European Commission

Rare diseases

How Europe is meeting the challenges

Research and Innovation

EUROPEAN COMMISSION

Directorate-General for Research and Innovation

Directorate F — Health

Unit F.5 — Personalised medicine

E-mail: RTD-FP7-HEALTH-PERSONALISED-MEDICINE@ec.europa.eu
RTD-PUBLICATIONS@ec.europa.eu

European Commission
B-1049 Brussels

EUROPEAN COMMISSION

Rare diseases

How Europe is meeting the challenges

Directorate-General for Research and Innovation
FP7 cooperation

Europe Direct is a service to help you find answers
to your questions about the European Union.

Freephone number (*):

00 800 6 7 8 9 10 11

(*) Certain mobile telephone operators do not allow access to 00 800 numbers or these calls may be billed.

More information on the European Union is available on the Internet (http://europa.eu).
Cataloguing data can be found at the end of this publication.
Luxembourg: Publications Office of the European Union, 2013

ISBN 978-92-79-28317-8
doi:10.2777/56070

Printed in Belgium
PRINTED ON ELEMENTAL CHLORINE-FREE BLEACHED PAPER (ECF)

Table of contents

Foreword

Dear Reader,

This booklet focuses on a group of diseases that are called 'rare' but actually affect over 30 million Europeans. Patients suffering from one of the estimated six to eight thousand rare diseases are few and far between, so pooling knowledge and scarce resources is the best way to find out how we can diagnose, treat or cure them.

Rare diseases are a challenge too big for any country or world region to master alone. This is why the European Commission, together with our national and international partners, initiated the International Rare Diseases Research Consortium (IRDiRC). It is the biggest collective rare diseases research effort which the world has ever seen. Its key objective is to deliver, by 2020, 200 new therapies for rare diseases and the means to diagnose most of them.

At the end of this publication, you will find a selection of over 110 recent projects on rare diseases, which the EU has funded with some €500 million since 2007. These projects bring together a vast array of know-how, experts and resources to improve our understanding of rare diseases in order to develop new diagnostics and therapies for patients, but also to promote best-practices used in hospitals and healthcare systems. It will help the many people who are affected by a rare disease and who all too often struggle to get medical attention and the help they desperately need.

We are committed to continue funding top quality research in rare diseases to the benefit of patients in Europe and around the world. Through IRDiRC, we will continue to strengthen the cooperation with our national and international partners.

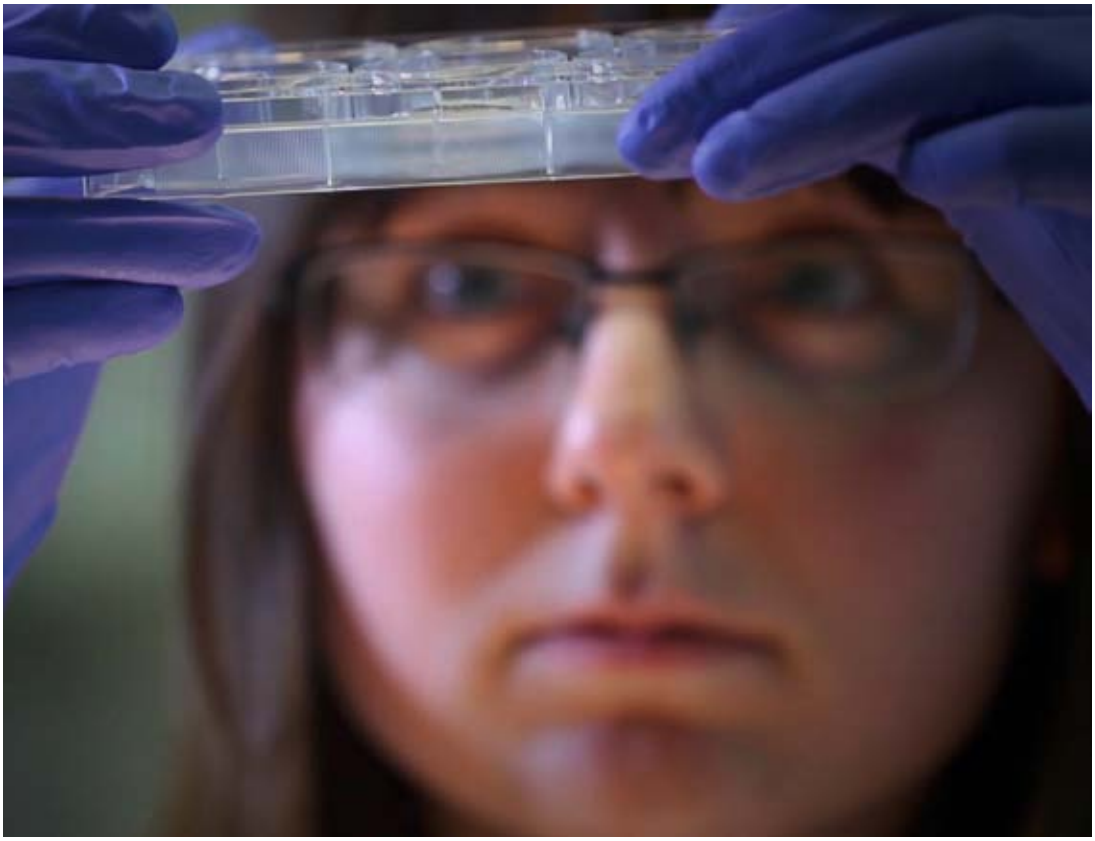
I hope you find this booklet interesting and informative.

Robert-Jan Smits,
Director-General, Directorate-General for Research and Innovation

Strength in numbers

New international consortium generates hope

Text by Brigid Grauman



Jane (not her real name) is a 15-year-old like any other, except that she isn't. She would like to go skiing with her cousin, she would like to do things other girls her age can do, but she can't because she has alternating hemiplegia, a rare disease that causes episodes of muscular spasms and paralysis. Physical effort, the cold, lights, foods or emotions of any kind can set off an episode that may last for anything from two hours to two weeks.

Jane doesn't take medicine because there isn't any that can help her condition. Instead, she tries to avoid situations that trigger an episode. Tsveta Schyns, a scientist who runs the European Network for Research on Alternating Hemiplegia Association (ENRAH), says the reality for patients like Jane is very much about 'living from day to day'. This year, the gene behind alternating hemiplegia was identified at last, offering cautious hope for patients.

Although there are only 500 known patients with alternating hemiplegia worldwide, rare diseases as a whole aren't rare. In the EU, a disease is defined as rare when it is life-threatening or chronically debilitating and when no more than 1 in 2 000 people has it. But while individually they may be rare, collectively they are not. Some 7 to 10 per cent of people have one of the 6 000–8 000 estimated rare diseases, and 30 million Europeans are affected by one or will be. Eighty per cent of rare diseases are genetic in origin.

The European Union has been funding cross-border research into rare diseases for well over a decade through its Framework Programmes for Research and Technological Development with complementary projects and actions funded via its Health Programmes (see the project section in this booklet). With the launch of an ambitious international consortium in 2011, it is hoping to bring research to a whole new level of collaboration.

The International Rare Diseases Research Consortium (IRDiRC) was the joint idea of the European Commission and the National Institutes of Health (NIH) in the US. It brings together a cross-section of everyone involved in rare diseases, from patients to researchers to biopharmaceutical industry representatives.

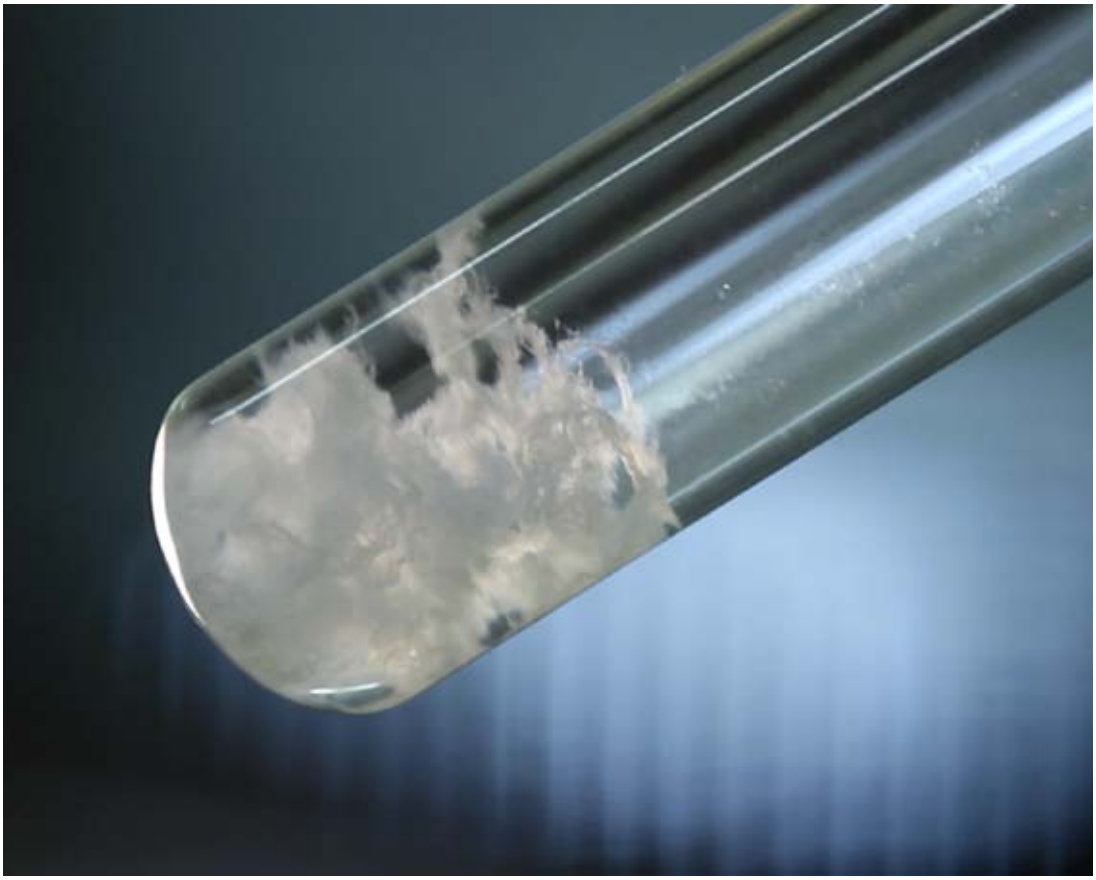
'The consortium's members have set themselves two ambitious goals for 2020 — to develop 200 new therapies for rare diseases and to find the means to diagnose most of them', says Ruxandra Draghia-Akli, who heads the Health Directorate at the Commission's Directorate-General for Research and Innovation, and is herself a noted scientist who worked during her PhD on a rare disease.

'The consortium's members have set themselves two ambitious goals for 2020 — to develop 200 new therapies for rare diseases and to find the means to diagnose most of them.'

'IRDiRC's aim is to fund projects that complement one another, while also encouraging healthy competition', says Draghia-Akli. 'At the same time, it is developing policies for how to deal with all aspects of research and innovation in this area, including data sharing and how to handle ethical problems and issues of intellectual property.'

The medical world has been revolutionised by new sequencing technology, which naturally is also changing the face of rare disease research. Over the past two years, the new Next Generation Sequencing Technologies have been applied to trying to discover the genetic variants, or changes in genomic sequences, that underlie rare diseases. These new technologies can be scaled up to many more families and rare diseases because they require fewer

Ruxandra Draghia-Akli, Director of the Health Directorate at the European Commission's Directorate-General for Research and Innovation.



researchers, and less time and money to tackle each rare disease.

'It's like iPods', says clinician-scientist Yanick Crow of the University of Manchester, 'these machines are everywhere. Mendelian genes are falling from the trees and the medical world will be a very different place five years from now.'

The patient's dilemma

In the meantime, what does this new research mean for patients? Most patient advocacy groups were started by parents of sufferers or patients seeking to have a louder collective voice to push for better diagnosis and data sharing. Nicolas Sireau, chairman of the Alkaptonuria (AKU) Society based in Cambridge, is one such parent. His sons, aged 9 and 12, have AKU, a genetic disease affecting some 1 000 known sufferers worldwide. AKU, a potentially debilitating condition that attacks the cartilage, causing brittleness that leads to severe osteoarthritis and a great deal of pain, is the first disease that led to the use of the expression 'inherited metabolic disease'. That was in 1901.

As with many rare diseases, the main problem with AKU is misdiagnosis. Urine of AKU sufferers is dark, and that starts at birth, but the diagnosis often comes later when the symptoms resemble those of osteoarthritis. 'When a person has been rightly diagnosed', says AKU Society Communication Manager Oliver Timmis, 'the advice is to eat less protein, and to avoid exercise that puts excessive strain on the joints.'

The Society is closely following the clinical trials launched with 12 partners across Europe on the use of nitisinone, used so

Willem Ouwehand, Professor of Experimental Haematology at the University of Cambridge and the Wellcome Trust Sanger Institute.

far to treat hereditary tyrosinemia. This EU-funded FP7 project is a good example of an international clinical trial with a patient group at its core, and could serve as a model for future rare disease research.

'From the discovery of the gene to a new treatment can take a long time. We have to manage expectations and not promise too much. The right medicine has to be identified and then it has to go through extensive safety and efficacy studies.'

Although the medicine won't reverse joint damage, it will prevent it from developing further. The earlier it is prescribed the better, so the sooner diagnosis is made the better the outcome for the patient.

A key player in patient welfare and policy reforms is Eurordis, a Paris-based non-governmental organisation representing 544 rare disease patient organisations in 49 countries, covering 4000 diseases. As Yann Le Cam, its chief executive officer, explains, it is essential to speak with one voice at national and European levels. The slogan for the 2012 Rare Disease Day was 'Rare but strong together', a call for solidarity for 'one of the most disadvantaged categories of population for centuries.'

New tools speed research

Since 2009, when the global research community started to apply modern genomics to rare disease research, scientists' ability to identify the causative genes of diseases has increased exponentially. The genes of some 3500–4000 diseases are still unknown, but 5 to 10 of these new genes are found almost every week. Medical research is being transformed.

Willem Ouwehand, Professor of Experimental Haematology at the University of Cambridge and the Wellcome Trust Sanger Institute, and the UK's NHS health representative on IRDiRC's Executive Committee, believes IRDiRC can achieve two important things. 'It can ensure that everyone adheres to common data-sharing rules in a pre-competitive way, which will speed up the process of gene discovery. And it ensures discoveries are rapidly translated to healthcare systems across the globe.'

New genomics technologies will simplify the diagnostic process, and thus reduce the period of diagnostic delay. 'This period is of about two years, but it can last as long as five years', says Ouwehand. 'This is an anx-

ious time for parents. The sooner a diagnosis is made the sooner parents can agree on a care plan for their child and make informed family planning choices.' Furthermore, if diagnosis is not made early enough the illness can cause lasting damage.

New treatments, the other area wherein lies much hope, can be a lengthy process and Ouwehand says one needs to be realistic. 'From the discovery of the gene to a new treatment can take a long time. We have to manage expectations and not promise too much. The right medicine has to be identified and then it has to go through extensive safety and efficacy studies.'

If the global research community could identify some 10 new causative genes every week, says Ouwehand, it would still take some 7 years to discover the remaining 3 500 or so genes that cause as yet unexplained rare diseases. 'So we must speed up', he says, 'and IRDiRC will help because data sharing among researchers will lead to faster discovery.'

Another potential benefit of research into rare diseases, which are mostly monogenic, or caused by the inheritance of a single defective gene, is that it can help us understand the cause of common disorders like obesity and cardiovascular diseases, including strokes and heart attacks. Ongoing work with families affected by rare diseases will, step-by-small-step, offer insights into the details of the molecular processes that underlie common diseases, and this will eventually lead to the development of new therapies that may also have wider applications.

Repurposing: using existing drugs

Among his many commitments, Lakshminarayan Ranganath runs Britain's new Alkaptonuria (AKU) Centre at the Royal Liverpool University Hospital, where they carry out genetic analysis and genotype/phenotype correlations. The UK has 80 AKU patients, who are involved in the Centre's clinical trial for repurposing nitisinone as part of the EU-funded FP7 project.

'In Liverpool, we are carrying out an active research programme in both basic and clinical science', Ranganath explains. 'In basic science we're still trying to understand this disease that resembles osteoarthritis. We're trying to develop gene and enzyme therapies, using new clinical assessment tools.'

For researchers like Ranganath, IRDiRC is a powerful voice for rare diseases, which don't get a fair share of research funds. 'It's very important for us to help generate funds', he says. Furthermore, he adds, research may be applied to other more common diseases. 'AKU research may help in the treatment of arthritis, which affects around 20 per cent of people over the age of 50.'

Why come at it from an AKU viewpoint? 'Because there are already a lot of people researching osteoarthritis. When you study a rare disease you come at it from a new angle and shed a different light.'

Also a clinician-scientist, Yanick Crow of the University of Manchester says the repurposing of drugs is what is speeding up treatment. 'The new genomic technology translates into trial therapies that allow us to be more optimistic than ever before. New drugs, however, take longer to develop.'

Thanks to the new technologies, Crow and his team have found the genes relevant to Nuclease Immune Mediated Brain and Lupus-like conditions, and therapeutic options may lie ahead. He has secured funding to undertake clinical trials with a treatment already used for HIV. 'With an immune disease where you can potentially switch off or temper an immune response, therapeutic options are a real possibility', says Crow.

He also sees an interesting development in the study of some rare diseases — the definition of disease pathways. 'Suddenly you have a set of diseases that have a common pathogenesis', he says. 'I believe that in five years' time the genetic basis of most Mendelian diseases, or monogenic diseases that follow simple laws of inheritance, will have been defined.' The grouping of conditions into disease pathways, Crow explains, will greatly help in the development and use of treatments.

For Crow, our very conception of complex and simple (Mendelian) diseases is changing. 'One reason people are interested in rare diseases is that they offer a relatively tractable approach to understanding an otherwise seemingly intractable problem. It's a different way of looking at the same problem.'

Orphan medicine: the need to join forces

Until the 1980s in the US and the late 1990s in Europe, few pharmaceutical companies were keen to concentrate on rare diseases, until they realised that designing a drug for a molecular target unequivocally defined by genetics is often a more focussed, more effective and safer route to drug development. They saw a new opportunity, with the concomitant hope that some of these drugs may turn out to have wider applications. One such example is oncology drugs developed for rare cancers that have been applied more widely after the first authorised indications.

'Some companies have in fact been investing in rare disease treatment for a long time', says health policy expert Wills Hughes-Wilson, 'but over recent years rare diseases have moved front and centre in the minds of pharmaceutical companies. This is due to an increasing awareness of rare diseases, along with a growing understanding and acceptance that these patients deserve treatment.' She should know. Among her many positions, Hughes-Wilson is vice-president for External Affairs at the biopharmaceutical company Swedish Orphan Biovitrum (Sobi), and chair of the industry associations' European biopharmaceutical Enterprises (EBE) and Europabio's Joint Taskforce on Rare Diseases.

As a member of the European Commission's Committee of Experts on Rare Diseases (EUCERD), Hughes-Wilson stresses that the orphan drug development model must be improved by bringing all stakeholders together. IRDiRC, she says, is a decisive step in that direction. 'Orphan medicinal product development is not less expensive or simpler. In fact, it's sometimes a lot more complicated because there are often few medical experts, an absence of animal models and computer simulations for pre-clinical studies, and small and geographically dispersed patient populations for the clinical trial programmes.'

'IRDiRC provides a platform for exchanging ideas and it offers a good cross-fertilisation of people with the same goals.'

As a result, she says it's increasingly important for industry regulators, investors, clinicians, patient groups and business to find creative ways to challenge the current development paradigm. 'We need tools like progressive or adaptive licensing, innovative funding programmes like the EU's FP7 research programme, new models for countries to work together to increase market access, and new models for collaborative consortium-based development. And we need to address commercialisation right from the very beginning of a drug's development. There's not much use having a great product if it doesn't reach the patient.'

Prosensa is a small biotech company in Leiden, the Netherlands, that focuses on rare diseases and works closely with the universities of Leiden and Nijmegen and pharmaceutical groups, like GlaxoSmithKline. They don't yet have therapies on the market but are working on nine programmes, including two products for Duchenne muscular dystrophy. One of these is in the last stage of development and should be ready in 2013.

'2013 is a very exciting year for us', says Chief Business Officer Luc Dochez. 'IRDiRC provides a platform for exchanging ideas and it offers a good cross-fertilisation of people with the same goals. Although the

Luc Dochez, Chief Business Officer at Prosensa, Leiden, the Netherlands.

Lucia Monaco, Chief Scientific Officer, Telethon.

stakeholders each have their own personal interests, we are all committed to helping as many patients as we can as soon as we can. The consortium helps us to work together more effectively and efficiently.'

