stage clinical evaluation in a coordinated effort to address the “innovation gap” that afflicts both industry and academic science worldwide.

http://www.eatris.eu/

ECARUCA

ECARUCA is a European-based database, that collects cytogenetic and clinical data of rare chromosomal aberrations from (cyto)genetic centres in Europe and the rest of the world. Many ECARUCA accountholders are also member of the European Cytogeneticists Association (ECA). During recent years there has been an enormous

improvement in diagnostic techniques, enabling cytogeneticists to find more and smaller chromosomal aberrations. However, accurate clinical knowledge about rare chromosome disorders is frequently lacking, as a considerable percentage of cases remains unpublished. The resulting gap in clinical knowledge is in sharp contrast with the increasing demand from parents and physicians for reliable information on the disorder of their child or patient.
http://umcecaruca01.extern.umcn.nl:8080/ecaruca

LOVD: Leiden Open (source) Variation Database

LOVD aims to provide a flexible, freely available tool for Gene-centered collection and display of DNA variations. LOVD 3.0 extends this idea to also provide patient-centered data storage and storage of NGS data, even of variants outside of genes. To maintain a high quality of the data stored, LOVD connects with various resources, like HGNC, NCBI, EBI and Mutalyzer. The LOVD team is located in Leiden, The Netherland.

http://www.lovd.nl/3.0/home

SPAIN

SEFALer: Laboratory Animals Phenotyping Network

SEFALer is a service coordinated by CIBERER through several of its research groups, unprecedented in Spain and specialising in phenotyping animal models with specific applications for rare diseases. The SEFALer is a network technology platform which research groups and services (SEFALer units) are joining to carry out work on phenotyping laboratory animals, particularly genetically modified mice. The SEFALer platform is permanently open to having new research groups join.
http://www.ciberer.es/en/platforms/sefaler

SWEDEN

INCF-DataSpace

The purpose of the INCF Dataspace is to enable collaboration between researchers through the sharing of neuroscience data, text, images, sounds, movies, models and simulations.

https://www.incf.org/network

UNITED-KINGDOM

COMET (Core Outcome Measures in Effectiveness Trials)

The COMET Initiative brings together people interested in the development and application of agreed standardised sets of outcomes, known as ‘core outcome sets’. These sets represent the minimum that should be measured and reported in all clinical trials of a specific condition, and are also suitable for use in clinical audit or research other than randomised trials. The existence or use of a core outcome set does not imply that outcomes in a particular trial should be restricted to those in the relevant core outcome set. Rather, there is an expectation that the core outcomes will be collected and reported, making it easier for the results of trials to be compared, contrasted and combined as appropriate; while researchers continue to explore other

outcomes as well. COMET aims to collate and stimulate relevant resources, both applied and methodological, to facilitate exchange of ideas and information, and to foster methodological research in this area.
http://www.comet-initiative.org/about/overview

DECIPHER (Database of Chromosomal Imbalance and Phenotype in Humans Using Ensembl Resources)

DECIPHER is an interactive web-based database which incorporates a suite of tools designed to aid the interpretation of submicroscopic chromosomal imbalance. DECIPHER enhances clinical diagnosis by retrieving information from a variety of bioinformatics resources relevant to the imbalance found in the patient. Known and predicted genes within an aberration are listed in the DECIPHER patient report, common copy-number changes in healthy populations are displayed and genes of recognized clinical importance are highlighted. DECIPHER is an IRDIRC recognized resource.
http://decipher.sanger.ac.uk/

Diagnostic Mutation Database (DMuDB)

The Diagnostic Mutation Database is a secure repository of clinical quality variant data collected from diagnostic genetics laboratories. Access to DMuDB is available by annual laboratory subscription, and must be for diagnostic purposes only. DMuDB is accessed through a secure website; the data can also be accessed through a graphical browser, which is the preferred method for viewing data and also allows access to other mutation databases. Access to DMuDB is not permitted for any purpose other than the investigation and interpretation of patient results in order to provide a diagnosis. Researchers or healthcare professionals wishing to query the database and obtain data that may be held there send a request, which will be passed on to laboratories that have submitted relevant data. It may be possible for data to be shared for research and other non-diagnostic purposes but this must be done with express permission of the submitting laboratory and with data transfer agreements in place. The web site is a private site operated and maintained by Certus Technology. Access to the site is restricted. The DMuDB is located in Manchester, United-Kingdom.
https://secure.dmudb.net/ngrl-rep/Home.do

EBI (European Bioinformatics Institute)

The EBI is part of EMBL, Europe's flagship laboratory for the life sciences. EMBL-EBI provides freely available data from life science experiments covering the full spectrum of molecular biology. While they are best known for their provision of bioinformatics services, about 20% of the institute is devoted to basic research. An extensive training program helps researchers in academia and industry to make the most of the incredible amount of data being produced every day in life science experiments. The EBI is a non- profit, intergovernmental organisation funded by EMBL member states. The 500 staff from 43 nationalities work on the Wellcome Trust Genome Campus in Hinxton, Cambridge in the United Kingdom.

http://www.ebi.ac.uk

The EBI coordinates several projects which are very relevant for RD: The project **Cosmos**, Coordination of Standards in Metabolomics, brings together European data providers to set and promote community standards that will make it easier to disseminate metabolomics data through life science e-infrastructures.
http://www.cosmos-fp7.eu/

The project **Impact** for Improving protein annotation and coordination through technology contributes to the further development and enhancement of the 'InterPro' database of predictive protein signatures, i.e. entities that are used to recognize a particular domain or protein family, and its other contributing databases.