'IRDiRC will provide added value to our research initiatives by identifying gaps that we can fill with specific funding initiatives'

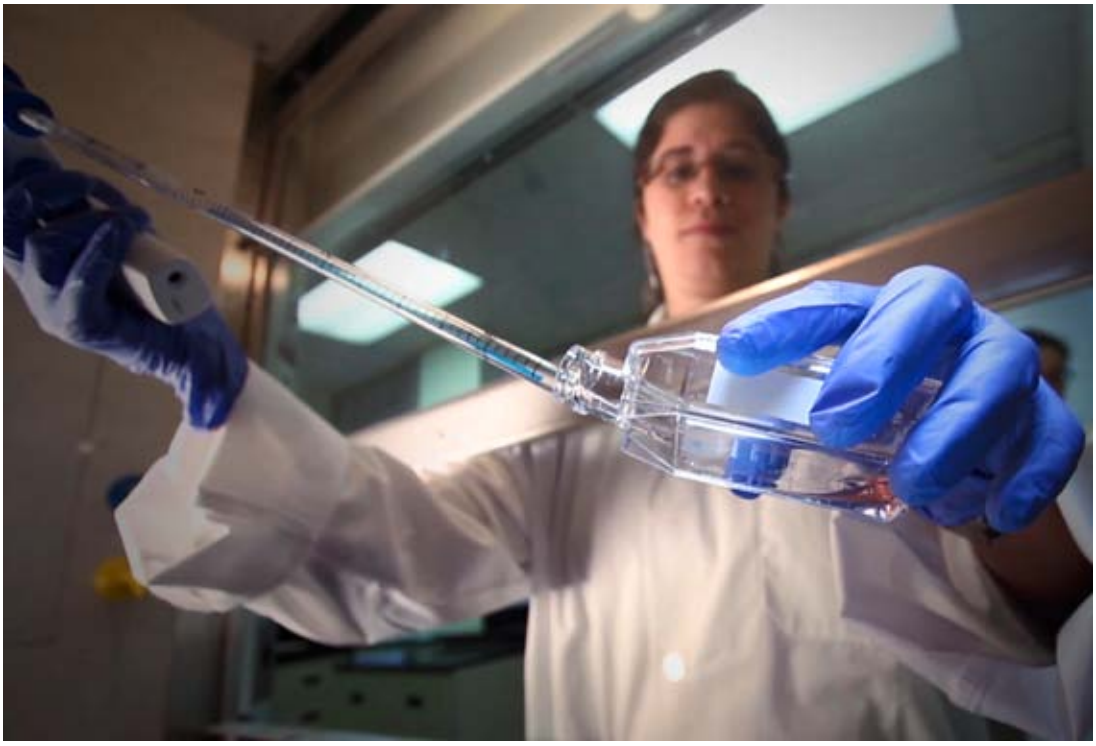
Funding agencies have their nose to the ground

Finding the funds to invest in research is a constant battle. In Italy, Telethon is a charity that funds research into hereditary genetic diseases. Started in 1990 by patients with muscular dystrophies, the objective has since broadened to include all genetic diseases. In 2012, they raised more than €30 million at their yearly TV fundraising event. The money is spent on research at the three Telethon Institutes, as well as at Italian non-profit research laboratories through calls for application.

'We decided to join IRDiRC because 80 per cent of rare diseases are genetic in origin', says Chief Scientific Officer Lucia Monaco, 'and IRDiRC's objectives of supporting the development of diagnostic tools and therapies for rare diseases are very much in line with our own.' Although Telethon raises funds and invests in Italy, they are convinced that research into rare diseases must have an international reach.

'IRDiRC will provide added value to our research initiatives by identifying gaps that we can fill with specific funding initiatives', says Monaco, 'and it will also help us by providing shared policies and guidelines issued by its scientific committees.'

In the view of Lucia Faccio, who heads Telethon's Business Development Office, our drug development model is unsatisfactory. 'The development guidelines are not yet set, the endpoints are still exploratory, the technical assessments are complicated and in most cases there are no benchmarks.' She says we need close collaboration with the regulatory authorities for an open assessment of a therapy's risks and benefits. Telethon believes in the importance of orphan drug designation for rare disease therapies, and has



so far obtained Orphan Drug Designation from the European Medicines Agency (EMA) and the United States Food and Drug Administration (FDA) for six rare genetic diseases.

Telethon has witnessed the rare disease field becoming increasingly relevant to pharmaceutical and biotech companies. In the past two years, the charity has signed two agreements with two major pharmaceutical companies for the development of innovative therapies for genetic diseases. 'We see this as an essential step to complete the path from laboratory to patient', says Faccio, 'since both the resources and the competences needed to reach therapy registration and to make them accessible to patients are in the hands of industry.'

National funding agencies have been among IRDiRC's early members, with the ambition being to know what was going on elsewhere and to streamline their efforts. Paul Lasko is director of the Canadian Institute of Genetics, and will take over the chairmanship of IRDiRC's Executive Committee in April 2013. He is actively engaged in cutting-edge science. 'What IRDiRC is already bringing to the table', he says, 'is better coordination among its member funding agencies, so we're actually talking to each other, addressing gaps and coordinating.'

It is also bringing about much better cooperation among researchers, he insists. 'All these different diseases make it a complicated area, and what's developing is a protected space where researchers can discuss plans while at the same time protecting proprietary data.'

A large number of therapies are currently being experimented on rare diseases, among them gene therapy, which may have applications for common diseases. 'We're learning about novel types of therapies in the rare diseases world and we're also identifying mutations and thinking of them

in terms of a patient stratification strategy', says Lasko. 'Several rare diseases may cause neuro-muscular degeneration, for instance, which allows us to stratify patients.'

Stratification is the identification of groups of patients who share 'biological' characteristics, and can thus be diagnosed and treated more effectively. Scientists are doing the same when stratifying cancer patients based on molecular markers, so again rare disease therapeutic research is at the scientific forefront. 'In fact, we can think of cancer as a huge collection of rare diseases', says Lasko. 'In Canada, this is why funding into rare diseases is seen as part of a larger personalised medicine. The market is small but if we can start addressing these genes collectively then it becomes much more attractive to pharmaceutical companies.'

Future world

Jeff Schloss heads the Division of Genome Sciences at the National Human Genome Research Institute, NIH, in Bethesda, Maryland, in the US. 'We're running the front rather than the back end of the programme', he says of their role within IRDiRC. Within this division, Lu Wang coordinates a four-year programme called Centers for Mendelian Genomics.

Their work is where we're heading in the future. It involves the Next Generation DNA Sequencing Technology that allows scientists to sequence the entire genome quite fast and quite cheaply, and thus be able to do this with several family members to identify the DNA changes that underlie rare diseases. Another approach, known as exome sequencing, is to study the roughly 5 % of the genome most likely to include the important DNA changes.

'The three centres' joint goal is to discover the genetic basis of as many rare and inherited disorders as we can', says Wang. 'Our long-term goal is to make the most of what genomic technology can do for the genetic basis of rare inherited disorders.'

The genetic basis of a dozen rare diseases has so far been discovered by using the new whole genome or whole exome methods, and the point of the programme is to accelerate this path by applying the new sequencing and analysis technologies to increasing success rates. 'As you do more of these studies you learn how to design them more successfully', says Schloss.

For genomic researchers like Schloss and Wang, IRDiRC helps identify scientists working on the same disease with whom to share patient samples or data. 'It's good to put genomics researchers together with people who know about drug development', says Schloss. 'Within IRDiRC, we have experts in gene discovery and people with extensive clinical experience. In some cases these people are one and the same, but for everyone the ultimate motivation is to figure out how to treat patients.'

Ruxandra Draghia-Akli of the European Commission sees IRDiRC as a major worldwide effort to increase awareness of rare diseases, to help understand their origin and how they function, and to promote joint international research across the public and private sectors. 'This is a large collaborative effort and I am very optimistic that IRDiRC will reach its goals. It's not an easy task, but we'll get there.'

'At the end of the day', says health policy expert Wills Hughes-Wilson, 'the attraction of rare diseases is the difference specific and effective therapies can make in patient communities that previously lacked hope.' Fifteen-year-old Jane, whose days are so blighted by alternating hemiplegia and who craves just a little independence from her illness, may be among the many thousands of patients to benefit.

Read more about IRDiRC on:
http://www.irdirc.org.

EU funding for rare diseases

Rare disease research in the *Seventh Framework Programme for Research and Technological Development* (FP7; 2007–13) focuses on Europe-wide studies of natural history, pathophysiology and the development of preventive, diagnostic and therapeutic interventions. FP7 has funded close to 100 collaborative research projects addressing various aspects of rare diseases with some 1 000 participants from over 38 countries.

Under the *Second Programme of Community Action in the Field of Health* (Health Programme; 2008–13) more than 30 projects on rare diseases have been funded, covering different types of actions and stakeholder groups. A number of EU-wide resources are in place to pool scarce expertise and provide patients and health professionals with improved access to medical information, treatment centres, patient support groups and epidemiological/research data.

Rare disease projects

a selection of EU-funded activities since 2007(*)

(*) Second Programme of Community Action in the Field of Health, Seventh Framework Programme for Research and Technological Development.

This section contains a selection of projects funded by the EU's Seventh Framework Programme for Research and Technological Development (FP7; 2007–13) and the Second Programme of Community Action in the Field of Health (Health Programme; 2008–13). Whilst the FP7 projects mostly deal with collaborative health research, the activities funded through the Health Programme are often complementary and focus on policy or implementation aspects.

The projects selected have been divided into seven categories:

- Cancer
- Cardiovascular, pulmonological and haematological disorders
- Dermatology, ophthalmology, urology and nephrology
- Immunology
- Metabolic disorders and endocrinology
- Neurology, mental health, neuromuscular and musculoskeletal disorders
- Systems biology, molecular genetics, databases, clinical pharmacology, support and coordination

More information about the projects can be found on the project websites or on the websites of the European Commission:

- FP7: http://cordis.europa.eu
- Health Programme: http://ec.europa.eu/health

Cancer

DARTRIX

DARPin Targeted Magnetic Hyperthermic Therapy for Glioblastoma

The DARTRIX project will develop high-affinity protein scaffolds to create a new generation of targeted therapeutics to fight glioblastoma. Brain cancer (glioblastoma) is nearly incurable and most patients die within a year after diagnosis, so there is an urgent need to improve the treatments for this disease.

Small, non-immunoglobulin human protein scaffolds binding specific targets with exceptionally high affinity (DARPins) will be coupled with a contrast agent (ferucarbotran). When stimulated by an appropriate alternating magnetic current, ferucarbotran generates heat that can kill cancer cells very effectively. The DARTRIX team aims to use DARPins to specifically target tumour cells before application of the magnetic current, to generate toxic heat in the tumour itself.

- Coordinator: **Kerry Chester, University College London (United Kingdom) (k.chester@ucl.ac.uk)**
- Participants: **UK (Coordinator), CH, DE, FR**
- Website: **http://cordis.europa.eu/**
- Duration: **from March 2012 to February 2017**
- Project costs: **€7.7 million**
- EU contribution: **€5.9 million**
- Project Number: **278580 (FP7-Health)**

ENCCA

European Network for Cancer Research in Children and Adolescents

The ENCCA Network has put its forces together for the benefit of young people suffering from cancer. ENCCA aims to establish a European Virtual Institute to set up an integrated research strategy and to facilitate clinical trials to introduce a new generation of biologically targeted drugs. This will increase the quality of life of cancer survivors through more efficacious and less toxic therapies.

The biologically-driven research agenda of ENCCA will improve training of the clinical investigators and translational scientists to spread excellence, increase capacity to participate in research and monitor outcomes across Europe. ENCCA aims to accelerate drug development in partnership with the industry by improving the access to young patients with cancer and to academic expertise in care, clinical and biological research.

Bringing all stakeholders to the table, ENCCA will address the needs of all current multinational clinical trial groups for the benefit of children with cancer.

- Coordinator: **Ruth Ladenstein, St. Anna Kinderkrebsforschung / Children's Cancer Research Institute (Austria) (ruth.ladenstein@ccri.at)**
- Participants: **AT (Coordinator), BE, DE, EL, ES, FR, IT, NL, PL, SE, UK**
- Website: **http://www.encca.eu/**
- Duration: **from January 2011 to December 2014**
- Total costs: **€13.4 million**
- EU contribution: **€11.9 million**
- Project Number: **261474 (FP7-Health)**

ENS@T-CANCER

European Network for the Study of Adrenal Tumours — Structuring clinical research on adrenal cancers in adults

Adrenal tumours are rare but have a very unfavourable prognosis. The rarity of the tumour impedes clinical studies, which are often fragmented and have small cohort sizes. The European Network for the Study of Adrenal Tumours aims to fill this gap in research, and also to increase treatment options for affected patients and harmonise diagnostic criteria.

ENS@T has set up a database of adrenal tumours and has defined an associated network of Biological Resource Centers for further research on molecular mechanisms and increasing the availability of specific diagnostic and therapeutic tools for adrenal cancers. In addition, the network will focus on structuring European clinical and translational research, conducting interventional trials for the benefit of patients, improving diagnosis and risk stratification of adrenal cancer and identifying novel biomarkers for treatment response, amongst other things.

- Coordinator: **Felix Beuschlein, Medizinische Klinik and Poliklinik IV, Ludwig-Maximilians University, Munich (Germany) (felix.beuschlein@med.uni-muenchen.de)**
- Participants: **DE (Coordinator), FR, IT, NL, UK**
- Website: **http://www.ensat.org/**
- Duration: **from January 2011 to December 2015**
- Total costs: **€8.1 million**
- EU contribution: **€5.9 million**
- Project Number: **259735 (FP7-Health)**

EUROSARC

EUROpean clinical trials in rare SARComas within an integrated translational trial network

EUROSARC focuses on the treatment of sarcomas, a rare and heterogeneous group of malignant tumours. Their treatment now needs to be adapted to histological and molecular subtypes and targeted therapies need to be developed. The integrated EUROSARC consortium gathers representatives of most European sarcoma groups and SMEs, all with proven track records of scientific and clinical excellence.

In the past, due to the rarity of sarcomas, very few clinical trials or systemic treatments have been carried out in specific subtypes of the tumour. EUROSARC comes in to establish new systemic treatment strategies and to set up innovative targeted therapies based on the scientific understanding of molecular alterations driving the tumours thereby developing paradigm-changing clinical research. Translational research and facilitating cooperation on the international level are also amongst the EUROSARC project objectives, but its main aim is still to further improve the duration of survival and the quality of life of patients.

- Coordinator: **Jean-Yves Blay, Université Claude Bernard Lyon 1 (France) (jean-yves.blay@lyon.unicancer.fr)**
- Participants: **FR (Coordinator), BE, DE, ES, IT, NL, PL, UK**
- Website: **http://www.eurosarc.eu/**
- Duration: **from December 2011 to November 2016**
- Total costs: **€7.9 million**
- EU contribution: **€5.9 million**
- Project Number: **278742 (FP7-Health)**

GAPVAC

Glioma actively personalised vaccine consortium

Gliablastoma (GB) is rare, but fatal. While 2 to 3 out of 100 000 people are hit by GB, there are 13 000 Europeans per year facing the diagnosis of this deadly disease with the chance to survive the next 5 years being less than 6 %.

Currently available therapeutic options are uniformly 'one medicine for all patients' approaches and therefore are actually neglecting the individuality of each patient's disease. These therapies are often accompanied by severe toxicities with only limited benefit for patients (tumour growth and survival times).

The GAPVAC team aims to introduce a novel, highly innovative approach of actively personalised immunotherapy which might have a tremendous impact for the life course of affected patients without additive toxicities. This will be achieved by an on-demand manufactured peptide vaccine specifically tailored to stimulate the patients´ immune system to defend the body against the cancerous disease.

GAPVAC's goal is to test the safety, feasibility and efficacy (biological and early clinical) of this new personalised approach to immunotherapy.

- Coordinator: **Sabrina Kuttruff, Immatics Biotechnologies GmbH (Germany) (kuttruff@immatics.com)**
- Participants: **DE (Coordinator), CH, DK, ES, IL, NL, UK, US**
- Website: **http://www.gapvac.eu/**
- Duration: **from November 2012 to January 2017**
- Total costs: **€7.9 million**
- EU contribution: **€6.0 million**
- Project Number: **305061 (FP7-Health)**

IMMOMEC

IMmune MOdulating strategies for treatment of MErkel cell Carcinoma

IMmune MOdulating strategies for treatment of MErkel cell Carcinoma (IMMOMEC) is a project that has been set up to establish and investigate a new and effective immunotherapy for merkel cell carcinoma (MCC). Although a very rare form of skin cancer (affecting 0.44 per 100 000), it is far more lethal, with a mortality rate of 37 %.

IMMOMEC has worked on developing a therapeutic approach for treatment of patients with MCC. It seeks to do so by testing and establishing an effective therapy for MCC before establishing the feasibility of effective immunotherapy. In addition, IMMOMEC tries to identify and characterise HLA-restricted immunodominant T cell epitopes as well as prognostic and predictive biomarkers.

Underlying this work is the objective to establish a European network for research and therapy of MCC.

- Coordinator: **Prof. Jürgen C. Becker, Medizinische Universitaet Graz (Austria) (juergen.becker@medunigraz.at)**
- Participants: **AT (Coordinator), DE, DK, ES, FR, IT, UK**
- Website: **http://www.immomec.eu/**
- Duration: **from January 2012 to December 2015**
- Total costs: **€7.4 million**
- EU contribution: **€5.7 million**
- Project Number: **277775 (FP7-Health)**

IntReALL

International study for treatment of childhood relapsed ALL 2010 with standard therapy, systematic integration of new agents, and establishment of standardised diagnostics and research

Leukaemia might hit adults and children alike, in either acute or chronic form. IntReALL concentrates on acute lymphoblastic leukaemia (ALL) in children, as relapse remains the main cause of mortality. IntReALL project partners are creating the world's largest study for children with ALL relapses to optimise treatment and to foster studies on the most promising new and targeted agents. This will establish the highest diagnostic and therapeutic standard and improve the survival of children with ALL.

IntReALL will set up an adequate trial structure, an optimised web-based database and standardised diagnostic methods. For standard risk patients, the best available treatment protocols will be randomly compared, and the additional effect on survival of the humanised monoclonal CD22 directed antibody epratuzumab will be investigated. High risk patients who have unsatisfying remission rates will receive an intensified induction with the new nucleoside analogue clofarabine compared to standard induction therapy.

- Coordinator: **Arend von Stackelberg, Charité Berlin (Germany) (arend.stackelberg@charite.de)**
- Participants: **DE (Coordinator), AT, BE, CH, CZ, DK, ES, FI, FR, IL, IT, NL, NO, PL, PT, SE, UK, US**
- Website: **http://paedonko.charite.de/**
- Duration: **from October 2011 to September 2016**
- Total costs: **€7.7 million**
- EU contribution: **€5.9 million**
- Project Number: **278514 (FP7-Health)**

LOULLA&PHILLA

Development of 6-Mercaptopurine and Methotrexate oral liquid formulations for the maintenance treatment of Acute Lymphoblastic Leukaemia in children

The French company Only for Children Pharmaceuticals coordinated a multinational and multidisciplinary consortium specialised in paediatric haemato-oncology. The team was composed of clinicians, paediatricians, pharmacokineticists, pharmacists, manufacturers, engineers, as well as regulatory and ethical experts. It performed the non-clinical and clinical development of Methotrexate and 6-Mercaptopurine oral liquid formulations adapted for maintenance treatment of acute lymphoblastic leukaemia in children.

The adapted formulations were developed and made available while the project was ongoing. In addition, a pharmacokinetic, palatability and safety study to assess the bioavailability of the new 6-Mercaptopurine oral liquid formulation was conducted on 15 patients, followed by registration at the European Medicines Agency (EMA).

- Coordinator: **Vincent Grek, Only for Children Pharmaceuticals, Paris (France) (vincent.grek@O4CP.com)**
- Participants: **FR (Coordinator), DE, DK**
- Website: **http://www.fp7-loullaphilla.eu/**
- Duration: **from November 2008 to April 2012**
- Total costs: **€4.2 million**
- EU contribution: **€3.3 million**
- Project Number: **223401 (FP7-Health)**

OCTIPS

Ovarian Cancer Therapy — Innovative Models Prolong Survival

Most epithelial ovarian cancer (EOC) patients first respond to surgery and chemotherapy, but then relapse and die. The high mortality rate is due to developed resistance to chemotherapy.

The international OCTIPS project team hypothesises that the primary tumour includes a small population of resistant cells that are ultimately responsible for relapse and that by targeting this population front-line it may prolong disease-free survival or even achieve a cure. OCTIPS will use unique retrospective and novel prospective paired tumour samples collected at the time of diagnosis and relapse to identify and validate molecules and pathways responsible for relapse.

OCTIPS aims to develop new targeted therapies through different model systems, translating its findings into patients' benefits and survival.

- **Coordinator:** Dan Cacsire Castillo-Tong, Medizinische Universität Wien (Austria) (dan.cacsire-castillo@meduniwien.ac.at)
- **Participants:** AT (Coordinator), BE, DE, FR, IL, NL, UK
- **Website:** http://www.octips.eu/
- **Duration:** from January 2012 to December 2015
- **Total costs:** €3.9 million
- **EU contribution:** €2.9 million
- **Project Number:** 279113 (FP7-Health)

OPTATIO

OPtimising TArgets and Therapeutics In high risk and refractOry Multiple Myeloma

OPTATIO seeks to develop new diagnostic methods and therapeutic options to tackle Multiple Myeloma, an incurable blood cancer with rapidly growing prevalence and poor prognosis.

Project members of OPTATIO will analyse clinical data to learn more about reasons for therapy resistance and disease relapse due to acquired drug resistance. These data will be used further on for in vitro screening and in innovative in vivo models, with the aim being to develop new lead compounds targeting myeloma cells within their microenvironment.

The clinical expertise of several oncological divisions, the research experience of academic laboratories and the pharmaceutical know-how of small and medium-sized enterprises as well as the biotech industry are joining their efforts within OPTATIO to tackle Multiple Myeloma. OPTATIO will ensure better diagnostics, more realistic new drug screening approaches and personalised therapies, all aiming to reduce the death toll of people hit by Multiple Myeloma.

- **Coordinator:** Wolfgang Willenbacher, Medical University Innsbruck (Austria) (wolfgang.willenbacher@uki.at)
- **Participants:** AT (Coordinator), CZ, DE, ES, HU, IT
- **Website:** http://www.cemit.at/projekte/eu-fp7-optatio.html
- **Duration:** from January 2012 to December 2014
- **Total costs:** €4.3 million
- **EU contribution:** €2.9 million
- **Project Number:** 278570 (FP7-Health)

OVER-MyR

Overcoming clinical relapse in multiple myeloma by understanding and targeting the molecular causes of drug resistance

OVER-MyR fights against multiple myeloma, a currently incurable rare malignant plasma cell disease. Patients suffering from this disease often relapse despite therapy. The OVER-MyR team aims to understand the reasons for the drug resistance, to develop new and better strategies to tackle the disease, and to provide input for further studies on safety, dosage levels and responses to new treatments.

OVER-MyR will investigate in particular some aspects of relapse, focusing on drugs and their specific sub-clones or sub-populations and alterations in cells of the niche that promote drug resistance. Further works will include a study on the molecular alternation in primary multiple myeloma and environment cells, as well as the implementation of in vitro and in vivo models of drug resistance to compare respective characteristics. The results of research to be carried out will permit the identification of ten prominent (altered) candidate genes involved in multiple myeloma relapse.

- Coordinator: **Karin Vanderkerken, Vrije Universiteit Brussel (Belgium) (Karin.Vanderkerken@vub.ac.be)**
- Participants: **BE (Coordinator), AU, DE, FR, IT, NL, UK**
- Website: **http://www.over-myr.eu/**
- Duration: **from January 2012 to December 2014**
- Total costs: **€3.9 million**
- EU contribution: **€2.9 million**
- Project Number: **278706 (FP7-Health)**

RARECARENet

Information network on rare cancers

RARECARENet is an information network on rare cancers, aiming to provide comprehensive information on unfamiliar forms of cancer to relevant target groups such as oncologists, general practitioners, researchers, health authorities and patients.

The network aims to develop information on the healthcare pathways for rare cancers, centres of expertise, clinical diagnosis and management (including very rare cancers), and updated epidemiological indicators, and information for patients. Dissemination of information amongst target groups and relevant national and international associations is at the heart of the network's work. The final objectives are to improve the timeliness and accuracy of diagnosis, to facilitate the access to high quality treatment for patients with rare cancers, and to standardise practices across EU countries.

- Coordinator: **Gemma Gatta, Fondazione IRCCS Istituto Nazionale dei Tumori, Milano (Italy) (gemma.gatta@istitutotumori.mi.it)**
- Participants: **IT (Coordinator), BE, BG, CH, FI, FR, IE, NL, SI, UK**
- Website: **http://www.rarecare.eu/**
- Duration: **from May 2012 to October 2015**
- Total costs: **€1.7 million**
- EU contribution: **€1.0 million**
- Project Number: **20111201 (EU Health Programme)**

Cardiovascular, pulmonological and haematological disorders

BESTCILIA

Better Experimental Screening and Treatment for Primary Ciliary Dyskinesia

Primary Ciliary Dyskinesia (PCD) is a rare genetically heterogeneous disorder which results from the dysfunction of motile hair-like organelles (cilia) that results in severe, chronic airways disease. The main objective of BESTCILIA is to improve the diagnosis and treatment of PCD patients, as the current lack of evidence-based management guidelines translates into a high burden of disease and related healthcare costs.

The BESTCILIA team will establish widespread, early diagnosis by the introduction of nasal Nitric Oxide measurement as a screening tool and by the introduction of high-speed videomicroscopy as a diagnostic tool. BESTCILIA will develop new outcome criteria, notably a PCD-specific quality of life questionnaire, and establish a PCD registry for both cross-sectional analysis of current disease status and longitudinal observational analysis of disease progression under different regimens.

- **Coordinator:** Heymut Omram, Westfälische Wilhelms-Universität Münster (Germany) (heymut.omran@ukmuenster.de)
- **Participants:** DE (Coordinator), CH, CY, DK, EL, NL, PL, UK, US
- **Website:** http://cordis.europa.eu/
- **Duration:** from December 2012 to November 2015
- **Total costs:** €3.8 million
- **EU contribution:** €2.9 million
- **Project Number:** 305404 (FP7-Health)

ChiLD-EU

Orphans Unite: chiLD better together — European Management Platform for Childhood Interstitial Lung Diseases

Lack of awareness or complex differential diagnosis leads to much morbidity and mortality (about 15%) of children suffering from diffuse lung diseases, called childhood interstitial lung diseases (chiLD). The chiLD-EU project will put forward evidence-based diagnostic and management clinical guidelines for the benefit of the young patients.

Leading European clinical scientists and paediatric pulmonologists collaborate to assemble cohorts in which children are followed in a pan-European database and biobank compatible with others worldwide to allow common projects. Outcomes and treatment schemes will be rigorously defined and their value systematically assessed. ChiLD-EU will put defined treatment protocols systematically into practice, allowing their evaluation, and perform a randomised controlled trial to put prescriptions for children on an evidence-based footing.

- **Coordinator:** Matthias Griese, Ludwigs-Maximilians-Universität München (Germany) (matthias.griese@med.uni-muenchen.de)
- **Participants:** DE (Coordinator), FR, IT, TR, UK
- **Website:** http://www.childeu.net/
- **Duration:** from January 2012 to May 2016
- **Total costs:** €3.8 million
- **EU contribution:** €3.0 million
- **Project Number:** 305653 (FP7-Health)

DEEP

DEferiprone Evaluation in Paediatrics

β-thalassaemia major is one of the most severe forms of rare anaemia. Survival and quality of life have dramatically improved through regular blood transfusions and chelating (removing heavy metals from the body) therapy removing iron accumulation. There are three iron chelating agents available in Europe, deferiprone being the first oral drug and considered the most efficacious in removing iron from the heart. Despite wide experience with deferiprone, limited data are available on its use in children, especially in 2–10 year-olds.

DEEP aims at integrating existing information on use of deferiprone in paediatrics, covering the lack of knowledge and providing a valid support to its usage in all age groups of children. Through conducting three studies, the project will provide data on pharmacokinetics, comparative efficacy/safety and long-term safety. DEEP's final aim is to provide deferiprone in efficacious dosages as a first line treatment for patients under 18 years of age.

- **Coordinator:** Adriana Ceci, Università degli Studi di Bari (Italy) (adriana.ceci@uniba.it; deep@cvbf.net)
- **Participants:** IT (Coordinator), AL, CA, CY, DE, EG, GR, NL, TN
- **Website:** http://www.deep.cvbf.net
- **Duration:** from January 2011 to December 2014
- **Total costs:** €8.1 million
- **EU contribution:** €5.2 million
- **Project Number:** 261483 (FP7-Health)

ENCE-CF-LAM-LTX

European Networks of Centres of Expertise for CF (Cystic Fibrosis), LAM (Lymphangioleiomyomatosis) and LTX (Lung Transplantation)

European Networks of Centres of Expertise for rare diseases have been identified by the European Commission as one important key to optimising the healthcare for European citizens. Within the European Networks of Centres of Expertise (ENCE), scientists joined forces to tackle rare diseases. One of these networks is ENCE-CF-LAM-LTX, which aims at designing a blueprint for the implementation of Networks of Centres of Expertise for Rare Diseases — exemplified here by Cystic Fibrosis, Lymphangioleiomyomatosis and Lung Transplantation, but ultimately to be applied to other rare diseases as well.

ENCE-CF-LAM-LTX stakeholders — patients, doctors and other care team members, clinical researchers, health administration and insurance organisations — formed a blueprint for networks on rare diseases, to make best use of all existing capacities and knowledge. They set up patient registries, biobanks and clinical trial networks, amongst other things.

- **Coordinator:** Thomas O.F. Wagner, Klinikum der Johan Wolfgang Goethe Universität Frankfurt (Germany) (t.wagner@em.uni-frankfurt.de)
- **Participants:** DE (Coordinator), AT, CZ, FR, IE, UK
- **Website:** http://www.ence-plan.eu/
- **Duration:** from April 2009 to March 2011
- **Total costs:** €1.0 million
- **EU contribution:** €0.9 million
- **Project Number:** 223355 (FP7-Health)

ENERCA 3

European Reference Network of Expert Centres in Rare Anaemias

The European Network for Rare and Congenital Anaemias (ENERCA) was set up in 2002 to help medical practitioners and patients deal with rare anaemias (RA) by improving the public health service in this regard. The main objective of its third phase was the establishment of a European Reference Network (ERN) of Expert Centres in RA.

As a first step, the project identified appropriate centres dealing with RA in each Member State. Linking these centres, the network is designed as a platform providing information and services to health professionals, patients, authorities, the pharmaceutical industry, health managers and other stakeholders. This network establishes cooperation between experts and organises the exchange of expertise between professionals. ENERCA 3 also prepared a publication of recommendations for the recognition of centres of expertise on RA (ENERCA White Book) that also includes a comprehensive catalogue for external quality assessment (EQAS) of procedures used in the diagnosis of RA.

- **Coordinator:** Joan-Lluis Vives Corrons, Hospital Clínic de Barcelona (Spain) (jlvives@clinic.ub.es)
- **Participants:** ES (Coordinator), BE, CY, DE, EL, FR, IT, NL, PT, UK
- **Website:** http://www.enerca.org/
- **Duration:** from June 2009 to May 2012
- **Total costs:** €2.0 million
- **EU contribution:** €1.2 million
- **Project Number:** 20081210 (EU Health Programme)

ESPOIR

European clinical study for the application of regenerative heart valves

The ESPOIR project gives hope to patients suffering from acquired or congenital heart diseases that require heart valve replacement. Current heart valve substitutes are not ideal as they need anticoagulation, thus bear the risk of bleeding when manufactured from non-organic material, or they degenerate when they derive from animals or human tissue donors (homografts).

An ideal heart valve substitute would overcome these limitations. The ESPOIR project has developed such an implant for heart valves. Implants derive from donated homografts, which are chemically treated to inactivate potential microorganisms and viruses. The heart valves are then decellularised chemically, so that only connective tissue remains, the matrix of the decellularised heart valve (DHV). In order to drive the translation of this promising regenerative approach towards practical clinical use, the ESPOIR team will undertake a prospective multi-centre trial to include at least 200 patients from eight leading European Centres for Congenital Heart Surgery.

- **Coordinator:** Axel Haverich, Medizinische Hochschule Hannover (Germany) (haverich.axel@mh-hannover.de)
- **Participants:** DE (Coordinator), BE, CH, FR, IT, MD, NL, UK
- **Website:** http://www.espoir-clinicaltrial.eu/
- **Duration:** from January 2012 to December 2015
- **Total costs:** €6.6 million
- **EU contribution:** €5.2 million
- **Project Number:** 278453 (FP7-Health)

EUHANET

European Haemophilia Network

To improve the available care for patients with inherited bleeding disorders, a project was launched to set up a network of European haemophilia centres. The European Haemophilia Network (EUHANET) aims to reduce health inequalities and enhance the quality of care delivered.

As there are huge differences in the care offered by the 420 European haemophilia centres, EUHANET will assess and standardise their services and develop a certification system. The Haemophilia Central website will give access to information relevant to patients with inherited bleeding disorders and their carers. The European Haemophilia Safety Surveillance (EUHASS) project launched in 2008 will be expanded within the EUHANET framework to include acquired haemophilia and acquired von Willebrand disease as well as serious inherited platelet disorders.

The Rare Bleeding Disorders Database (RBDD) will also become part of EUHANET. In addition to data on the natural history of rare bleeding disorders already collected, it will collate data on afibrinogenemia and factor XIII deficiency.

- **Coordinator:** Michael Makris, University of Sheffield (USFD) (United Kingdom) (m.makris@sheffield.ac.uk)
- **Participants:** UK (Coordinator), BE, IT, NL
- **Website:** http://www.euhanet.org
- **Duration:** from June 2012 to November 2015
- **Total costs:** €1.5 million
- **EU contribution:** €0.9 million
- **Project Number:** 20111207 (EU Health Programme)

eurIPFnet

European IPF Network: Natural course, Pathomechanisms and Novel Treatment Options in Idiopathic Pulmonary Fibrosis

IPF affects around 360 000 patients in the European Union, who experience a gradual decrease in quality of life due to breathlessness (progressive dyspnoea) and coughing. People hit by IPF usually die within three to five years upon diagnosis. Within the eurIPFnet consortium, leading European scientists joined their forces to develop new therapeutic strategies for patients with Idiopathic Pulmonary Fibrosis (IPF).

The eurIPFnet experts came together to decipher the natural course and molecular pathomechanisms and to develop new therapeutic strategies for IPF patients. EurIPFnet set up a European IPF registry (eurIPFreg) with data regarding the natural course, familiar background and other factors relevant to IPF, and a European IPF biobank (eurIPFbank) of blood, cells and tissue specimens of IPF. Those samples were the basis for further studies.

- **Coordinator:** Andreas Guenther, Justus-Liebig-Universität Giessen (Germany) (andreas.guenther@innere.med.uni-giessen.de)
- **Participants:** DE (Coordinator), AT, FR, IT, UK
- **Website:** http://www.pulmonary-fibrosis.net/
- **Duration:** from January 2008 to June 2011
- **Total costs:** €3.9 million
- **EU contribution:** €3.0 million
- **Project Number:** 202224 (FP7-Health)

EUROFANCOLEN

Phase I/II Gene Therapy Trial of Fanconi anemia patients with a new Orphan Drug consisting of a lentiviral vector carrying the FANCA gene: A Coordinated International Action

Fanconi anemia (FA) is a rare inherited syndrome characterised by the early development of bone marrow failure and increasing predisposition to cancer with age. Allogeneic hematopoietic cell transplantation is the only definitive curative therapy for the bone marrow failure of FA patients, although it is associated with complications. The EUROFANCOLEN project aims to develop a safe and efficient therapy for FA.

Difficulties in the collection of sufficient numbers of hematopoietic stem cells (HSC) from FA patients and the use of sub-optimal transduction protocols with gammaretroviral vectors have limited the success of previous FA gene therapy trials. The innovative gene therapy approach proposed by EUROFANCOLEN relies on the use of two recent biotechnology innovations:

- the discovery of new drugs with potent activity to mobilise HSCs from the bone marrow to peripheral blood;
- the development of a new lentiviral vector by members of this Consortium, which was designated as a new Orphan Drug for FA by the European Commission in December 2010.

- **Coordinator:** Juan A. Bueren, Centro de Investigaciones Energéticas, Medioambientales y Tecnológicas (CIEMAT) (Spain) (juan.bueren@ciemat.es)
- **Participants:** ES (Coordinator), DE, FR, UK
- **Website:** http://www.ciemat.es/
- **Duration:** from January 2013 to December 2017
- **Total costs:** €7.0 million
- **EU contribution:** €5.3 million
- **Project Number:** 305421 (FP7-Health)

IMPACTT

Immunoglobulin lgY pseudomonas: a clinical trial for cystic fibrosis treatment

The IMPACTT team conducts clinical studies to prove that a single daily gargle with the Anti-Pseudomonas lgY improves the condition of cystic fibrosis (CF) patients. This alternative therapeutic strategy aims to fight continuous pulmonary deterioration and death of individuals suffering from CF, when antibiotics alone are not enough.

CF is a chronic disease, considerably lowering the quality of life, and is even life threatening through respiratory insufficiency and complications of chronic lung infections. Bacterial infections with Pseudomonas aeruginosa (PA) are typical for CF, and repeated courses of antibiotics in heavy doses have more than doubled the median survival age. IgY could be used as an alternative to antibiotics and thus reduce antibiotics resistance.

No preventive or eradicative treatments of PA infection in the lungs exist today, even though PA is a life-threatening bacterium that survives in the lungs, causing morbidity and mortality. This is where the IMPACTT study comes in, demonstrating that the `Anti-pseudomonas lgY` has a preventive effect in fighting the fatal chronic infection of PA.

- **Coordinator:** Anders Larsson, Uppsala University (Sweden) (anders.larsson@akademiska.se)
- **Participants:** SE (Coordinator), BE, DE, DK, FR, IT, LT
- **Website:** http://www.impactt.eu/
- **Duration:** from January 2011 to December 2014
- **Total costs:** €7.0 million
- **EU contribution:** €5.4 million
- **Project Number:** 261095 (FP7-Health)

IMPROVED

IMproved Pregnancy Outcomes by Early Detection; personalised medicine for pregnant women: novel metabolomic and proteomic biomarkers to detect pre-eclampsia and improve outcome

Pre-eclampsia is one of the leading causes of maternal death in Europe; one in twenty first time pregnancies are complicated by this disease, which presents in late pregnancy with high blood pressure and often poor fetal growth. The IMPROVED project aims to develop an early pregnancy screening test for pre-eclampsia to reduce the life-threatening complications of this disease.

IMPROVED will include a clinical study of 5 000 first-time pregnant women to assess and refine novel and innovative prototype tests based on emerging metabolomic and proteomic technologies developed by SMEs that are part of the consortium.

The team will also establish a biobank, assess the potential synergy of a combined metabolomic and proteomic approach, and advance regulatory approval and development of the selected test into the clinical arena. The application of new technologies to identify 'at risk' patients in early pregnancy will allow stratified care with personalised fetal and maternal surveillance, early diagnosis and timely intervention.

- **Coordinator:** Louise Kenny, University College Cork (Ireland) (l.kenny@ucc.ie)
- **Participants:** IE (Coordinator), DE, DK, NL, SE, UK
- **Website:** http://www.fp7-improved.eu/
- **Duration:** from November 2012 to October 2016
- **Total costs:** €7.7 million
- **EU contribution:** €5.9 million
- **Project Number:** 305169 (FP7-Health)

INHERITANCE

INtegrated HEart Research In TrANslational genetics of dilated Cardiomyopathies in Europe

Inherited dilated cardiomyopathies (DCM) are monogenic disorders caused by mutations in more than 30 genes. DCM affects one out of 2 500 individuals in Europe and is the major cause of heart transplantation and death due to non-ischaemic heart failure in adolescents and young adults. The INHERITANCE team aims to gain new insights and knowledge on the disease, translating this into innovative, disease-specific diagnostic and treatment strategies.

Currently, less than 1% of patients with familial DCM are genotyped in Europe. INHERITANCE aims to conduct further research on this rare disease, with help from over 2 000 DCM patients and their relatives. The INHERITANCE strategy is to integrate genomic, proteomic, structural and functional studies exploring the molecular cascades arising from causative mutations in order to understand disease expression and evolution and to explore novel therapeutic strategies both in humans and in animal models.

- **Coordinator:** Eloisa Arbustini, Fondazione IRCCS Policlinico St Matteo (Italy) (e.arbustini@smatteo.pv.it)
- **Participants:** IT (Coordinator), DE, DK, ES, FR, NL, SE, UK
- **Website:** http://www.inheritanceproject.eu/
- **Duration:** from January 2010 to December 2013
- **Total costs:** €4.0 million
- **EU contribution:** €2.9 million
- **Project Number:** 241924 (FP7-Health)

InterPregGen

Genetic studies of pre-eclampsia in Central Asian and European populations

Around 50 000 pregnant women and their unborn babies lose their lives per year to pre-eclampsia, a cardiometabolic complication in pregnancy. The incidence of pre-eclampsia in Central Asian countries is over twice as high as in Western Europe.

The InterPregGen team aims to set up links between research groups in Central Asia (Kazakhstan and Uzbekistan) and Europe, in order to identify and compare the genetic variants which are predisposed to pre-eclampsia. Scientific cooperation, training Central Asian researchers in European centres of excellence and addressing the limited knowledge of genetic diversity in Central Asian populations by undertaking whole genome sequencing are key parts of this project.

InterPregGen will establish pre-eclampsia biobanks of DNA and plasma samples from a total of 4 000 affected women, their partners and babies, and matched control samples from healthy pregnant women, in Kazakhstan and Uzbekistan. Further studies will be conducted to identify pre-eclampsia susceptibility genes and their variants, to get insights into the underlying pathological mechanism.

- **Coordinator:** Linda Morgan, University of Nottingham (United Kingdom) (linda.morgan@nottingham.ac.uk)
- **Participants:** UK (Coordinator), FI, IS, NO, KZ, UZ
- **Website:** http://www.interpreggen.org/
- **Duration:** from November 2011 to April 2016
- **Total costs:** €7.8 million
- **EU contribution:** €5.9 million
- **Project Number:** 282540 (FP7-Health)

NEUROSIS

Efficacy and safety of inhaled budesonide in very preterm infants at risk of bronchopulmonary dysplasia

The Neonatal European Study of Inhaled Steroids (NEuroSIS) project focuses on preterm infants born at less than 28 weeks of gestational age (GA). The project seeks to determine whether the early inhalation of budesonide reduces the risk of mortality and bronchopulmonary dysplasia (BPD). BPD contributes to the mortality of preterm infants and is associated with impaired neurosensory development and an increased risk of pulmonary morbidity in adolescence and young adulthood.

Within 2 years, 850 infants between 23 and 27 weeks GA have been randomised during the first 12 hours of life for a multi-centre clinical trial of budesonide or a placebo to prevent BPD. The primary objective is survival without BPD at 36 weeks GA. The results of NEuroSIS will provide valuable and useful indications about the efficacy and safety of inhaled steroids in a population of very preterm infants.

- **Coordinator:** Dirk Bassler, Eberhard Karls Universität Tübingen (Germany) (dirk.bassler@med.uni-tuebingen.de)
- **Participants:** DE (Coordinator), CZ, DE, FI, FR, IL, IT, NL, UK
- **Website:** http://www.neurosis-study.eu/
- **Duration:** from March 2009 to February 2014
- **Total costs:** €7.4 million
- **EU contribution:** €5.6 million
- **Project Number:** 223060 (FP7-Health)

PRATH

Preclinical study of Recombinant human Anti-C5 for the Treatment of atypical HUS

In collaboration with international partners, the Italian company Adienne S.r.l. set up a preclinical study on a potential drug Recombinant human minibody for the treatment of the atypical Haemolytic Uraemic Syndrome (HUS). HUS is a systemic disease characterised by damage to endothelial cells and erythrocytes, thrombocytopenia, micro thrombosis and kidney failure, and has already shown complement involvement in its pathogenesis.