http://www.ebi.ac.uk/impact

The European Genome-Phenome Archive (EGA) provides a service for the permanent archiving and distribution of personally identifiable genetic and phenotypic data resulting from biomedical research projects. Data at EGA was collected from individuals whose consent agreements authorise data release only for specific research use to bona fide researchers. Strict protocols govern how information is managed, stored and distributed by the EGA project.

https://www.ebi.ac.uk/ega/home

ELIXIR

ELIXIR is an intergovernmental organisation that brings together life science resources from across Europe. These resources include databases, software tools, training materials, cloud storage and supercomputers.The goal of ELIXIR is to coordinate these resources so that they form a single infrastructure. This infrastructure makes it easier for scientists to find and share data, exchange expertise, and agree on best practices. Ultimately, it will help them gain new insights into how living organisms work. ELIXIR includes 21 member states and over 180 research organisations. It was founded in 2014, and is currently implementing its first five-year scientific programme. The scientific and technical activities in ELIXIR are run by five Platforms (Data, Tools, Interoperability, Compute and Training) and four Use Cases (Human Data, Rare Disease, Marine Metagenomics and Plant Sciences). Platforms bring together experts to define the strategy and provide services in a particular area e.g. training, data. Use Cases bring together scientists who work in a specific domain (e.g. Plant Sciences). These scientists develop services targeted for their own domains. They also give feedback on the services the Platforms provide, to make sure that the services solve real world problems.

http://www.elixir-europe.org/

GEN2PHEN

The GEN2PHEN project aims to unify human and model organism genetic variation databases towards increasingly holistic views into Genotype-To-Phenotype (G2P) data, and to link this system into other biomedical knowledge sources via genome browser functionality. The project establishes the technological building-blocks needed for the evolution of today's diverse G2P databases into a future seamless G2P biomedical knowledge environment, by the projects end. This will consist of a European-centred but globally-networked hierarchy of bioinformatics GRID-linked databases, tools and standards, all tied into the Ensembl genome browser.

http://www.p3p.org/biobank-toolkit/gen2phen

International Mouse Phenotype Consortium (IMPC)

The International Mouse Phenotype Consortium is a research infrastructure of excellence for translational research and functional genomics.
After completing the mouse genome sequence, an international consortium was developed, the International Knock-out Mouse Consortium (IKMC) to systematically generate mutant ES cells for every gene in the mouse genome (20,000 plus genes).
The IMPC builds on the efforts of International Knock-out Mouse Consortium (IKMC) to produce knockout mice and carry out high-throughput phenotyping of each line in order

to determine the function of every gene in the mouse genome. These mice are preserved in repositories and made available to the scientific community representing a valuable resource for basic scientific research as well as generating new models for human diseases.

https://www.mousephenotype.org

Instruct

Instruct, the Integrated Structural Biology Infrastructure, consists of distributed centres for structural biology. All centres maintain a set of core technologies (e.g. protein production, NMR, crystallography, microscopy) accessed by users to obtain multi-scale structural data.

http://www.structuralbiology.eu/

RD-Connect

RD-Connect is a unique global infrastructure project that links up databases, registries, biobanks and clinical bioinformatics data used in rare disease research into a central resource for researchers worldwide. In a six-year project funded by the European Union but uniting researchers across the world, it will develop an integrated research platform in which complete clinical profiles are combined with -omics data and sample availability for rare disease research, in particular research funded under the International Rare Diseases Research Consortium (IRDiRC). RD-connect is an IRDiRC Recognized recource. RD-Connect's scientific coordination is moved from Newcastle University to CNAG-CRG in Barcelona. RD-Connect's objectives are:

- Harmonisation and development of common standards for databases and patient registries for rare diseases by collaborating internationally to implement common registry infrastructure and data elements across a federated system.
- Harmonisation and development of common standards and a common catalogue for rare disease biobanks that collect and provide standardised, quality-controlled biomaterials for translational research.
- Development of a suite of clinical bioinformatics tools, including data mining and knowledge discovery tools for analysis and integration of molecular and clinical data to discover new disease genes, pathways and therapeutic targets.
- Development of an integrated platform to host the processed data from the research projects Neuromics, EURenOmics and future IRDiRC projects.
- Development of best ethical practices for balancing patient-related interests associated with rare disease research using databases/registries, biobanks and omics databases, engaging with relevant stakeholders, including patient organisations, clinical and research networks, legislators and policymakers and the pharmaceutical industry.
- Development of a proposal for an expedient regulatory framework for linking of medical and personal data related to rare disease on a European and global level.
- Ensuring access to project results and broad and global impact in science, diagnostics and translational research including industrial collaborations.

http://rd-connect.eu/

Please note that all data presented in this report are available for download at www.orphadata.org

For any questions or comments, please contact us: *contact.orphanet@inserm.fr*

Editor-in-chief: Ana Rath ● Editor of the report: Driss El Moustaine ● Visual design : Julie Christ ● Photography : Patrice Latron/Inserm

The correct form when quoting this document is:

« List of research infrastructures useful to rare diseases in Europe », Orphanet Report Series, Rare Diseases collection, May 2018
http://www.orpha.net/orphacom/cahiers/docs/GB/Research_Infrastructures_for_rare_diseases_in_Europe.pdf

This Orphanet Report Series is part of the project / joint action '677024 / RD-ACTION' which has received funding from the European Union's Health Programme (2014-2020).