Adienne S.r.l. obtained the orphan designation EU/3/08/571 for its Recombinant human minibody against Complement component C5 for the treatment of atypical HUS in September 2008. The PRATH project focused on pharmacological, pharmacokinetic and toxicological studies, with one objective being a pre-clinical evaluation of the therapeutic efficacy of the anti-C5 antibody in mouse models of atypical HUS and characterisation of GMP-grade anti-C5 antibody production. Data collected in the project will serve for further development of this potential drug.

- **Coordinator:** Antonio Francesco Di Naro, Adienne S.r.l. (Italy) (antonio.dinaro@adienne.com)
- **Participants:** IT (Coordinator), FR, UK
- **Website:** http://www.prath.eu/home.htm
- **Duration:** from May 2010 to April 2012
- **Total costs:** €2.6 million
- **EU contribution:** €1.8 million
- **Project Number:** 242273 (FP7-Health)

THALAMOSS

THALAssaemia MOdular Stratification System for personalised therapy of beta-thalassaemia

Thalassaemia is an inherited blood disorder, and beta-thalassaemia patients might require blood transfusions for the rest of their life. THALAMOSS tools and technologies will facilitate identification of novel diagnostic tests, drugs and treatments specific to patient subgroups and guide conventional and novel therapeutic approaches for beta-thalassaemia, including personalised medical treatments.

THALAMOSS aims to provide new biomarkers for distinct treatment subgroups in beta-thalassaemia (500–1 000 samples from four European medical centres). Translation of these activities into the product portfolio and research and development methodology of participating SMEs will be a major issue. The scientific work packages of THALAMOSS will focus on: i) the recruitment, patient characterisation and development of erythroid precursor cell cultures; ii) omics analyses; iii) novel therapeutic approaches.

- **Coordinator:** Roberto Gambari, Università degli studi di Ferrara (Italy) (gam@unife.it)
- **Participants:** IT (Coordinator), CY, CZ, EL, IL, NL, UK, US
- **Website:** http://cordis.europa.eu/
- **Duration:** from November 2012 to October 2016
- **Total costs:** €6.7 million
- **EU contribution:** €5.0 million
- **Project Number:** 306201 (FP7-Health)

TRAUMAKINE

Interferon-beta treatment of acute respiratory distress syndrome (ARDS)

Acute respiratory distress syndrome (ARDS) kills 35–40% of Europe's 175 000 annual patients, despite the much improved mechanical ventilation techniques and improved supportive therapies. TRAUMAKINE focuses on interferon-beta treatment of ARDS, producing further results based on a clinical study with affected patients that demonstrated a significant drop in all-cause mortality.

TRAUMAKINE members will conduct a pan-European study for further safety and pharmacokinetics of IFN-beta. Improved data would allow for a marketing application for European regulatory authorities but also for a much improved understanding what clinical parameters and biomarkers can attribute to the outcome of this deadly process in lungs. The project also aims to harmonise European ARDS treatment and to create ARDS-specific analytics for future diagnosis and treatment efficacy. This will further reduce the mortality rate and costs for hospitals, societies and insurance companies.

- **Coordinator:** **Markku Jalkanen, Faron Pharmaceuticals (Finland) (markku.jalkanen@faronpharmaceuticals.com)**
- **Participants:** **FI (Coordinator), IT, UK**
- **Website:** **http://cordis.europa.eu/**
- **Duration:** **from December 2012 to November 2016**
- **Total costs:** **€7.8 million**
- **EU contribution:** **€5.9 million**
- **Project Number:** **305853 (FP7-Health)**

Dermatology, ophthalmology, urology and nephrology

AAVEYE

Gene therapy for inherited severe photoreceptor diseases

Mutations in genes preferentially expressed in the photoreceptor cells of the retina give rise to many inherited blinding diseases for which no treatment is currently available. Vectors based on the adeno-associated virus (AAV) efficiently revert retinal pigment epithelium (RPE) defects; however gene transfer to photoreceptors remains challenging. The project aims at overcoming this challenge.

Gene therapy for inherited severe photoreceptor diseases (AAVEYE) uniquely brings together leading European scientists who will work on four priorities, including: developing AAV-based, long-term, safe gene transfer to photoreceptors and assessing the impact of AAV-mediated photoreceptor transduction on rescuing retinal function in animals.

The project consortium will set out to provide pre-clinical proof-of-concept to move gene therapies for severe blinding retinal photoreceptor diseases from the laboratory into the healthcare system.

- Coordinator: **Alberto Auricchio, Fondazione Telethon (Italy) (auricchio@tigem.it)**
- Participants: **IT (Coordinator), CH, EE, UK**
- Website: **http://www.aaveye.eu/**
- Duration: **from November 2008 to October 2011**
- Total costs: **€3.8 million**
- EU contribution: **€2.9 million**
- Project Number: **223445 (FP7-Health)**

CRUMBS IN SIGHT

Restoring Mueller glia cell photoreceptor interactions with Crumbs

The 'Crumbs In Sight' consortium is involved in groundbreaking research to develop novel therapies and to understand the basis of retinal degeneration, in particular the role and function of the Crumbs homologue 1 (CRB1) gene in inherited blindness. Mutations in the CRB1 gene cause photoreceptor degeneration resulting in progressive retinitis pigmentosa (RP) or Leber congenital amaurosis (LCA), which both currently are untreatable blinding diseases.

The goal of this specific project was to provide a therapeutic approach to CRB1-related diseases of the retina with a focus on the recovery of interactions between Mueller glial cells and photoreceptors. Using fruit fly and mouse genetics, Crumbs In Sight analysed the biochemical, cellular, developmental and physiological functions of CRB1 and the effect of loss of interaction between Mueller glia cells and photoreceptors and subsequent retinal degeneration.

- Coordinator: **Jan Wijnholds, Koninklijke Nederlandse Akademie van Wetenschappen (KNAW) (The Netherlands) (j.wijnholds@nin.knaw.nl)**
- Participants: **NL (Coordinator), DE, FR, UK**
- Website: **http://crfb.univ-mrs.fr/Crumbs**
- Duration: **from April 2008 to May 2012**
- Total costs: **€4.0 million**
- EU contribution: **€3.0 million**
- Project Number: **200234 (FP7-Health)**

DRUGSFORD

Preclinical development of drugs and drug delivery technology for the treatment of inherited photoreceptor degeneration

Hereditary photoreceptor degeneration is a collective term that describes a group of diseases that lead to severe visual impairment and blindness through retinal damage. It is estimated to affect a quarter of a million people in Europe alone. Mutations behind many of the diseases are known, but there are as yet no treatments.

The project will target a factor that seems to occur in many types of hereditary photoreceptor degeneration, a decision supported by several scientific reports showing that the degeneration could be slowed down or stopped if this is rebalanced. DRUGSFORD will have access to new regulating substances and these will be combined with drug delivery techniques that will help the compounds to cross the blood-brain-barrier and to reach the photoreceptors, so that these can be protected.

- Coordinator: **François Paquet-Durand, Eberhard Karls Universität, Tübingen (Germany) (francois.paquet-durand@klinikum.uni-tuebingen.de)**
- Participants: **DE (Coordinator), IT, NL, SE**
- Website: **http://www.drugsford.eu/**
- Duration: **from September 2012 to August 2015**
- Total costs: **€6.5 million**
- EU contribution: **€4.9 million**
- Project Number: **304963 (FP7-Health)**

DSD-LIFE

Clinical European study on the outcome of surgical and hormonal therapy and psychological intervention in disorders of sex development (DSD)

Disorders of sex development (DSD) mostly demand genital constructive surgery. Frequently, decisions on sex rearing are difficult and sex hormone substitution is indicated in many cases through puberty and adult life. As things stand there are no dedicated treatments.

DSD-Life is intending to develop evidence-based guidelines for treatment of the condition. To realise this aim, the influences and interrelations of a range of medical interventions, hormonal effects and characteristics along with cultural and psychological influences will all be investigated. The long-term impact of the study will see individuals with DSD benefitting from improved care and a subsequently higher quality of life, along with greater social inclusion.

- Coordinator: **Birgit Köhler, Charité — Universitätsmedizin, Berlin (Germany) (Birgit.Koehler@charite.de)**
- Participants: **DE (Coordinator), FR, NL, PL, SE, UK**
- Website: **http://cordis.europa.eu/**
- Duration: **from October 2012 to September 2016**
- Total costs: **€3.8 million**
- EU contribution: **€2.9 million**
- Project Number: **305373 (FP7-Health)**

EUCILIA

Pathophysiology of Rare Diseases Due to Ciliary Dysfunction: Nephronophthisis, Oral-Facial-Digital Type 1 and Bardet-Biedl Syndromes

Ciliary defects underlie a wide range of human disorders, including the rare and heritable Bardet-Biedl (BBS), Oro-facial-digital type 1 (OFD1) and nephronophthisis (NPHP) syndromes. While each of these disorders presents different symptoms, all are characterised by polycystic renal disease. The EUCILIA project used BBS, OFD1 and NPHP syndromes as model systems to study the physiological role of primary cilia, with special emphasis on their role in the genitourinary tract and in the development of renal cysts. These form a major cause of mortality in this group of patients.

The EUCILIA consortium brought together the best scientists in Europe working on cilia function. Together with the generated in vitro and in vivo models to study the physiological role of primary cilia and the analysis of the ciliary protein interaction network as well as of the downstream pathway, the project allowed for the identification, testing and validation of potential therapeutic agents for the amelioration and prevention of renal cysts.

- Coordinator: **Brunella Franco, Fondazione Telethon (Italy) (franco@tigem.it)**
- Participants: **IT (Coordinator), DE, UK**
- Website: **http://www.eucilia.eu/**
- Duration: **from February 2008 to January 2011**
- Total costs: **€3.8 million**
- EU contribution: **€2.9 million**
- Project Number: **201804 (FP7-Health)**

@EUNEFRON

European Network for the Study of Orphan Nephropathies

The EUNEFRON consortium was created to investigate the natural history and pathophysiology of rare inherited diseases affecting important structures of the kidney. It mobilised a critical mass of expertise at European level to develop preventive, diagnostic and therapeutic interventions alleviating the burden of these diseases, particularly in children.

The project used and developed multiple models, both in vitro and in vivo. It aimed to foster more interaction between physicians and researchers, to promote research and to efficiently disseminate knowledge by creating a European registry and a network of genetic laboratories.

The project examined the complex relationship between different nephron segments and the multi-systemic involvement of renal diseases. It also yielded new insights into basic processes relevant for the general population such as progression of renal disease.

- Coordinator: **Olivier Devuyst, Université catholique de Louvain (Belgium) (olivier.devuyst@uclouvain.be) and University of Zurich (Switzerland) (olivier.devuyst@uzh.ch)**
- Participants: **BE (Coordinator), CH, DE, DK, FR, IT, NL, UK**
- Website: **http://www.eunefron.org/**
- Duration: **from May 2008 to April 2012**
- Total costs: **€3.9 million**
- EU contribution: **€3.0 million**
- Project Number: **201590 (FP7-Health)**

EURenOmics

European Consortium for High-Throughput Research in Rare Kidney Diseases

The EURenOmics consortium has access to the largest clinical cohorts of patients with rare kidney disorders available, amounting to more than 10000 patients, including detailed phenotypic information and comprehensive biorepositories containing DNA, blood, urine, amniotic fluid and kidney tissue. The resources from such an extensive cohort will further the project's aims to progress in both diagnosis and treatment.

By integrating comprehensive data sets from next generation exome and whole-genome sequencing, tissue transcriptome, tissue transcriptome and antigen/epitope profiling, the project hopes to develop innovative testing techniques and define a new mechanistic disease ontology beyond phenotypical or morphological description, among other objectives.

These efforts will converge in the development of innovative diagnostic tools and biomarkers and efficient screening strategies for novel therapeutic agents.

- Coordinator: **Prof. Jürgen C. Becker, Universitaetsklinikum Heidelberg (Germany) (franz.schaefer@med.uni-heidelberg.de)**
- Participants: **DE (Coordinator), BE, CH, ES, FI, FR, IT, NL, TR, UK, US**
- Website: **http://www.eurenomics.com/**
- Duration: **from October 2012 to September 2017**
- Total costs: **€15.8 million**
- EU contribution: **€11.9 million**
- Project Number: **305608 (FP7-Health)**

EuroDSD

Investigation of the molecular pathogenesis and pathophysiology of Disorders of Sex Development (DSD)

Disorders of Sex Development (DSD) constitute a group of mostly heritable disorders affecting the genito-urinary tract and, in most cases, also the endocrine-reproductive system. The EuroDSD project focused on Europe-wide studies of natural history and pathophysiology and on the development of preventive, diagnostic and therapeutic interventions.

The project helped establish a basis for evidence-based medicine regarding sex assignment and conservative and surgical treatment options. Among other activities, it carried out research in order to identify patients with monogenic and non-defined DSD and searched for methylation patterns as 'footprints' of hormone-dependent genetic alterations. It defined the functional aspects of androgen action as the main basis for sex-related phenotypes. This allows for better decision-making in gender assignment and therapeutic approaches to DSD while improving gender medicine in general.

- Coordinator: **Olaf Hiort, Universität zu Lübeck (Germany) (olaf.hiort@uksh.de)**
- Participants: **DE (Coordinator), BE, FR, IT, NL, SE, UK**
- Website: **http://www.eurodsd.eu/**
- Duration: **from May 2008 to October 2011**
- Total costs: **€3.9 million**
- EU contribution: **€3.0 million**
- Project Number: **201444 (FP7-Health)**

EuroVisionNet

Visual Impairment and Degeneration: a Road Map for Vision Research within Europe

The EuroVisionNet project aimed to overcome national fragmentation among the European vision research community by better linking research activities and policies. This involved improved scientific integration of European vision research and closer collaboration between public and private sectors, as well as targeted policies and guidelines. The project also aimed to improve the communication between researchers, patients and the general public.

A number of different activities were implemented to put this in practice. The project brought together major scientific actors in the research fields of visual impairment and degeneration to enhance coordination between their research activities. It facilitated the exchange of information between participants from different disciplines and initiated strategic discussions on future activities. The project also encouraged collaboration between vision research and the industry.

- Coordinator: **Thomas H. Wheeler, European Vision Institute EEIG (Belgium) (info@europeanvisioninstitute.org)**
- Participants: **BE (Coordinator), CH, DE, FR, PT, UK**
- Website: **http://cordis.europa.eu/**
- Duration: **from March 2008 to February 2012**
- Total costs: **€0.8 million**
- EU contribution: **€0.8 million**
- Project Number: **200641 (FP7-Health)**

GENEGRAFT

Phase I/II ex vivo gene therapy clinical trial for recessive dystrophic epidermolysis bullosa using skin equivalent grafts genetically corrected with a COL7A1-encoding SIN retroviral vector (Orphan drug designation (EU/3/09/630))

Characterised by skin blistering, RDEB is a rare skin disease caused by the lack of expression of type II collagen. GENEGRAFT has demonstrated the feasibility of a treatment approach in pre-clinical studies in mice. Now they aim to undertake a clinical trial on three patients.

This involves the transfer and adaptation of the entire experimental procedure for genetic correction of RDEB skin equivalents suitable for transplantation in patients. Alongside this 'bench to bedside' element of the project, three type VII collagen tolerant patients will provide material for the establishment of a clinical-grade cell bank of primary keratinocytes and fibroblasts. GENEGRAFT has the potential to bring clinical improvement to patients of this devastating skin disease.

- Coordinator: **Alain Hovnanian, Institut national de la santé et de la recherche médicale (INSERM) (France) (alain.hovnanian@inserm.fr)**
- Participants: **FR (Coordinator), AT, DE, UK**
- Website: **http://www.genegraft.eu/**
- Duration: **from March 2011 to February 2016**
- Total costs: **€6.3 million**
- EU contribution: **€4.9 million**
- Project Number: **261392 (FP7-Health)**

PREVENTROP

New approach to treatment of the blinding disease Retinopathy of Prematurity (ROP)

Due to improved medical care, survival rates for preterm babies are higher than ever, although infants are more likely to be affected by morbidity impacting on their quality of life. The Preventrop project intends to conduct preclinical and clinical studies to develop a new preventative intervention for one such condition. Retinopathy of prematurity (ROP) is a disease impacting on preterm children, which may cause visual impairment and blindness.

The consortium will build on the research it has conducted to produce a growth factor complex registered under the name Premiplex, and administered to preterms to prevent ROP. It will make a significant contribution towards the goal of the International Rare Diseases Research Consortium (IRDiRC) by delivering one new therapy for a rare disease.

- Coordinator: **Ann Hellström, Goeteborgs Universitet (Sweden) (ann.hellstrom@medfak.gu.se)**
- Participants: **SE (Coordinator), DE, IT, NL, NO, UK, US**
- Website: **http://www.rop.gu.se/**
- Duration: **from October 2012 to September 2017**
- Total costs: **€7.6 million**
- EU contribution: **€5.9 million**
- Project Number: **305485 (FP7-Health)**

RdCVF

Rod-derived Cone Viability Factor

The Rod-derived Cone Viability Factor (RdCVF) project is hoping to lead to a proof of safety and concept in advanced retinitis pigmentosa leading to a new and widely applicable approach to a currently untreatable blinding condition.

The discovery of RdCVF has furthered the understanding of secondary loss of cone photoreceptors as a consequence of mutations expressed only in rods in most cases of rod-cone degenerations. Rodent trials have shown that the intraocular administration of RdCVF significantly increases cone survival and function and the drug has been awarded orphan status.

Amongst other objectives, the project will focus on innovative delivery systems such as the use of nanoparticles to reduce the dosage and provide a steady level of the medication. Pharmacokinetic and pharmacodynamic studies will determine the dosage, half-life and site of injection of the protein.

- Coordinator: **Jose-Alain Sahel, Institut national de la sante et de la recherche médicale (INSERM) (France) (j.sahel@gmail.com)**
- Participants: **FR (Coordinator), DE, PT**
- Website: **http://www.rdcvf.eu/**
- Duration: **from March 2010 to February 2013**
- Total costs: **€3.9 million**
- EU contribution: **€2.6 million**
- Project Number: **241683 (FP7-Health)**

STRONG

European Consortium for the Study of a Topical Treatment of Neovascular Glaucoma

The second most common cause for the removal of the eye-ball across all eye diseases, neovascular glaucoma (NVG), is very aggressive, causing patients intractable pain. Today's therapeutic approaches are inadequate, such as the destruction of the retia by coagulation. STRONG proposes to assess the topical administration of Aganirsen to interrupt the production of a growth factor, which plays a major role in the pathogenesis of NVG.

The Mainz University Medical Centre will coordinate a randomised, double-masked, 3-group, placebo-controlled trial to assess Aganirsen's ability to slow neovascularisation. 333 subjects, one of the largest patient cohorts ever collected, across 30 sites will participate in the assessment of this new therapeutic approach, which, hopefully, will result in conditional authorisation.

- Coordinator: **Norbert Pfeiffer, Johannes Gutenberg-Universität Mainz (Germany) (norbert.pfeiffer@unimedizin-mainz.de)**
- Participants: **DE (Coordinator), FR, IL, PT, UK**
- Website: **http://cordis.europa.eu/**
- Duration: **from October 2012 to March 2016**
- Total costs: **€7.7 million**
- EU contribution: **€5.7 million**
- Project Number: **305321 (FP7-Health)**

TAG

Improving Healthcare and Social Support for Patients and Family affected by Severe Genodermatoses — Together Against Genodermatoses

Genodermatoses are inherited genetic skin conditions which can be chromosomal, single gene or polygenetic. The TAG network contributes to the improvement of healthcare and social support for patients suffering from severe genodermatoses in European, Mediterranean and Middle Eastern countries.

By getting together stakeholders from the EU and its neighbours involved in the healthcare and social support of patients, the network harnesses the extensive experience members have in the management of genodermatoses. It seeks to establish a new website to highlight the actions taken by network partners, develop a directory and list of services provided in each country and gather together a group of industries that are interested in improving patient care.

- Coordinator: **Louis Dubertret, Fondation René Touraine (France) (louis.dubertret@gmail.com, marie.guillon@fondation-r-touraine.org)**
- Participants: **FR (Coordinator), CY, EL, FR, IT, PT, RO, SI, TR**
- Website: **http://asso.orpha.net/TAG/cgi-bin**
- Duration: **from November 2008 to November 2011**
- Total costs: **€0.8 million**
- EU contribution: **€0.5 million**
- Project Number: **2007335 (EU Health Programme)**

TREATRUSH

Fighting blindness of Usher syndrome: diagnosis, pathogenesis and retinal treatment (TreatRetUsher)

Important scientific advances have been made into the auditory aspects of Usher syndrome, the most frequent hereditary cause of deafness associated to blindness. However, while the deafness is congenital, the retinitis pigmentosa is not detected before the age of eight to ten. The TREATRUSH project is setting out to halt what they define as an unacceptable under-diagnosis of the syndrome. Children with the most severe form are usually diagnosed as severely or profoundly deaf only.

To help parents make a fully informed choice of treatment, the project will develop new clinical and molecular tools with guidelines, clarify the retinal pathogenesis of Usher syndrome and conduct tests to evaluate phenotype rescuing. TREATRUSH also hopes to prevent and treat the retinal defect by associated adenovirus (AAV) gene therapy.

- Coordinator: **Christine Petit, Université Pierre et Marie Curie, Paris (France) (christine.petit@pasteur.fr)**
- Participants: **FR (Coordinator), CH, DE, IT, NL, UK, US**
- Website: **http://www.treatrush.eu/**
- Duration: **from February 2010 to January 2014**
- Total costs: **€7.9 million**
- EU contribution: **€6.0 million**
- Project Number: **242013 (FP7-Health)**

Immunology

CELL-PID

Advanced Cell-based Therapies for the treatment of Primary ImmunoDeficiency

Primary immune deficiencies are inherited disorders that can cause severe infections, autoimmunity and cancer. The Advanced Cell-based Therapies for the treatment of Primary ImmunoDeficiency (CELL-PID) project will use rigorous preclinical efficacy and toxicology evaluation with a view to launching new clinical trials.

This new approach will evaluate therapies involving the use of genetically modified haemotopoietic stem cells (HSC) as immunotherapeutic cells to build up a healthy immune system. The work will be carried out by clinical centres, scientists and industrial partners in the field of advanced therapies.

The successful completion of the project will lead to a wider clinical application of medicinal products able to rebuild and modulate the immune system. The impact will extend beyond PID to acquired immune disorders, allogenic HSCT and cancer treatment.

- Coordinator: **Alessandro Aiuti, Università Vita-Salute San Raffaele (Italy) (a.aiuti@hsr.it)**
- Participants: **IT (Coordinator), BE, CH, DE, FR, IL, NL, TR, UK**
- Website: **http://dev.cell-pid.eu/index.pl**
- Duration: **from November 2010 to May 2015**
- Total costs: **€15.7 million**
- EU contribution: **€11.8 million**
- Project Number: **261387 (FP7-Health)**

CureHLH

European initiative to improve knowledge, treatment and survival of haemophagocytic syndromes in children

The European initiative to improve knowledge, treatment and survival of haemophagocytic syndromes in children (CureHLH) will develop a diagnostic algorithm that brings together, and optimises, knowledge from all European scientists active in research and treatment of HLH. Across Europe, scientists in the field have formed a consortium to provide access to material and data.

Four disease-causing genes have been identified in about half of the patients. Diagnosis is difficult, pathophysiology poorly understood, and treatment unsatisfactory with about 40% of the children dying from treatment failure or toxicity.

Only combined efforts at a European-wide level will lead to the identification of risk factors for treatment failure and toxicity, resulting in improved treatment strategies.

- Coordinator: **Gritta Janka, Universitätsklinikum Hamburg-Eppendorf (Germany) (janka@uke.uni-hamburg.de)**
- Participants: **DE (Coordinator), FR, IT, SE, UK**
- Website: **http://www.uke.de/kliniken/haematologie/index_45263.php**
- Duration: **from June 2008 to May 2011**
- Total costs: **€3.9 million**
- EU contribution: **€2.9 million**
- Project Number: **201461 (FP7-Health)**

DeSScipher

To decipher the optimal management of systemic sclerosis

Systemic sclerosis (SSc) is a disorder which can affect the skin, internal organs and blood vessels. The DeSScipher project aims to overcome the shortcomings of the current approach to diagnosis and management of the disease, which offers few validated recommendations for therapy.

To achieve this, the project will develop evidence-based clinical guidelines for the management of SSc, based on the results of observational trials. These trials will namely evaluate methods to identify SSc patients at risk of developing digital ulcers at an early stage and methods to prevent and treat these ulcers. They will also analyse the efficacy of different immunosuppressive agents in treating pulmonary fibrosis and the treatment options for pulmonary hypertension and heart disease in SSc. The guidelines will be disseminated to physicians and patients.

- **Coordinator:** Ulf Müller-Ladner, Justus-Liebig-Universität Gießen (Germany) (u.mueller-ladner@kerckhoff-klinik.de)
- **Participants:** DE (Coordinator), BE, CH, FR, HU, IT, UK
- **Website:** http://www.uni-giessen.de/cms/forschung/einrichtungen/eup/coop
- **Duration:** from December 2012 to November 2015
- **Total costs:** €3.8 million
- **EU contribution:** €3.0 million
- **Project Number:** 305495 (FP7-Health)

Euradrenal

Pathophysiology and natural course of autoimmune adrenal failure in Europe

Autoimmune Addison's Disease (AAD) is frequently diagnosed after a life-threatening adrenal crisis, often resulting in untimely fatalities. Euradrenal is setting out to unravel the pathogenesis and natural course of AAD through a European network of patient registries and biobanks. Parallel research will examine the cellular and molecular mechanisms of autoimmunity directed at the adrenal cortex.

Exploiting these resources, the project consortium will describe the natural course of the disease with a focus on factors limiting quality of life. It aims also to identify and characterise the disease-causing genes.

The project will not only lead to the development of novel diagnostic and therapeutic interventions for Addison patients, but also increase our understanding of the pathogenesis of autoimmune diseases in general.

- **Coordinator:** Eystein Husebye, Universitetet i Bergen (Norway) (eystein.husebye@helse-bergen.no)
- **Participants:** NO (Coordinator), CH, DE, IT, PL, SE, UK
- **Website:** http://www.euradrenal.org/
- **Duration:** from April 2008 to March 2012
- **Total costs:** €3.9 million
- **EU contribution:** €2.9 million
- **Project Number:** 201167 (FP7-Health)

EuroFever

The PRES European Network of Registries for Autoinflammatory Diseases in childhood

Autoinflammatory diseases are a group of disorders in which the patient's innate immune system attacks the body's own tissues. The EuroFever project was launched to raise awareness among paediatricians and paediatric rheumatologists about the prompt recognition of these diseases and to help them provide adequate information to families affected by these conditions. It also aimed to increase knowledge on these rare disorders, namely with regard to diagnosis, treatment and complications.

Activities to achieve these objectives included the creation of an international registry for autoinflammatory diseases and of web pages for patients and physicians on each disorder. Two surveys were carried out to examine the efficacy of available treatments and the prevalence of these diseases among European paediatric rheumatology centres.

- Coordinator: **Marco Gattorno, Istituto Giannina Gaslini IRCCS — IGG (Italy) (marcogattorno@ospedale-gaslini.ge.it)**
- Participants: **IT (Coordinator), BE, DE, FR, NL, TR, UK**
- Website: **http://www.printo.it/eurofever/**
- Duration: **from July 2008 to June 2011**
- Total costs: **€0.6 million**
- EU contribution: **€0.3 million**
- Project Number: **2007332 (EU Health Programme)**

EURO-GENE-SCAN

European Genetic Disease Diagnostics

Mutations in almost 150 genes have been found to cause primary immunodeficiencies (PID) which means that even for well-defined subgroups of PID, mutations in different genes result in identical, or overlapping, phenotypes.

Although significant collaboration has already been underway in Europe over the last two decades, current mutation analysis is very complex, involving many European laboratories: in each, mutation detection normally only covers a few per cent of all disease genes. If multiple genes need to be analysed, the cost rises proportionately and obtaining a correct diagnosis is both difficult and time consuming.

Amongst other objectives, EURO-GENE-SCAN aimed to develop an innovative multiplexing technology and, through the use of high-throughput sequencing, bring the cost of analysing all 150 known PID genes in a single run to around the current cost for mutation detection in single disease genes.

- Coordinator: **C.I. Edvard Smith, Karolinska Institutet (Sweden) (edvard.smith@ki.se)**
- Participants: **SE (Coordinator), DE, PL, UK**
- Website: **http://www.gatc-biotech.com/en/gatc/contact.html**
- Duration: **from January 2009 to December 2011**
- Total costs: **€3.8 million**
- EU contribution: **€2.9 million**
- Project Number: **223293 (FP7-Health)**

EURO-HISTIO-NET 2008

A reference network for Langerhans cell histiocytosis and associated syndromes in the EU

Langerhans cell histiocytosis (LCH) is a disease characterised by excess immune system cells called Langerhans building up in the body. About 80% of patients form tumours called granulomas which cause pain and swelling and may lead to bone fracture.

The EURO-HISTIO-NET 2008 project was set up to improve knowledge of the disease and improve the quality of available care for patients. It worked towards the creation of a network of reference centres organising care and clinical research for LCH and associated syndromes in EU countries. Project activities included the creation of a web portal and of a web database to disseminate information and the publication of guidelines for diagnosis, treatment and follow-up of LCH.

- Coordinator: **Jean Donadieu, Assistance Publique Hôpitaux de Paris (France) (jean.donadieu@trs.aphp.fr)**
- Participants: **FR (Coordinator), AT, BE, BG, BR, DE, EL, ES, LB, MA, IT, PL, SE, UK, US**
- Website: **http://www.eurohistio.net/**
- Duration: **from September 2008 to August 2011**
- Total costs: **€0.6 million**
- EU contribution: **€0.2 million**
- Project Number: **2007120 (EU Health Programme)**

EURO-PADnet

The Pathophysiology and Natural Course of Patients with Primary Antibody Deficiencies (PAD)

The consortium that makes up the Pathophysiology and Natural Course of Patients with Primary Antibody Deficiencies (PAD) project cares for more than 1 000 patients with Primary Antibody Deficiencies. This represents about half of all people registered in Europe, many being children. Those affected have defective immunity leading to an increased susceptibility to recurrent infections of the respiratory and gastro-intestinal tract. Ill-defined co-morbidity is also a feature.

The consortium combines clinical and research data in an online registry complimented by a sample repository. It also used linkage analysis and candidate gene approaches to elucidate the genetic cause of PADs, to use mouse models of PAD and establish in vitro models for B cell differentiation.

- Coordinator: **Bodo Grimbacher, University College London, Medical School (United Kingdom) (b.grimbacher@medsch.ucl.ac.uk)**
- Participants: **UK (Coordinator), CZ, DE, FR, IT, NL**
- Website: **http://www.europadnet.eu/home**
- Duration: **from May 2008 to April 2011**
- Total costs: **€3.9 million**
- EU contribution: **€2.9 million**
- Project Number: **201549 (FP7-Health)**

EUROTRAPS

Natural course, pathophysiology, models for early diagnosis, prevention and innovative treatment of TNF Receptor Associated Periodic Syndrome TRAPS with application for all hereditary recurrent fevers

EUROTRAPS is a multidisciplinary consortium that combines ideas, resources and data to gain insights into the natural course and pathophysiology of TNF Receptor Associated Syndrome (TRAPS). This rare disease of innate immunity causes recurrent bouts of fever and pain. The development of renal amyloidosis in 20% of cases makes it potentially fatal.

The creation of a European registry for TRAPS patients, set up by the project, has facilitated delineative scores and outcome measures for diagnosis and treatment. The project developed kit prototypes to facilitate identification of mutations and prognosis factors. EUROTRAPS developed in vitro and animal models to investigate innovative therapies.

- **Coordinator:** Isabelle Touitou, Centre Hospitalier Universitaire de Montpellier (France) (isabelle.touitou@inserm.fr)
- **Participants:** FR (Coordinator), AT, DE, IT, IS, UK
- **Website:** http://fmf.igh.cnrs.fr/ISSAID/EUROTRAPS/index.php
- **Duration:** from April 2008 to September 2011
- **Total costs:** €3.8 million
- **EU contribution:** €2.9 million
- **Project Number:** 200923 (FP7-Health)

FIGHT-HLH

First Targeted Therapy to FIGHT Haemophagocytic Lymphohistiocytosis (HLH): A novel approach to HLH

No drug has been formally developed for the treatment of haemophagocytic lymphohistiocytosis (HLH), a disease characterised by uncontrolled immune response that primarily affects young children. If untreated it is usually fatal and even when treated, survival rates are as low as 60-70%.

The project aims to provide data needed for market access authorisation of NI-0501 for the treatment of HLH. NI-0501 is a monoclonal antibody which neutralises the biological activity of human interferon-gamma, a cytokine believed to play a key role in the pathogenesis of the disease.

The clinical programme foresees a pilot study involving patients who have reactivated following initial treatment and a pivotal study which will also recruit newly diagnosed patients, once a favourable benefit risk profile is established.

- **Coordinator:** Cristina de Min, NOVIMMUNE SA (Switzerland) (cdemin@novimmune.com)
- **Participants:** CH (Coordinator), BE, IT, UK
- **Website:** http://cordis.europa.eu/
- **Duration:** from July 2012 to May 2016
- **Total costs:** €11.2 million
- **EU contribution:** €5.9 million
- **Project Number:** 306124 (FP7-Health)

MABSOT

Development of OPN-305 as an orphan drug for the treatment of Delayed Graft Function post solid organ transplantation

The MABSOT project has developed a novel antibody to prevent delayed graft function (DGF), defined as the need for dialysis within seven days of renal transplantation. This can result in allograft rejection. Prolonged dialysis, hospitalisation and an impact on the duration of renal graft survival are also possible consequences. DGF occurs in 21–44% of those receiving a cadaveric renal graft.

The successful completion of the project will allow the OPN-305 antibody, which has received OMP designation, to be developed for the treatment of DGF in a range of solid organ transplant situations. Anticipated benefits include the reduction of the duration of hospitalisation, greater longevity associated with the transplanted organ and enhanced quality of life for transplant patients.

- **Coordinator:** Mary Reilly, Opsona Therapeutics Limited (Ireland) (mreilly@opsona.com)
- **Participants:** IE (Coordinator), BE, CZ, ES, NL, UK
- **Website:** http://www.mabsot.eu/
- **Duration:** from December 2010 to November 2013
- **Total costs:** €7.8 million
- **EU contribution:** €5.9 million
- **Project Number:** 261468 (FP7-Health)

Net4CGD

Gene Therapy for X-linked Chronic Granulomatous Disease (CGD)

Net4CGD is hoping to build on the results of research by members of its consortium conducted on haematopoietic gene correction of X-CGD using gp91 gammaretroviral gene transfer vectors. The project focuses on the clinical development of a new orphan drug that could help patients with a rare immune deficiency resulting in infections and inflammatory granulomas.

Encouraging results have been obtained already in preclinical studies and these have prompted the consortium to undertake the testing of a new lentiviral vector in several European centres with expertise in the disease. If successful, the study will be used to register the orphan drug, which is expected to improve patients' quality of life and reduce the economic burden on health systems.

- **Coordinator:** Anne Galy, Association Genethon (France) (galy@genethon.fr)
- **Participants:** FR (Coordinator), CH, DE, UK
- **Website:** http://www.finovatis.com/en/
- **Duration:** from December 2012 to November 2016
- **Total costs:** €8.2 million
- **EU contribution:** €5.9 million
- **Project Number:** 305011 (FP7-Health)

NIMBL

Nuclease Immune Mediated Brain and Lupus-like conditions (NIMBL): natural history, pathophysiology, diagnostic and therapeutic modalities with application to other disorders of autoimmunity

The NIMBL project brings together European and US clinical and other scientists currently at the forefront of research into Nuclease Immune Mediated Brain and Lupus-like (NIMBL) conditions. Very recent discoveries of the cell-intrinsic initiation of autoimmunity have major implications for how researchers understand the discrimination of self from non-self.

The project will use this new biological paradigm to gain a better understanding of the natural course of these disorders and their underlying pathological basis. NIMBL conditions greatly reduce the quality of life for patients and have a high mortality rate especially in children. The conditions are rare, but under-diagnosed, and no cures exist at the moment.

- **Coordinator:** Yanick Crow, The University of Manchester (United Kingdom) (yanickcrow@mac.com)
- **Participants:** UK (Coordinator), ES, IT, NL, US
- **Website:** http://www.nimbl.eu
- **Duration:** from June 2010 to May 2013
- **Total costs:** €6.9 million
- **EU contribution:** €5.3 million
- **Project Number:** 241779 (FP7-Health)

Pemphigus

Pemphigus — From autoimmunity to disease

The Pemphigus project brought European scientists and clinicians together in a consortium to provide a critical mass of patients and research tools to address this potentially lethal bullous disease of the skin and mucosa.

The condition of pemphigus may be considered as a paradigmatic organ-specific autoimmune disease, and despite enormous progress in research into the disease, no specific therapy is available.

The consortium set out to improve the definition of the immune pathogenesis of pemphigus and to analyse the autoAb-driven effector phase frequently involving epitope spreading which ultimately leads to a more severe disease. As only a few medical centres in Europe can deal with pemphigus, the consortium's efforts in understanding the pathogenesis of the disease may be crucial to understanding the mechanisms leading from autoimmunity to clinically overt autoimmune disease.

- **Coordinator:** Michael Hertl, Philipps Universität Marburg (Germany) (hertl@med.uni-marburg.de)
- **Participants:** DE (Coordinator), CH, FR, IT
- **Website:** http://www.pemphigus.eu/
- **Duration:** from May 2008 to October 2011
- **Total costs:** €3.6 million
- **EU contribution:** €2.8 million
- **Project Number:** 200515 (FP7-Health)

PROFNAIT

Development of a prophylactic treatment for the prevention of foetal/neonatal alloimmune thrombocytopenia (FNAIT)

Foetal/Neonatal Alloimmune Thrombocytopenia (FNAIT) is a rare but potentially serious condition resulting in severe bleeding, foetal death and lifelong disabilities. The transferral of the HPA-1 antigen from the foetus may lead to anti-HPA-1a production in the mother, resulting in the destruction of platelets in a HPA-1a positive foetus and causing FNAIT in a subsequent pregnancy.

The project hopes to develop a prophylactic treatment by working with leading European hospitals, blood banks and companies. The objective is to develop the orphan drug anti HPA-1a immunoglobulin (IgG), Tromplate®, through clinical trials to establish efficacy and safety in treatment.

- Coordinator: **Jens Kjeldsen-Kragh, Prophylix Pharma AS (Norway) (jkk@prophylixpharma.com)**
- Participants: **NO (Coordinator), DE, DK, SE**
- Website: **www.prophylixpharma.com/profnait-project**
- Duration: **from August 2012 to July 2018**
- Total costs: **€7.7 million**
- EU contribution: **€5.9 million**
- Project Number: **305986 (FP7-Health)**

SHARE

Single Hub and Access point for paediatric Rheumatology in Europe

Paediatric rheumatic diseases (PRD) include vasculitis, scleroderma, juvenile idiopathic arthritis (JIA), antiphospholipid syndrome (APS), juvenile dermatomyositis (JDM) and juvenile systemic lupus erythematosus (SLE). The objective of the SHARE project is to improve the quality of care for patients suffering from one of these diseases.

This is to be achieved by reducing barriers in the process of developing new medical technology, drugs or treatments for patients, and by improving patients' access to relevant information about their disease. The project also supports the exchange of ideas, results, data and best practices and the implementation of results in training programmes for healthcare professionals.

SHARE is expected to improve the treatment and management of PRD by boosting progress in research, harmonising treatment and supporting regulatory decisions.

- Coordinator: **Nico Wulffraat, Universitair Medisch Centrum Utrecht — UMCU (the Netherlands) (N.Wulffraat@umcutrecht.nl)**
- Participants: **NL (Coordinator), CZ, DE, ES, FR, HU, IT, UK**
- Website: **http://ec.europa.eu/eahc/projects/database.html?prjno=20111202**
- Duration: **from September 2012 to August 2015**
- Total costs: **€1.5 million**
- EU contribution: **€0.9 million**
- Project Number: **20111202 (EU Health Programme)**

Metabolic disorders and endocrinology

AIPgene

Augmenting PBGD Expression in the Liver as a Novel Gene Therapy for Acute Intermittent Porphyria

Acute Intermittent Porphyria (AIP) is a rare genetic disease in which mutations in the porphobilinogen deaminase (PBGD) gene result in a wide variety of problems including abdominal pains, psychiatric and neurological disorders as well as muscular weakness. Acute porphyric attacks can be life-threatening and the long-term consequences include irreversible nerve damage, liver cancer and kidney failure. As therapies currently available do not prevent the symptoms or consequences of such attacks, the aim of the AIPgene project is the clinical development of the orphan drug AAV-AAT-PBGD for the treatment of AIP.

The project covers the development of a process to produce the drug for clinical trials, the constitution of cohorts to improve the follow-up of patients and determine clinical criteria to select patients for gene therapy, and a trial to verify the safety and efficacy of the drug.

- Coordinator: **Gloria González, Fundación para la Investigación Médica Aplicada (Spain) (ggasegui@unav.es)**
- Participants: **ES (Coordinator), DE, NL, SE**
- Website: **http://www.aipgene.org/**
- Duration: **from January 2011 to December 2013**
- Total costs: **€4.4 million**
- EU contribution: **€3.3 million**
- Project Number: **261506 (FP7-Health)**

ALPHA-MAN

Clinical Development of Enzyme Replacement Therapy in alpha-Mannosidosis Patients Using Recombinant Human Enzyme

Alpha-Mannosidosis is a devastating disease caused by the deficiency of the lysosomal alpha-mannosidase (LAMAN) which can lead to severe problems including mental retardation, skeletal changes, hearing loss and recurrent infections. While no causative treatment for alpha-Mannosidosis has been available to date, an early initiated therapy could contribute to a normal development. Since pharmaceutical interest in this disease is low, different EU-funded projects have worked towards developing a therapeutic agent.

The ALPHA-MAN project aims to take these initiatives further. It implements clinical trials in alpha-Mannosidosis patients to provide an effective drug and to determine the minimal effective dose by chronic treatment studies. The project also examines how recombinant human LAMAN crosses the Blood Brain Barrier and studies the impact of chronic Enzyme Replacement Therapy (ERT) treatment.

- Coordinator: **Paul Saftig, Christian-Albrechts-Universität zu Kiel (Germany) (psaftig@biochem.uni-kiel.de)**
- Participants: **DE (Coordinator), BE, DK, FR, NO, PL, UK**
- Website: **http://www.alpha-man.eu/**
- Duration: **from October 2010 to September 2013**
- Total costs: **€8.0 million**
- EU contribution: **€5.9 million**
- Project Number: **261331 (FP7-Health)**

AP-HP_Porphyria_FY2011 (EPNET)

Porphyria is a rare disorder where chemicals called porphyrias accumulate in the body causing symptoms such as stomach aches and skin problems. EPNET's (European Porphyria Network) objective is to provide an effective network of specialist porphyria centres in each country, in order to improve the lives of porphyria patients through better diagnosis and treatment of these rare conditions.

In all, there are 33 such centres working together to develop an up-to-date approach to the management of patients and families and that conform to uniform standards. In this context, EPNET focuses on: providing information to patients and healthcare professionals (HCPs); collecting information on safety of drugs; using external quality assessment to develop quality standards for diagnosis and clinical advice; a web-based registry to collect data about the porphyrias.

- Coordinator: **Jean-Charles Deybach, Assistance Publique — Hôpitaux de Paris (France) (jean-charles.deybach@lmr.aphp.fr)**
- Participants: **FR (Coordinator) — EPNET consists of 33 EU specialist centres from 21 European and candidate countries**
- Website: **http://www.porphyria-europe.org; http://www.drugs-porphyria.org**
- Duration: **from January 2011 to January 2012**
- Total costs: **€0.2 million**
- EU contribution: **€0.1 million**
- Project Number: **20103209 (EU Health Programme)**

BALANCE

Development of a bioartificial liver therapy in acute liver failure

Acute Liver Failure (ALF) is a highly lethal disorder where transplants are the only life-saving therapy. BALANCE aims to offer patients a bioartificial liver support system, to bridge the liver transplant waiting or recovery period, since the limited availability of donor livers means many patients are not treated in time.

It is helping to develop a bioartificial liver (BAL), which it believes will support ALF patients by treatment of their plasma through a bioreactor with functional human cells. The approach will involve two main steps: in-vitro optimisation of the BAL and human cell line and testing and validation of the optimised and upscaled BAL on pigs and secondly on humans with ALF.

The consortium consists of private and academic partners and aims for three main results: an optimised and validated BAL, a GMP (good manufacturing practice) manufacturing process and a GMP grade and stable human liver cell line.

- Coordinator: **Robert A.F.M. Chamuleau, Academisch Medisch Centrum, Universiteit van Amsterdam (The Netherlands) (r.a.chamuleau@amc.uva.nl)**
- Participants: **NL (Coordinator), FR, UK**
- Website: **http://cordis.europa.eu/**
- Duration: **from June 2012 to May 2015**
- Total costs: **€7.8 million**
- EU contribution: **€6.0 million**
- Project Number: **304914 (FP7-Health)**

DevelopAKUre

Clinical Development of Nitisinone for Alkaptonuria

Alkaptonuria (AKU), also known as Black Bone Disease, is a rare genetic disorder in which an enzyme called homogentisate 1, 2-dioxygenase (HGD) is absent. This leads to a build-up of toxic homogentisic acid (HGA) in the body. Some of this HGA reacts to form black pigment which is deposited in connective tissues, leading to arthritis, heart disease and disability. Currently, multiple arthroplasty is inevitable since AKU is incurable and there is no effective disease-modifying therapy. DevelopAKUre is working towards the clinical development of an orphan drug, nitisinone, for the treatment of AKU.

This will involve a dose-finding study, a phase 3 clinical trial to prove efficacy and a cross-sectional study in children and young adults to determine when to start treatment. Building on the results of DevelopAKUre, a request for marketing authorisation of nitisinone for AKU will be put forward to the European Medicines Agency.

- Coordinator: **Lakshminarayan Ranganath, Royal Liverpool and Broadgreen University Hospitals Trust (United Kingdom) (lrang@liverpool.ac.uk)**
- Participants: **UK (Coordinator), DK, FR, NL, IT, SE, SK**
- Website: **http://cordis.europa.eu/**
- Duration: **from November 2012 to April 2018**
- Total costs: **€11.0 million**
- EU contribution: **€6.0 million**
- Project Number: **304985 (FP7-Health)**

E-IMD

European registry and network for Intoxication type Metabolic Diseases

The European registry and network for Intoxication type Metabolic Diseases (E-IMD) has been established to help those affected by rare organic acidurias (OADs) or urea cycle defects (UCDs). It aims to do so through the assimilation of data on a web-based registry, where information on follow-up investigations of people affected by such a disease will be stored.

This registry will describe the disease course, epidemiology, diagnostic and therapeutic strategies for OADs and UCDs and will be available to national and EU health authorities. It will come up with European consensus care protocols for such patients to try to identify the best means of diagnosis and treatment. These protocols will be translated into the official EU languages and used as the basis for national guidelines and patient brochures.

- Coordinator: **Stefan Kölker, Universitätsklinikum Heidelberg (Germany) (Stefan.Koelker@med.uni-heidelberg.de)**
- Participants: **DE (Coordinator), AT, BE, CZ, DK, EL, ES, FR, IT, NL, PL, PT, RO, UK**
- Website: **http://www.e-imd.org/en/index.phtml, https://www.eimd-registry.org**
- Duration: **from January 2011 to January 2014**
- Total costs: **€1.3 million**
- EU contribution: **€0.8 million**
- Project Number: **20101201 (EU Health Programme)**

EUCLYD

A European Consortium for Lysosomal Disorders

Lysosomal storage diseases (LSD) are rare disorders, each due to a specific lysosomal enzyme deficiency causing deposits to accumulate in organs and tissues. The EUCLYD consortium was set up to develop a scientific network among communities of basic and clinical investigators in European countries to study various aspects of LSD. Of the 40 to 50 LSDs presently known, EUCLYD focused on Gaucher disease, Pompe disease, MPS VI and Multiple sulfatase deficiency as prototypes of disorders with different stored materials in organs and tissues outside the central nervous system.

The project examined the pathophysiology and the mechanisms underlying the symptoms with a view to developing clinical applications. It also investigated the disease's natural history. These issues were addressed through patients' studies and mouse models recapitulating the phenotype of LSDs. The project also focussed on achieving a better understanding of these processes triggered by substrate storage.

- Coordinator: **Generoso Andria, Dipartimento di Pediatria Universita di Napoli Federico II (Italy) (andria@unina.it)**
- Participants: **IT (Coordinator), DE, NL, SE, UK**
- Website: **http://www.euclyd.eu/**
- Duration: **from May 2008 to April 2011**
- Total costs: **€3.9 million**
- EU contribution: **€3.0 million**
- Project Number: **201678 (FP7-Health)**

The EURO-WABB Project

An EU Rare Diseases Registry for Wolfram syndrome, Alström syndrome, Bardet-Biedl syndrome and other rare diabetes syndromes

The general objective of the EURO-WABB Project is to support efficient diagnosis, treatment and research for the overlapping Wolfram, Alström and Bardet-Biedl syndromes, as well as other rare diabetes syndromes. WABB syndromes constitute a group of rare, heritable disorders linked by intolerance of the body to glucose. Each of these syndromes affects different parts of the body, including hearing and vision.

An EU registry for Rare Diabetes Syndromes (RDS) containing clinical, genetic diagnostic and outcome data has been created to achieve this goal. More specifically, the registry has been established to:

- establish the natural history of RDS (their characteristics, management and outcomes);
- assess the clinical effectiveness of management and quality of care;
- provide an inventory of patients for recruitment into intervention studies;
- establish genotypes-phenotypes.

- Coordinator: **Timothy Barrett, University of Birmingham C/O Diabetes Unit (United Kingdom) (t.g.barrett@bham.ac.uk)**
- Participants: **UK (Coordinator), DK, ES, ET, FR, IT, PL**
- Website: **http://www.euro-wabb.org**
- Duration: **from January 2012 to January 2014**
- Total costs: **€1.5 million**
- EU contribution: **€0.9 million**
- Project Number: **20101205 (EU Health Programme)**

InnovaLiv

Innovative Strategies to Generate Human Hepatocytes for Treatment of Metabolic Liver Diseases: Tools for Personalised Cell Therapy

Transplantation of donor hepatocytes has become an alternative to liver transplantation for the treatment of liver diseases. As adult hepatocytes cannot be expanded in vitro, there is a critical need to explore the potential of human stem cells such as human Embryonic Stem (hES) cells for generating sufficient quantities of functional human hepatocytes. The InnovaLiv project aims to provide the EU healthcare system with a renewable and reliable source of functional clinical-grade hepatocytes generated from hES cell lines.

To achieve this, it will work towards the development of scale-up procedures for hES cells and the production of GMP-grade tissue culture reagents that will facilitate large-scale differentiation of hES cells to hepatocytes. Rigorous standards will be developed to ensure the safety and quality of these cells. The GMP-compliant hepatocytes will be prepared as a prototype therapy.

- Coordinator: **Anne Weber-Benarous, Institut national de la santé et de la recherche médicale (INSERM) (France) (anne.weber@inserm.fr)**
- Participants: **FR (Coordinator), DE, ES, SE, UK**
- Website: **http://www.innovaliv.eu/**
- Duration: **from December 2011 to November 2014**
- Total costs: **€7.7 million**
- EU contribution: **€5.9 million**
- Project Number: **278152 (FP7-Health)**

MeuSIX

Clinical Trial of Gene Therapy for MPS VI, a Severe Lysosomal Storage Disorder

Mucopolysaccharidosis VI (MPS VI), or Maroteaux-Lamy syndrome, is a rare lysosomal storage disease characterised by growth retardation, corneal clouding, cardiac valve disease, organomegaly and skeletal dysplasia. It is caused by deficient activity of arylsulfatase B (ARSB). Gene therapy based on a single intravascular administration of adeno-associated viral (AAV) vectors targeting the liver has the potential to provide a lifelong source of ARSB. The MeuSIX consortium will investigate the safety and efficacy of AAV-mediated gene therapy in patients.

This will be achieved through a clinical trial. An orphan drug designation for the MPS VI therapeutic AAV vector has been obtained from the European Medicinal Agency and the US Food and Drug Administration. The results of the trial could significantly improve the quality of life of patients while facilitating the development of similar approaches for other inborn errors of metabolism.

- Coordinator: **Alberto Auricchio, Fondazione Telethon (Italy) (auricchio@tigem.it)**
- Participants: **IT (Coordinator), FR, NL, TR, US**
- Website: **http://cordis.europa.eu/**
- Duration: **from December 2012 to November 2017**
- Total costs: **€7.9 million**
- EU contribution: **€6.0 million**
- Project Number: **304999 (FP7-Health)**

PERSIST

Persisting Transgenesis

For many disabling or fatal diseases, there is evidence for the potential efficacy of gene therapy, especially in the areas of inherited immune and enzyme deficiencies. However, current gene transfer technologies have limitations and may result in undesirable mutagenic effects.

The PERSIST project addresses the development of emerging gene therapy tools and technologies for clinical application. It explores the use of highly innovative gene-modifying and delivery technologies, capitalising on recent discoveries on artificial endonucleases and gene expression control. The project brings together 22 European experts in the field of genetic engineering for persisting gene expression from different European countries. Target diseases include inherited immune deficiencies, lysosomal storage disorders and haemophilias.

- Coordinator: **Luigi Naldini, Vita Salute San Raffaele University (Italy) (naldini.luigi@hsr.it)**
- Participants: **IT (Coordinator), BE, CH, DE, ES, FR, NL, SE, UK**
- Website: **http://www.persist-project.eu/**
- Duration: **from January 2009 to June 2013**
- Total costs: **€14.8 million**
- EU contribution: **€11.2 million**
- Project Number: **222878 (FP7-Health)**

TAIN

Treatment of Adrenal Insufficiency in Neonates — Development of a Hydrocortisone Preparation for the Treatment of Adrenal Insufficiency in Neonates and Infants

Adrenal Insufficiency is a rare disorder which prevents the body from producing sufficient cortisol. The aim of the TAIN project is to develop a new formulation of hydrocortisone that can be used from birth in replacement therapy, especially in the 0–2 year age range. The problem of effective hydrocortisone replacement is particularly acute among young patients for whom no licensed therapy currently exists.

TAIN involves European leaders in drug development, neonatology and paediatric pharmacology. A Paediatric Investigation Plan has been developed that will enable clinical trials to be carried out to provide sufficient evidence of drug safety and efficacy, to allow submission of a Paediatric Use Medicines Authorisation to the European Medicines Agency. The project also aims to raise awareness of Adrenal Insufficiency to maximise its positive impact.

- Coordinator: **Martin Whitaker, University of Sheffield (United Kingdom) (martin.whitaker@sheffield.ac.uk)**
- Participants: **UK (Coordinator), CH, DE**
- Website: **http://www.tain-project.org/**
- Duration: **from December 2011 to November 2015**
- Total costs: **€5.6 million**
- EU contribution: **€4.2 million**
- Project Number: **281654 (FP7-Health)**

Neurology, mental health, neuromuscular and musculoskeletal disorders

BIO-NMD

Identifying and validating pre-clinical biomarkers for diagnostics and therapeutics of Neuromuscular Disorders

Knowledge of Neuromuscular Disorder genetic diagnosis is rapidly expanding, leading to earlier diagnosis, new targets for disease characterisation, and drug discovery and development. It is also leading to more questions about how to translate this knowledge into clinical practice: clinical trials typically do not last long enough for clinical improvement to be expected.

Biomarkers represent measurable bio-parameters, which can be used for monitoring disease progression, prognosis and drug response, therefore optimising the choice of appropriate and often personalised therapies. Through the use of OMIC sciences, BIO-NMD is working on developing biomarkers that will increase therapy efficiency and efficacy. These are tested and validated in both animal models and human samples, and the qualified biomarkers resulting from the BIO-NMD project will be ready for ongoing and further clinical trials for the patients' benefit.

- Coordinator: **Alessandra Ferlini, Università degli Studi di Ferrara (Italy) (fla@unife.it)**
- Participants: **IT (Coordinator), DE, FR, NL, SE, UK, US**
- Website: **http://www.bio-nmd.eu/**
- Duration: **from December 2009 to December 2012**
- Total costs: **€7.5 million**
- EU contribution: **€5.6 million**
- Project Number: **241665 (FP7-Health)**

CARE-NMD

Dissemination and Implementation of the Standards of Care for Duchenne Muscular Dystrophy in Europe (including Eastern countries)

CARE-NMD was established with the aim of optimising the treatment of Duchenne muscular dystrophy (DMD) in participating countries, thus improving the quality of life for DMD patients.

Specifically, the project identified the status of DMD treatment approaches in each country through online questionnaires and then, according to the results obtained, organised training sessions with healthcare providers at national level. These sessions sought to support providers in their efforts to bring healthcare practices in line with the recommended and established standards of care.

Additionally, the project increased awareness and knowledge about DMD treatment recommendations through an online discussion forum and national multidisciplinary training workshops.

- Coordinator: **Janbernd Kirschner, Universitätsklinikums Freiburg (Germany) (eu-drittmittel@uniklinik-freiburg.de)**
- Participants: **DE (Coordinator), BG, BY, CZ, DK, FR, HR, HU, IE, MK, NL, NO, PL, RO, RS, RU, SE, SK, UA, UK**
- Website: **http://en.care-nmd.eu/**
- Duration: **from October 2009 to September 2012**
- Total costs: **€1.6 million**
- EU contribution: **€0.9 million**
- Project Number: **20091205 (EU Health Programme)**

DEM-CHILD

A Treatment-Oriented Research Project of NCL Disorders as a Major Cause of Dementia in Childhood

Neuronal ceroid lipofuscinoses (NCL) is a neurodegenerative disease that affects children. Currently there is no cure for this disease which causes dementia, blindness, epilepsy, physical decline and ultimately an early death. NCL are under-diagnosed, and large therapeutic studies have traditionally been difficult to initiate, since it is difficult to find and study genetically similar patients given genetic heterogeneity.

The DEM-CHILD project brings together recognised European research teams, high-technology SMEs and Indian experts to work towards the goal of developing innovative and cost- and time-effective testing and screening as well to support the development of innovative therapies. To carry out this work, a large patient base will be brought together and studied and the therapeutic strategies that are developed will be tested in mouse models.

- **Coordinator:** Angela Schulz, Universitätsklinikum Hamburg-Eppendorf (Germany) (an.schulz@uke.de)
- **Participants:** DE (Coordinator), FI, IN, IT, UK
- **Website:** http://www.dem-child.eu/
- **Duration:** from October 2011 to October 2014
- **Total costs:** €3.9 million
- **EU contribution:** €3.0 million
- **Project Number:** 281234 (FP7-Health)

EFACTS

European Friedreich's Ataxia Consortium for Translational Studies

Friedreich's ataxia (FRDA) is a rare autosomal recessive neurological disease that is severely debilitating and leads to loss of mobility and dependency for all activities. Onset is usually in childhood and symptoms include cardiomyopathy, visual and auditory loss, diabetes, pes cavus and kyphoscoliosis. The EFACTS initiative's primary aim is to adopt a translational research strategy on the disease.

Since FRDA affects individuals and clinical specialists are often dispersed, its approach is to bring together a critical mass of researchers and clinicians to examine the patient base, research reagents and knowledge for progress. It uses IT services as crucial support in this collaborative work as a means of collecting patient data and material and making it available to leading researchers for advanced analysis, research and drug development.

- **Coordinator:** Massimo Pandolfo, Université Libre de Bruxelles (Belgium) (massimo.pandolfo@ulb.ac.be)
- **Participants:** BE (Coordinator), AT, DE, ES, FR, IT, UK, US
- **Website:** http://www.e-facts.eu/
- **Duration:** from May 2010 to May 2014
- **Total costs:** €7.9 million
- **EU contribution:** €6.0 million
- **Project Number:** 242193 (FP7-Health)

ENDOSTEM

Activation of vasculature associated stem cells and muscle stem cells for the repair and maintenance of muscle tissue

The ENDOSTEM project has two overall goals: it seeks to come up with innovative biotherapeutics for tissue repair by developing new strategies that target endogenous skeletal muscle tissue-related stem cells; in parallel, this project explores new approaches that limit tissue damage with a specific focus on agents that modify muscle and muscle vasculature progenitor cells.

Three clinical trials will run in tandem as part of the project, with the most promising drugs first validated in small and large animal models. This work is complemented by novel bio-delivery systems for effective targeting, since a key issue that this project addresses is the tissue environment in which endogenous stem cells are activated. Advances in this field will not only address muscle diseases, but also provide potential cures for broad application in regenerative medicine in general.

- **Coordinator:** David Sassoon, Institut national de la santé et de la recherche médicale (INSERM) (France) (david.a.sassoon@gmail.com)
- **Participants:** FR (Coordinator), CH, DE, DK, ES, FR, IT, UK
- **Website:** http://www.endostem.eu/
- **Duration:** from January 2010 to December 2014
- **Total costs:** €15.8 million
- **EU contribution:** €12.0 million
- **Project Number:** 241440 (FP7-Health)

EU-CHS

European network for central hypoventilation syndromes: Optimising healthcare for patients

The EU-CHS project was created to optimise healthcare for patients with central hypoventilation syndromes (CHS) in Europe. CHS are extremely rare disorders involving the autonomic nervous system, which controls functions such as breathing. CHS include a varied group of not fully characterised diseases, with severe chronic central hypoventilation being the hallmark and the most life-threatening common feature.

The main aims of the EU-CHS project were to provide information about CHS through a multi-lingual website and to implement a European CHS register. The register identifies a critical mass of CHS patients in the 11 participating countries and facilitates epidemiological and clinical studies. More specific aims for the project included: defining European guidelines for diagnosis and treatment of CHS and providing an overview of the state of existing services.

- **Coordinator:** Ha Trang, Assistance Publique, Hôpitaux de Paris (France) (ha.trang@rdb.aphp.fr)
- **Participants:** FR (Coordinator), AT, CH, DE, DK, ES, HR, IT, NO, PL, PT, SE, SI, UK
- **Website:** http://www.ichsnetwork.eu/
- **Duration:** from June 2009 to May 2012
- **Total costs:** €1.1 million
- **EU contribution:** €0.7 million
- **Project Number:** 20081206 (EU Health Programme)

Euro-MOTOR

European multidisciplinary ALS network identification to cure motor neuron degeneration

Amyotophic Lateral Scelrosis (ALS) is a devastating neurological disease affecting in Europe 50 000 individuals at any time, causing around 10 000 deaths each year. It is characterised by progressive degeneration of motor neurons in the brain and spinal cord leading to muscle weakness. Although there have been a number of scientific breakthroughs, there is no cure at the moment. Euro-MOTOR will use a large integrative effort at European level with a systematic biological approach to aid this progress.

The consortium aims to detect key genetic drivers of disease susceptibility / progression, while parametric modelling of the causal connections in identified molecular networks will generate a model of the disease. Large quantitative omics data from new functional models and from patients in two prospective European, population-based inception cohorts will be analysed, with major findings validated in a second prospective patient cohort and functional models.

- **Coordinator:** Leonard Van den Berg, Universitair Medisch Centrum Utrecht (The Netherlands) (lberg@umcutrecht.nl)
- **Participants:** NL (Coordinator), BE, FR, DE, IE, IT, NL, UK
- **Website:** http://www.euromotorproject.eu/
- **Duration:** from February 2011 to January 2016
- **Total costs:** €11.9 million
- **EU contribution:** €9.0 million
- **Project Number:** 259867 (FP7-Health)

FIGHT-MG

Myasthenias, a group of immune mediated neurological diseases: from etiology to therapy

Myasthenia Gravis (MG) is a heterogeneous rare autoimmune neurological disease affecting the neuromuscular junction (NMJ). Research into the disease is still at an early stage, the molecular events causing and maintaining MG are still unknown and current treatments are not effective and lead to unwanted side-effects.

The project aims to improve therapies, by linking basic researchers with clinical neurologists, SMEs and European patient associations. More specifically, research will go into determining what factors are associated with the onset/affecting the course of the disease as well as the etiology of MG and the pathogenic mechanisms at the NMJ. Ultimately, the initiative aims to put in place new diagnostic and monitoring assays and to come up with novel therapies to combat the disease.

- **Coordinator:** Sonia Berrih-Aknin, Institut national de la santé et de la recherche médicale (INSERM) (France) (sonia.berrih-aknin@upmc.fr)
- **Participants:** FR (Coordinator), CH, EL, DE, IL, IT, NO
- **Website:** http://www.fight-mg.eu/
- **Duration:** from December 2009 to December 2013
- **Total costs:** €7.8 million
- **EU contribution:** €5.9 million
- **Project Number:** 242210 (FP7-Health)

LeukoTreat

Therapeutic challenge in Leukodystrophies: Translational and ethical research towards clinical trials

The LeukoTreat programme aims to combat Leukodystrophies (LDs), rare inherited neurodegenerative diseases of the white matter and its main component, myelin, which predominantly affect children. Despite major advances in the past decade, no current curative therapy exists, so the development of therapeutic approaches for myelin repair and neuro-protection constitute the primary objectives of the project.

To achieve its goal and develop efficient and effective therapies, it uses five complementary approaches. The programme:

- collects information on the epidemiology of patients;
- identifies and validates biomarkers;
- develops pharmacological strategies;
- develops innovative gene and cell therapies;
- tackles ethical impacts of the proposed therapeutic challenges.

- **Coordinator:** Catherine Vaurs-Barrière, Université d'Auvergne Clermont-Ferrand 1 (France) (catherine.barriere@u-clermont1.fr)
- **Participants:** FR (Coordinator), AT, AU, DE, ES, IT, NL, UK
- **Website:** http://www.leukotreat.eu/
- **Duration:** from March 2010 to March 2013
- **Total costs:** €9.0 million
- **EU contribution:** €6.0 million
- **Project Number:** 241622 (FP7-Health)

MEFOPA

European Project on Mendelian Forms of Parkinson's Disease

The Collaborative Project on Mendelian Forms of Parkinson's Disease (MEFOPA) is a consortium of people involved in basic and clinical research on rare Mendelian forms of Parkinson's Disease (PD) with autosomal-dominant and autosomal-recessive inheritance. This variant of the disease is chosen as it has become increasingly clear that the best way of developing effective disease-modifying treatments is by focusing on rare variants with known defects.

Their aim is to identify and validate relevant disease-related molecular pathways, drug targets and biomarkers for disease susceptibility and progression. By employing an integrated, translational approach combining basic and clinical research groups, the consortium aims to achieve measurable progress for disease-modifying therapies, before testing their findings with designed drug trials on a selected group of patients.

- **Coordinator:** Thomas Gasser, Eberhard Karls Universität Tübingen (Germany) (thomas.gasser@uni-tuebingen.de)
- **Participants:** DE (Coordinator), BE, CH, DK, EL, ES, FR, HU, IT, NL, NO, PT, SE, UAE, UK
- **Website:** http://www.mefopa.eu/
- **Duration:** from April 2010 to September 2013
- **Total costs:** €8.1 million
- **EU contribution:** €5.8 million
- **Project Number:** 241791 (FP7-Health)

MitoTarget

Mitochondrial dysfunction in neurodegenerative diseases: towards new therapeutics

In order to understand neurodegenerative diseases, we need to understand the circumstantial evidence linking mitochondrial dysfunction with neuronal dysfunction. MitoTarget is a 36-month translational research programme whose aim is to gain an insight into the mechanisms leading to mitochondrial impairments and establish their clinical relevance in a severe orphan neurodegenerative disease, ALS.

If the initiative is successful, a new class of therapeutic agents will emerge, targeting underlying mitochondrial dysfunction in neurons or their supporting cells, will pave the way for a whole new school of thought and should lead to further breakthroughs.

The consortium brings together scientists, clinical investigators and an SME, which was responsible for identifying a powerful neuroprotective, first-in-class compound, TRO19622, which targets mitochondria.

- **Coordinator:** Rebecca Pruss, Trophos S.A. (France) (rpruss@trophos.com)
- **Participants:** FR (Coordinator), BE, DE, UK
- **Website:** http://cordis.europa.eu/
- **Duration:** from February 2009 to April 2012
- **Total costs:** €10.3 million
- **EU contribution:** €6.0 million
- **Project Number:** 223388 (FP7-Health)

NEURINOX

NOX enzymes as mediators of inflammation-triggered neurodegeneration: modulating NOX enzymes as novel therapies

NADPH oxidase (NOX) enzymes have emerged as key regulators of neuroinflammation and play a role in the progression of neurodegenerative diseases (ND). NEURINOX aims at clarifying exactly what role NOX enzymes play in this process, as well as evaluating the potential of novel ND therapeutic approaches targeting NOX activity.

NOX generates reactive oxygen species (ROS), whose presence or absence, in turn, can cause various different ND. The specific aim, therefore, is to understand how NOX controls neuroinflammation, to identify novel molecular pathways and biomarkers, and to develop specific therapies based on NOX modulation.

The results will be tested in clinical trials and on animal models, and will contribute to a better understanding of brain dysfunction and help identify new therapeutic targets for ND. The consortium consists of researchers, experts and clinicians from six different countries.

- **Coordinator:** Vincent Jaquet, Université de Genève (Switzerland) (Vincent.Jaquet@unige.ch)
- **Participants:** CH (Coordinator), AU, EL, FR, IT, SE
- **Website:** http://www.neurinox.eu/
- **Duration:** from January 2012 to January 2016
- **Total costs:** €15.4 million
- **EU contribution:** €11.4 million
- **Project Number:** 278611 (FP7-Health)

NEUROMICS

Integrated European Omics Research Project for Diagnosis and Therapy in Rare Neuromuscular and Neurodegenerative Diseases

Neurodegenerative (ND) and neuromuscular (NM) diseases are affecting the lives and mobility of 500 000 patients in Europe and millions of their carers, family members and employers. The NEUROMICS project aims to develop pathomechanism-based treatment for ten major ND and NM diseases.

It brings together 13 leading European research groups, 5 innovative SMEs and 4 overseas experts, and uses the most sophisticated Omics technologies. A number of major disease categories were selected, some of which are in a promising stage of etiological and therapeutic research while others are in great need of further classification.

The project will use next generation whole exome sequencing (WES) to increase the number of known gene loci. It will increase patient cohorts and develop biomarkers for clinical application. Activities also include the identification of disease modifiers in disease subgroup cohorts with extreme age of disease onset and the development of targeted therapies.

- Coordinator: **Olaf Riess, Eberhard Karls Universität Tübingen (Germany) (olaf.riess@med.uni-tuebingen.de)**
- Participants: **DE (Coordinator), AU, BE, CA, FR, IT, IS, NL, SE, UK, US**
- Website: **http://www.rd-neuromics.eu/**
- Duration: **from October 2012 to September 2017**
- Total costs: **€16.9 million**
- EU contribution: **€12.0 million**
- Project Number: **305121 (FP7-Health)**

nEUroped

European Network of Reference for Rare Paediatric Neurological Diseases

nEUroped is a network for children with rare nervous system disorders which brings together patients and their families, patient organisations, research groups and other interested parties across Europe. The project built on the results of the ENRAH project (www.enrah.net) also funded by the EU.

The nEUroped project aimed to improve the diagnosis, management and dissemination of information relating to a number of rare nervous system disorders in children, covering: Alternating Hemiplegia of Childhood (AHC), Narcolepsy and Rare Surgically Treatable Epileptic Syndromes (RSTES); Sturge-Weber; Hypothalamic hamartoma, Landau-Kleffner syndrome; Cerebellar Hamartomas and Rasmussen syndrome.

Apart from establishing an active and engaged network, the project sought to identify the main research, healthcare and social needs of the selected diseases by surveying patients and patients' registries. It then reviewed and analysed data to develop and disseminate recommendations as guidelines.

- Coordinator: **Alexis Arzimanoglou, Hospices Civils de Lyon (France) (aarzimanoglou@orange.fr)**
- Participants: **FR (Coordinator), BE, CZ, DE, DK, ES, IT, NL, PT, SI, UK**
- Website: **http://www.neuroped.eu/**
- Duration: **from April 2008 to December 2011**
- Total costs: **€1.1 million**
- EU contribution: **€0.7 million**
- Project Number: **2007122 (EU Health Programme)**

NEuroStemCell

European Consortium for Stem Cell Therapy for Neurodegenerative Diseases

The NEuroStemCell consortium aims to maximise the prospects for successful clinical trials of stem cell therapy for the neurodegenerative diseases Parkinson's (PD) and Huntington's (HD). Their goal is to develop safe and validated cells and clinical grade reagents to be used in clinical trials and, eventually, also in drug discovery.

In the first place, this involves comparing different stem cell sources with respect to their capacity to generate neurons. Extrinsic cues are then used to specify neuronal differentiation, different human stem cell lines and their ability to affect long-term behavioural recovery. Next, functional motor and cognitive recovery is evaluated, as well as the various impacts of the donor cells in the host brain.

If the research is successful, three SMEs in the consortium will generate the technologies for the manufacture and scale-up of safe, fully traceable, efficacious and banked stocks of cells ready for clinical use.

- **Coordinator:** Elena Cattaneo, Università degli Studi di Milano (Italy) (elena.cattaneo@unimi.it)
- **Participants:** IT (Coordinator), DE, DK, FR, SE, UK
- **Website:** http://cordis.europa.eu/
- **Duration:** from December 2008 to May 2013
- **Total costs:** €15.8 million
- **EU contribution:** €11.9 million
- **Project Number:** 222943 (FP7-Health)

NeuroXsys

Genomic Regulatory Systems of Human X-linked neurological diseases

In an effort to learn more about neurological diseases arising from the X chromosome, the NeuroXsys initiative was created to generate regulatory maps and models of the X chromosome. Vertebrate chromosomes are first subdivided into domains of genomic regulatory blocks (GRBs) and after these are mapped and the gene regulatory sequences extracted, the activities are modelled through transgenic reporter assays in the zebrafish juvenile and adult brain.

A key deliverable of NeuroXsys will be the publication of an online database that stores the findings of this research. The initiative will seek to identify human disease mutations in neural regulatory elements, with implicated elements being studied as regulators at single cell resolution in the zebrafish, and mouse brain being studied to define expression patterns.

- **Coordinator:** Thomas Becker, Universitetet i Bergen (Norway) (tbecker@med.usyd.edu.au)
- **Participants:** NO (Coordinator), AU, DE, DK, ES, FR, IT, UK
- **Website:** http://neuroxsys.net/
- **Duration:** from June 2009 to November 2012
- **Total costs:** €4.0 million
- **EU contribution:** €3.0 million
- **Project Number:** 223262 (FP7-Health)

NMD-Chip

Development of targeted DNA-Chips for High Throughput Diagnosis of NeuroMuscular Disorders

Inherited neuromuscular diseases form a large group of diseases that either directly or indirectly impair muscles. Their diagnosis requires extensive clinical examination and targeted complementary tests and as this is both highly complex and time consuming, many patients are not properly diagnosed. This is made worse by the fact that new cutting edge therapies cannot be used where there is no genetic confirmation of the disease.

DNA chips have the potential to address this issue. The objective of the NMD-Chip project is to design and validate such a chip for sequencing genes responsible for these diseases. This technology will then be used to identify new genes/mutations involved in these inherited NMD in order to increase the molecular diagnosis/patients ratio. Ultimately this will give patients easy access to molecular diagnosis and will thus allow them to benefit from the existing cutting edge therapies.

- **Coordinator:** Nicolas Levy, Institut national de la santé et de la recherche médicale (INSERM) (France) (nicolas.levy@univ-amu.fr)
- **Participants:** FR (Coordinator), DE, FR, HU, IT, NL, SE, UK
- **Website:** http://www.nmd-chip.eu/
- **Duration:** from October 2008 to October 2011
- **Total costs:** €3.8 million
- **EU contribution:** €2.9 million
- **Project Number:** 223026 (FP7-Health)

OPTIMISTIC

Observational Prolonged Trial in Myotonic Dystrophy Type 1 to Improve QoL-Standards, a Target Identification Collaboration

OPTIMISTIC is a European collaborative project of doctors, scientists, SMEs and other stakeholders, including patient organisations, aiming to improve clinical practice for patients suffering from myotonic dystrophy type 1 (DM1) disease. This rare, inherited and neglected disorder is one of the most variable human diseases with complex, multi-systemic and progressively worsening clinical manifestations.

There is no cure for DM1. The aim of treatment is to relieve impairments, reduce limitations and support participation in everyday activities. OPTIMISTIC investigates the effect of exercise training to improve functional capacity and of cognitive behavioural therapy (CBT) to stimulate an active lifestyle with a view to improving quality of life. The project also aims to develop clinical guidelines and to ensure their rapid uptake to achieve tangible improvements in DM1 care.

- **Coordinator:** Baziel Van Engelen, Stichting Katholieke Universiteit (The Netherlands) (b.vanengelen@neuro.umcn.nl)
- **Participants:** NL (Coordinator), DE, FR, UK
- **Website:** http://cordis.europa.eu/
- **Duration:** from November 2012 to October 2016
- **Total costs:** €3.8 million
- **EU contribution:** €3.0 million
- **Project Number:** 305697 (FP7-Health)

PADDINGTON

Pharmacodynamic Approaches to Demonstration of Disease Modification in Huntington's Disease by SEN0014196

The Paddington Consortium is composed of five specialised partners who will undertake research activities together aimed at establishing the feasibility of a range of pharmacodynamic readouts for use in clinical development of SEN0014196. This is a novel and selective SirT1 inhibitor used to tackle Huntington's disease, and the partners hope to demonstrate the disease-modifying properties of the compound.

The inhibitor is currently in Phase II of clinical development and a multi-factorial approach will be used for the project. This will include assessment of:

- novel and compound-specific measures of molecular action;
- previously identified predictors of disease progression.

Ultimately, the translational approaches will be instrumental in the progression of SEN0014196 to clinical proof-of-concept and will play a pivotal role in patient stratification and outcomes research.

- **Coordinator:** Giovanna Tripepi, Siena Biotech SPA (Italy) (gtripepi@sienabiotech.it)
- **Participants:** IT (Coordinator), DE, PL, UK
- **Website:** http://www.paddingtonproject.eu/
- **Duration:** from July 2010 to December 2013
- **Total costs:** €8.6 million
- **EU contribution:** €5.8 million
- **Project Number:** 261358 (FP7-Health)

SKIP-NMD

A Phase I/IIa Clinical Trial in Duchenne Muscular Dystrophy Using Systemically Delivered Morpholino Antisense Oligomer to Skip Exon 53

Duchenne muscular dystrophy (DMD) is a lethal muscle-degenerative condition which affects boys. It arises from the absence of dystrophin in skeletal and cardiac muscles. Modulation of pre-mRNA splicing by exon skipping using antisense oligonucleotides (AOs) is the most promising molecular intervention in DMD. The SKIP-NMD project aims to develop a Morpholino (PMO) AO to skip exon 53 and perform a clinical trial in boys with DMD using a pan-European consortium including world leading experts.

This will contribute to advancing this class of AO therapy in DMD by assessing the safety and efficacy of targeting another exon, and by exploring the use of non-invasive techniques to monitor response to treatment. The new PMO will be administered over 12 weeks in three groups, each of four boys with DMD receiving between 4 and 30 mg/kg or a placebo. If well tolerated, all boys will be treated for another 24 weeks at a dose of 30 mg/kg.

- **Coordinator:** Francesco Muntoni, University College London (United Kingdom) (f.muntoni@ucl.ac.uk)
- **Participants:** UK (Coordinator), BE, FR, IT, US
- **Website:** http://www.cordis.eu/
- **Duration:** from November 2012 to October 2015
- **Total costs:** €7.5 million
- **EU contribution:** €5.5 million
- **Project Number:** 305370 (FP7-Health)

TIRCON

Treat Iron-Related Childhood-Onset Neurodegeneration

Neurodegeneration with brain iron accumulation (NBIA) is a group of rare, inherited neurodegenerative disorders. The most common form is pantothenate kinase-associated neurodegeneration (PKAN). NBIA disorders usually begin in childhood and cause severe disability, eventually leading to a premature death. The TIRCON project aims to set up a structured network to improve diagnosis and treatment of NBIA. It brings together the outstanding, but scattered expertise in NBIA research and care throughout Europe and worldwide.

The project will include a large-scale clinical trial of deferiprone in PKAN. Together with a European SME, it will carry out studies to define the potential of pantethine and its derivatives to treat PKAN. The project partners will develop a harmonised patient registry and a biomaterial bank to allow natural history studies and biomarker development, two critical needs in NBIA research.

- **Coordinator:** Thomas Klopstock, Ludwig-Maximilians University, Munich (Germany) (thomas.klopstock@med.uni-muenchen.de)
- **Participants:** DE (Coordinator), CA, IT, NL, PL, SI, UK, US
- **Website:** http://tircon.eu/
- **Duration:** from November 2011 to October 2015
- **Total costs:** €6.7 million
- **EU contribution:** €5.2 million
- **Project Number:** 277984 (FP7-Health)

Systems biology, molecular genetics, databases, clinical pharmacology, support and coordination

Academic GMP

The impact of Regulation (EC) No 1394/2007 on the development of Advanced Therapy Medicinal Products (ATMPs): an academic perspective

Academic GMP is a research project which investigates the impact of current EU legislation on the development of Advanced Therapy Medicinal Products (ATMPs) in academia.

ATMPs are complex medicinal products for human use, based on gene therapy, somatic cell therapy or tissue engineering, which pose particular challenges to the regulation of medicines. Academic GMP facilities are major contributors to the development of such ATMPs.

The Academic GMP project assesses the impact of the EU Regulation on these facilities in order to yield comprehensive evidence and concrete suggestions to policy makers. It does so by: conducting a Europe-wide survey; organising workshops and a major conference on the issue; establishing a web-based platform for information exchange; and analysing publications, guidance and innovation statistics in relation to ATMPs.

- **Coordinator:** Martin Hildebrandt, Technische Universität München (Germany) (Martin.Hildebrandt@mri.tum.de)
- **Participants:** DE (Coordinator), AT, SE, UK
- **Website:** http://www.academic-gmp.eu/
- **Duration:** from September 2010 to May 2013
- **Total costs:** €0.6 million
- **EU contribution:** €0.5 million
- **Project Number:** 260773 (FP7-Health)

ADVANCE_HTA

Advancing and strengthening the methodological tools and practices relating to the application and implementation of Health Technology Assessment (HTA)

The use of Health Technology Assessment (HTA) allows decisions about health coverage to be made based on evidence and also improves efficiency in resource allocation. The ADVANCE_HTA project seeks to contribute to advancements in HTA methods by addressing areas of intense methodological debate in the application, use and implementation of HTA.

ADVANCE_HTA takes steps to involve the wider stakeholder community in areas of healthcare that are being widely debated due to their implications for decision-making and resource allocation. Among the many issues that ADVANCE_HTA addresses are: value for money, the different approaches surrounding thresholds for resource allocation, the concept of value assessment, and the factors that need to be considered beyond cost effectiveness, such as disease severity. One of the objectives is to improve the quality of the evidence required for and the methods associated with the assessment of rare diseases.

- **Coordinator:** Panos Kanavos, London School of Economics and Political Science (United Kingdom) (p.g.kanavos@lse.ac.uk)
- **Participants:** UK (Coordinator), BE, DE, ES, FR, IT, PL, SE, SI, US
- **Website:** http://www.cordis.eu/
- **Duration:** from January 2013 to December 2015
- **Total costs:** €4.0 million
- **EU contribution:** €2.9 million
- **Project Number:** 305983 (FP7-Health)

EUCERD Joint Action

Working for rare diseases

The EU Committee of Experts on Rare Diseases (EUCERD) assists the European Commission in formulating and implementing the EU's activities in the field of research and development in rare diseases. By fostering exchanges of relevant experience, the Committee promotes policies and good practices between the 27 EU Member States, specialised bodies in the EU Member States and relevant European authorities in the fields of research and public health. The current Joint Action is set up to support this mandate. It will in particular address the following priorities:

- enhancing the visibility and recognition of rare diseases;
- contributing to the development and dissemination of knowledge on rare diseases;
- contributing to the improvement of access to quality healthcare services (diagnosis, care, social support, innovative therapies, etc.).

- **Coordinator:** Kate Bushby, University of Newcastle upon Tyne (United Kingdom) (kate.bushby@newcastle.ac.uk)
- **Participants:** UK (Coordinator), DE, ES, FI, FR, IT, PT
- **Website:** http://www.eucerd.eu/
- **Duration:** from March 2012 to August 2015
- **Total costs:** €5.5 million
- **EU contribution:** €3.0 million
- **Project Number:** 20112201 (EU Health Programme)

EPIRARE

Building Consensus and Synergies for the EU Registration of Rare Disease Patients

The general objective of the EPIRARE project is to build consensus and synergies between the rare disease (RD) community in order to address the regulatory, ethical and technical issues linked to the registration of rare disease (RD) patients.

To achieve this aim, EPIRARE has embarked on a feasibility study for an EU platform for registries and databases collecting data on RD patients, considering a number of policy scenarios which may develop in the near future.

Specifically, the project will define the needs of EU registries and databases on rare diseases and assess the status of existing registries. It will also seek to identify key issues to prepare a legal basis for registration, as well as agree on a common data set, the governance and the scope of the platform, which can ensure the long-term sustainability of the participating registries.

- **Coordinator:** Domenica Taruscio, Istituto Superiore di Sanità (Italy) (domenica.taruscio@iss.it)
- **Participants:** IT (Coordinator), AM, BE, CN, BG, DE, EL, ES, FR, GE, HR, HU, NL, PT, RO, RU, UA, UK, US
- **Website:** http://www.epirare.eu/
- **Duration:** from April 2011 to October 2013
- **Total costs:** €1.1 million
- **EU contribution:** €0.7 million
- **Project Number:** 20101202 (EU Health Programme)

E-Rare-2

ERA-Net on Rare Diseases

The E-Rare-2 project builds on the success of E-Rare-1 which linked research funding organisations leading to joint activities on rare disease projects. E-Rare-2 deepens and extends cooperation among the existing network and involves four new partners' countries.

The project seeks to address the fragmentation of resources and knowledge on rare diseases and to develop a coordinated European response with enhanced coordination and transnational funding of research on rare diseases. As such, E-Rare-2 continues the systematic exchange of information and the annual launching of joint calls, while also maintaining a thorough assessment of the funding mechanisms and the results of the funded research projects. Additionally, E-Rare-2 engages in strategic activities aimed at developing and extending the network, and defining a strategic agenda for E-Rare-2 activities and beyond.

The project gives special attention to outreach and knowledge exchange with new Member States and countries.

- **Coordinator:** Sophie Koutouzov, Institut national de la santé et de la recherche médicale (INSERM) (France) (sophie.koutouzov@inserm.fr)
- **Participants:** FR (Coordinator), AT, BE, DE, EL, ES, HU, IL, IT, NL, PT, TR
- **Website:** http://www.e-rare.eu/
- **Duration:** from October 2010 to September 2014
- **Total costs:** €2.9 million
- **EU contribution:** €2.0 million
- **Project Number:** 266608 (FP7-Health)

EUCBCC

EUropean Cross Border Care Collaborations

The EUCBCC project was established with the overall aim of aiding European citizens in making informed decisions about whether to seek healthcare in another Member State. Additionally, if they choose to do so, the project seeks to ensure that the administrative and clinical processes are straightforward and that continuity of care is guaranteed.

EUCBCC conducts pan-European surveys and focused studies in key areas in order to examine specific aspects of healthcare delivery in cases where procedural compatibility is necessary in order to deliver safe, high-quality care with adequate continuity. The project also looks at areas where there is already cross-border collaboration, namely collaborations between hospitals in border areas, telemedicine and dentistry, to identify practical issues that have arisen and how they have or have not been addressed. Both quantitative and qualitative methods are used by the project team.

- **Coordinator:** Elias Mossialos, London School of Economics and Political Science (United Kingdom) (e.a.mossialos@lse.ac.uk)
- **Participants:** UK (Coordinator), AT, BE, CH, DE, EE, ES, FI, HU, IT, NL, SI
- **Website:** http://cordis.europa.eu/
- **Duration:** from May 2010 to October 2013
- **Total costs:** €5.7 million
- **EU contribution:** €4.4 million
- **Project Number:** 242058 (FP7-Health)

EUROCAT

Platform for sharing best practices for management of rare diseases

The EUROCAT project surveys 1.7 million births in Europe every year in order to gather information on congenital anomalies (CA). Over 30 years in operation, it has developed a network of 42 registries in 23 countries for the epidemiologic surveillance of CA.

The information gathered by EUROCAT facilitates early warning of new teratogenic exposures and contributes to the evaluation of the effectiveness of primary prevention and the impact of developments in prenatal screening. With 30% of the European birth population covered by EUROCAT, the project provides vital information and resources for the general public, health professionals and managers regarding clusters, exposures or risk factors of concern.

It also provides a network and infrastructure for research related to the causes and prevention of CA, and the treatment and care of affected children.

- **Coordinator:** Helen Dolk, University of Ulster (United Kingdom) (h.dolk@ulster.ac.uk)
- **Participants:** UK (Coordinator), AT, BE, CH, CZ, DE, DK, ES, FI, FR, HR, HU, IE, IT, LV, MT, NL, NO, PL, PT, SE, SI, UA
- **Website:** http://www.eurocat-network.eu/
- **Duration:** from January 2011 to December 2013
- **Total costs:** €3.3 million
- **EU contribution:** €1.1 million
- **Project Number:** 20102204 (EU Health Programme)

EuroGentest2

Genetic testing in Europe — Network for the further development, harmonisation, validation and standardisation of services

The EuroGentest network was established with the aim of harmonising the process of genetic testing, from sampling to counselling, across Europe. Ultimately the goal is to ensure that all aspects of genetic testing are of high quality and provide accurate and reliable results for the benefit of the patients. The project seeks to counter technical errors and poor reporting within genetic services in Europe by structuring, harmonising and improving the overall quality of these services.

The EuroGentest2 project, meanwhile, is concerned with setting the targets for laboratory and health professional accreditation, by contributing to guidelines and standards, and actively interacting with the professional organisations and the policy makers. EuroGentest2 also provides the research community with tools for quality management and coordinates training activities.

- **Coordinator:** Gert Matthijs, Katholieke Universiteit Leuven (Belgium) (gert.matthijs@uzleuven.be)
- **Participants:** BE (Coordinator), CH, CZ, DE, ES, FI, FR, IE, NL, SE, UK
- **Website:** http://www.eurogentest.org/
- **Duration:** from January 2011 to December 2013
- **Total costs:** €2.2 million
- **EU contribution:** €2.0 million
- **Project Number:** 261469 (FP7-Health)

EUROmediCAT

EUROmediCAT: Safety of Medication use in Pregnancy in Relation to Risk of Congenital Malformations

EUROmediCAT is a research project aimed at building a European system for evaluating the safety of medication use during pregnancy, specifically in relation to the risk of congenital anomalies. As such, the project aims to develop a European reproductive pharmaco-vigilance system.

The system is being developed based on an existing network of congenital anomaly registers in Europe, such as EUROCAT, as well as existing healthcare databases.

Specifically, the project seeks to quantify the risk of congenital anomalies related to four drug classes: new antiepileptics, insulin analogues, antiasthmatics, and antidepressants, in particular the selective serotonin re-uptake inhibitors. Additionally, it aims to develop a framework for evaluating the effectiveness of pregnancy-related drug safety measures.

- **Coordinator:** Helen Dolk, University of Ulster (United Kingdom) (h.dolk@ulster.ac.uk)
- **Participants:** UK (Coordinator), DK, IT, NL, PL
- **Website:** http://euromedicat.eu/
- **Duration:** from March 2011 to February 2015
- **Total costs:** €4.0 million
- **EU contribution:** €3.0 million
- **Project Number:** 260598 (FP7-Health)

EUROPLAN

European Project for Rare Diseases National Plans Development

The European Project for Rare Diseases National Plans Development (EUROPLAN) seeks to improve prevention, diagnosis, treatment and care for patients with rare diseases. Through the dissemination of data and recommendations, EUROPLAN contributes to the implementation of national plans and strategies to tackle rare diseases throughout the EU.

Between 2008 and 2011 EUROPLAN involved 57 associated and collaborating partners from 34 countries, including healthcare professionals, researchers, health authorities, patients' groups and EURORDIS, the European organisation for patients with rare diseases. The project managed to provide National Health Authorities with valuable tools and support to develop and monitor national plans and strategies for rare diseases. In addition, a common set of indicators will contribute to the comparability of data among the 27 EU Member States.

- **Coordinator:** Domenica Taruscio, Istituto Superiore di Sanità, Rome (Italy) (domenica.taruscio@iss.it)
- **Participants:** IT (Coordinator), BG, EE, ES, FR, NL, SE, UK
- **Website:** http://www.europlanproject.eu/
- **Duration:** from April 2008 to March 2011
- **Total costs:** €1.1 million
- **EU contribution:** €0.6 million
- **Project Number:** 2007119 (EU Health Programme)

GRiP

Global Research in Paediatrics

The Global Research in Paediatrics (GRiP) project, involving 21 institutions and at least another 16 major networks, aims to improve the health of children globally by facilitating the development and safe use of paediatric medicine.

GRiP is implementing a comprehensive educational programme in paediatric pharmacology and aims to build an infrastructure which allows for the integrated use of existing research capacity, thus reducing the fragmentation and duplication of activities.

Specifically, the project primarily focuses on: the development of a Paediatric Clinical Pharmacology Training Programme; the validation and harmonisation of research tools specifically for paediatrics; the sharing of strategies and plans; the utilisation of ongoing/planned research studies (including pharmacoepidemiology) to evaluate the feasibility of proposed research tools and strategies; and paediatric formulation and neonatal issues.

- **Coordinator:** Carlo Giaquinto, Azienda Ospedaliera di Padova (Italy) (giaquinto@pediatria.unipd.it)
- **Participants:** IT (Coordinator), CA, CH, ES, FI, FR, JP, NL, PL, UK, US
- **Website:** http://www.grip-network.org/
- **Duration:** from January 2011 to December 2015
- **Total costs:** €12.6 million
- **EU contribution:** €10.0 million
- **Project Number:** 261060 (FP7-Health)

JA-Orphanet Europe

Development of the European portal of rare diseases and orphan drugs

JA-Orphanet Europe seeks to improve the diagnosis, care and treatment of patients with rare diseases by offering a freely accessible reference portal for information on rare diseases and orphan drugs. By improving the update of data, the encyclopaedia and the directory of services, this project has further developed the Orphanet portal of rare diseases and orphan drugs.

The project has also improved the governance of Orphanet to ensure its mission at the international level. In addition, the website has been adapted to offer national front pages in national language(s) and the possibility to disseminate information on national policy documents and events. This ensures that each Member State will benefit from the core infrastructure already developed and will have the opportunity to offer its citizens a national portal at a marginal cost.

- **Coordinator:** Ségolène Aymé, Institut national de la santé et de la recherche médicale, (INSERM) Paris (France) (segolene.ayme@inserm.fr)
- **Participants:** FR (Coordinator), AU, BG, CA, DE, DK, ES, FI, IT, KR, NO, PT, RO, SE, TW, UK, US
- **Website:** http://www.orpha.net/
- **Duration:** from April 2011 to March 2012
- **Total costs:** €7.2 million
- **EU contribution:** €0.7 million
- **Project Number:** 20102206 (EU Health Programme)

OptiStem

Optimisation of stem cell therapy for clinical trials of degenerative skin and muscle diseases

OptiStem is a research project that brings together stem cell biologists and clinical experts from 18 partner institutions in six European countries to investigate stem cells in skeletal muscle and epithelia. It aims to develop and implement clinical trials that use stem cells from adult tissues, such as muscle, skin or the surface of the eye, to treat degenerative diseases.

OptiStem combines research on stem cells with pre-clinical work and clinical trials. Specifically, the project identifies and manipulates the genes that regulate self-renewal, migratory ability, survival and in vivo differentiation of cells that could potentially be used to treat disease. The team also evaluates how modifications in cultivation procedures affect stem cell behaviour so that safe, reproducible regenerative therapies can be developed in the future.

- **Coordinator:** Giulio Cossu, Universita delgi Studi di Milano (Italy) (giulio.cossu@unimi.it)
- **Participants:** IT (Coordinator), CH, DE, ES, FR, UK
- **Website:** http://www.optistem.org/
- **Duration:** from January 2009 to December 2013
- **Total costs:** €16.7 million
- **EU contribution:** €11.9 million
- **Project Number:** 223098 (FP7-Health)

PatientPartner

Identifying the Needs for Patients Partnering in Clinical Research

The PatientPartner project aimed to promote the role of patient organisations in the context of clinical trials, based on the belief that involving patient organisations as equal partners contributes to research that is better adjusted to the real needs of patients. The study focused particularly on clinical trials with children, the use of biobanks and ethical issues.

PatientPartner also sought to establish a communication platform and guidelines to enable mutually beneficial interactions between patients and clinical trial professionals.

The results of interviews with patients and patient organisations were combined with literature reviews and descriptions of best practices. Additionally, the project arranged workshops which brought together patients, patient organisations and other stakeholders in the clinical trial context.

- **Coordinator:** Cor Oosterwijk, Vereniging Samenwerkende Ouder- en Patiëntenorganisaties betrokken bij erfelijkheidsvraagstukken (The Netherlands) (C.Oosterwijk@vsop.nl)
- **Participants:** NL (Coordinator), BE, UK
- **Website:** http://www.patientpartner-europe.eu/
- **Duration:** from May 2008 to April 2011
- **Total costs:** €1.0 million
- **EU contribution:** €0.9 million
- **Project Number:** 201720 (FP7-Health)

RARE-Bestpractices

Platform for sharing best practices for management of rare diseases

As their name suggests, rare diseases (RD) are characterised by their low prevalence, meaning that their treatment is often hampered by limited knowledge. The RARE-Bestpractices project aims to address this problem by developing a sustainable networking platform which supports the collection of standardised and validated data and the efficient exchange of knowledge and reliable information on RD.

The platform promotes communication on the clinical management of rare diseases by disseminating trustworthy best practices guidelines globally, narrowing the existing gap among EU Member States and other countries. It exploits and integrates contributions from experts, patient representatives, policy makers, institutions, agencies, etc. in all EU Member States, and across the world, and identifies additional research needs to further improve clinical practice.

- **Coordinator:** Domenica Taruscio, Istituto Superiore di Sanità (Italy) (domenica.taruscio@iss.it)
- **Participants:** IT (Coordinator), BE, BG, DE, ES, FR, IT, NL, SE, UK
- **Website:** http://www.rarebestpractices.eu/
- **Duration:** from January 2013 to December 2016
- **Total costs:** €2.3 million
- **EU contribution:** €2.0 million
- **Project Number:** 305690 (FP7-Health)

RareDiseasePlatform

A European Platform of Integrated Information Services for Researchers in the Field of Rare Diseases and Orphan Drugs Supporting Team and Project Building

The RareDiseasePlatform (RDPlatform) project was established to create a set of tools to facilitate collaborations between academic teams, SMEs and even major companies, in the field of rare diseases (RD).

The project ultimately aimed to speed up RD research and development to provide diagnostic tools and therapies as quickly as possible. Specifically, the project team identified expert groups, research projects, technological platforms, databases and biobanks relevant to RD research, as well as opportunities for partnership between them. It then shared this information on the existing websites, presenting it in an accessible, 'searchable' and user-friendly manner. Information on partnership requests was made available via a newsletter, and potential collaborations were nurtured during two workshops for experts.

- **Coordinator:** Ségolène Aymé, Institut national de la santé et de la recherche médicale (INSERM) (France) (ayme@orpha.net)
- **Participants:** FR (Coordinator), AT, BE, CZ, DE, EE, ES, FI, IT, NL, PL, SE, UK
- **Website:** http://www.rdplatform.org/
- **Duration:** from May 2008 to April 2011
- **Total costs:** €1.0 million
- **EU contribution:** €0.9 million
- **Project Number:** 201230 (FP7-Health)

RD-Connect

RD-CONNECT: An integrated platform connecting registries, biobanks and clinical bioinformatics for rare disease research

Rare disease (RD) research remains quite fragmented by data type and by disease with far too little systematic connection of vital information. The RD-Connect project was thus established with the aim of developing robust mechanisms and standards for linking detailed clinical information with genetic information, biomaterial availability and research/trial datasets; in particular those generated by the omics research projects EURenOmics and Neuromics.

As such, the project is developing a critical mass for harmonisation and provides an impetus for a global 'trial-ready' infrastructure which will ultimately improve diagnostics and therapies for rare diseases. RD-Connect builds on and transforms the current state-of-the-art across databases, registries, biobanks, bioinformatics and ethical considerations to develop a comprehensive, user-friendly integrated platform through which researchers worldwide can share data.

- **Coordinator:** Hanns Lochmüller, University of Newcastle upon Tyne (United Kingdom) (hanns.lochmuller@ncl.ac.uk)
- **Participants:** UK (Coordinator), AT, AU, CH, CZ, DE, EL, ES, FR, IT, MT, NL, PT, SE, US
- **Website:** http://www.rd-connect.eu/
- **Duration:** from November 2012 to October 2018
- **Total costs:** €17.5 million
- **EU contribution:** €12.0 million
- **Project Number:** 305444 (FP7-Health)

SUPPORT-IRDiRC

Support for international rare disease research to serve the IRDiRC objectives

Rare diseases (RD) are, by their very nature, so rare that research faces some specific constraints. Naturally, a global coordination of research efforts would avoid duplication, fragmentation, redundancy and gaps. With this in mind, the International Rare Diseases Research Consortium (IRDiRC) was launched to coordinate and foster international collaborative research on RD, ambitiously aiming to develop 200 new therapies and produce diagnostic tools for a majority of RD by 2020.

In order to provide organisational and communication support to IRDiRC, the SUPPORT-IRDiRC project was conceived. Working in collaboration with the European Commission, research funding agencies in all participating countries, as well as with specific research projects, SUPPORT-IRDiRC contributes to the development of policies and guidelines aimed at accelerating research on RD and reinforcing international research cooperation.

- **Coordinator:** Segolene Aymé, Institut national de la santé et de la recherche médicale (INSERM) (France) (segolene.ayme@inserm.fr)
- **Participants:** FR (Coordinator)
- **Website:** http://www.irdirc.org/
- **Duration:** from October 2012 to September 2018
- **Total costs:** €2.2 million
- **EU contribution:** €2.0 million
- **Project Number:** 305207 (FP7-Health)

SYSCILIA

A systems biology approach to dissect cilia function and its disruption in human genetic disease

SYSCILIA is a large-scale project which brings together 18 partners from 7 different countries with the aim of identifying the molecular mechanisms characterising cilium function. It also applies a systems biology approach to identify the discrete perturbations associated with dysfunction caused by mutations in inherited ciliopathies.

The overall objectives of the project are to establish a paradigm for studying and modelling complex eukaryotic systems, to understand how system perturbation contributes to the modulation of clinical phenotypes, and to provide a better understanding of ciliary processes in biology and their associated diseases.

Concretely, the work of the project involves iterative cycles of quantitative data generation, model building, experimental testing and model refinement.

- **Coordinator:** Ronald Roepman, Radboud Universiteit Nijmegen — Stichting Katholieke Universiteit (Netherlands) (R.Roepman@antrg.umcn.nl)
- **Participants:** NL (Coordinator), DE, FR, IE, IT, UK, US
- **Website:** http://syscilia.org/
- **Duration:** from June 2010 to May 2015
- **Total costs:** €14.9 million
- **EU contribution:** €11.0 million
- **Project Number:** 241955 (FP7-Health)

TECHGENE

High throughput molecular diagnostics in individual patients for genetic diseases with heterogeneous clinical presentation

The TECHGENE project, which involved collaboration between 12 partners from 9 different countries, focused on the use of massively parallel sequencing techniques for the development, optimisation and implementation of diagnostic tools for genetic disorders.

It aimed to extend genetic diagnostics from relatively simple monogenic disorders to more complex genetically heterogeneous disorders. To do this, a number of model disorders with increasing genetic complexity and representing the majority of non-multifactorial genetic disorders were selected to act as prototypes. New massively parallel sequencing diagnostics were developed for each of them and a proof-of-principle was delivered. The project moves European laboratories and SMEs into a front-running position in the field.

- **Coordinator:** Hans Scheffer, Stichting Katholieke Universiteit — Radboud University Nijmegen Medical Centre (The Netherlands) (h.scheffer@gen.umcn.nl)
- **Participants:** NL (Coordinator), BE, CZ, DE, EE, ES, FR, IT, UK
- **Website:** http://www.techgene.eu/
- **Duration:** from February 2009 to January 2012
- **Total costs:** €3.8 million
- **EU contribution:** €3.0 million
- **Project Number:** 223143 (FP7-Health)

TissueGEN

The production of a 3D Human Tissue Disease Platform to enable regenerative medicine therapy development

The TissueGEN project focuses on the production of an in vitro human disease tissue platform technology to enable and accelerate the development of regenerative medicine therapies for a diverse range of diseases.

The project integrates differentiated Pluripotent Stem (iPS) cell cultures onto 3D tissue bioreactors to produce 3D human tissue disease cultures. The bioreactors are constructed using a range of innovative techniques to produce systems compatible with the analysis systems that are commonly used in laboratories worldwide.

The work of TissueGEN will allow regenerative therapies to be developed and tested on batteries of human tissues in the laboratory in a rapid, cost-effective manner, producing a key platform resource and marking a significant step forward for the regenerative medicine industry.

- **Coordinator:** Marcus Yeo, Zyoxel Limited (United Kingdom) (marcus@zyoxel.com)
- **Participants:** UK (Coordinator), DE, NL, SE
- **Website:** http://www.tissuegen.org/
- **Duration:** from January 2012 to December 2015
- **Total costs:** €4.3 million
- **EU contribution:** €3.0 million
- **Project Number:** 278955 (FP7-Health)

Alphabetical index

EUROPEAN COMMISSION

Rare diseases - How Europe is meeting the challenges

Luxembourg: Publications Office of the European Union

2013 — 96 pp. — 17,6 x 25 cm

ISBN 978-92-79-28317-8
doi:10.2777/56070

HOW TO OBTAIN EU PUBLICATIONS

Free publications:

- via EU Bookshop (http://bookshop.europa.eu);
- at the European Union's representations or delegations. You can obtain their contact details on the Internet (http://ec.europa.eu) or by sending a fax to +352 2929-42758.

Priced publications:

- via EU Bookshop (http://bookshop.europa.eu).

Priced subscriptions (e.g. annual series of the *Official Journal of the European Union* and reports of cases before the Court of Justice of the European Union):

- via one of the sales agents of the Publications Office of the European Union (http://publications.europa.eu/others/agents/index_en.htm).

KI-32-13-051-EN-C

Despite their name, rare diseases affect over 30 million Europeans. Patients suffering from one of the estimated six to eight thousand rare diseases are few and far between, so pooling knowledge and scarce resources is the best way to work out how to diagnose, treat or cure them.

The European Union has funded cross-border research and other activities related to rare diseases for well over a decade; over 110 current projects are presented in this booklet. The newly launched International Rare Diseases Research Consortium (IRDiRC) will take collaboration to a whole new level.

IRDiRC is the biggest collective rare diseases research effort the world has ever seen. Its key objective is to deliver 200 new therapies for rare diseases and the means to diagnose most of them, by 2020.

Research and Innovation policy

Publications Office

ISBN 978-92-79-28317-8

doi:10.2777/56070