IRDiRC Achievements and Road Map

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Achievements so far

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Launched in April, 2011, with ambitious goals by 2020

BIOMEDICAL RESEARCH

Rare-disease project has global ambitions

Consortium aims for hundreds of new therapies by 2020.

BY ALISON ABBOTT

Prader–Willi syndrome. Fabry renal disease. Spinocerebellar ataxia. Few people have heard of these and the other 'rare diseases', some of which affect only hundreds of patients worldwide. Drug companies searching for the next blockbuster pay them little attention. But the diseases are usually incurable — and there are thousands of them.

This week, the US National Institutes of Health (NIH) and the European Commission launch a joint assault on these conditions, whose small numbers of patients make it difficult to test new treatments and develop diagnostic methods. The International Rare Disease Research Consortium being formed under the auspices of the two bodies has the ambitious goal of developing a diagnostic tool for every known rare disease by 2020, along with new therapies to treat 200 of them. "The number of individuals with a particular rare disease is so small that we need to be able to pool information from patients in as many countries as possible," says Ruxandra Draghia-Akli, the commission's director of health research.

At the launch meeting in Bethesda, Maryland, on 6–8 April, prospective partners will map out research strategies to identify diagnostic biomarkers, design clinical trials and coordinate genome sequencing in these diseases. Nearly all the rare diseases, of which there are an estimated 6,000–8,000, are the result of small genetic changes.

The meeting will also discuss the governance of the project, which is most likely to be modelled on the pioneering Human Genome Project. As such, the consortium is open to research agencies and organizations from all over the world. Representatives from countries including Canada, Japan and some individual European nations are all attending the meeting, and may join the consortium. Those wishing to participate will have to pledge a minimum financial contribution, which has not yet been agreed, and share all relevant data. Indeed, the project will have to overcome numerous obstacles to information sharing, such as the fact that physicians in different countries often use entirely different words to describe the same disease.

Draghia-Akli points out that the project could yield major benefits for the emerging field of personalized medicine — another political priority for the NIH and the commission — which also faces the challenge of small populations of patients.

"We need to be able to pool information from patients in as many countries as possible."

Regulatory agencies such as the US Food and Drug Administration and the European Medicines Agency rely on large, randomized and controlled clinical trials when deciding whether to approve new medicines, and one of the aims of the consortium will be to develop alternative clinical-trial methods for diseases that affect few people.

These methods are becoming ever more important now that genome analysis is helping to break down common diseases into ever smaller subclasses. "Soon there will be no disease called breast cancer," says Draghia-Akli. Instead, the catch-all term will be replaced by "a large number of rare diseases, each of which causes malignant growth in breast tissue and requires individual treatment", she says.

The commission will launch a €100-million (US$140-million) call for research proposals in July, which will support the consortium's scientific goals by focusing heavily on developing appropriate clinical trials. ■

- 200 new therapies for rare diseases

- Means to diagnose most rare diseases

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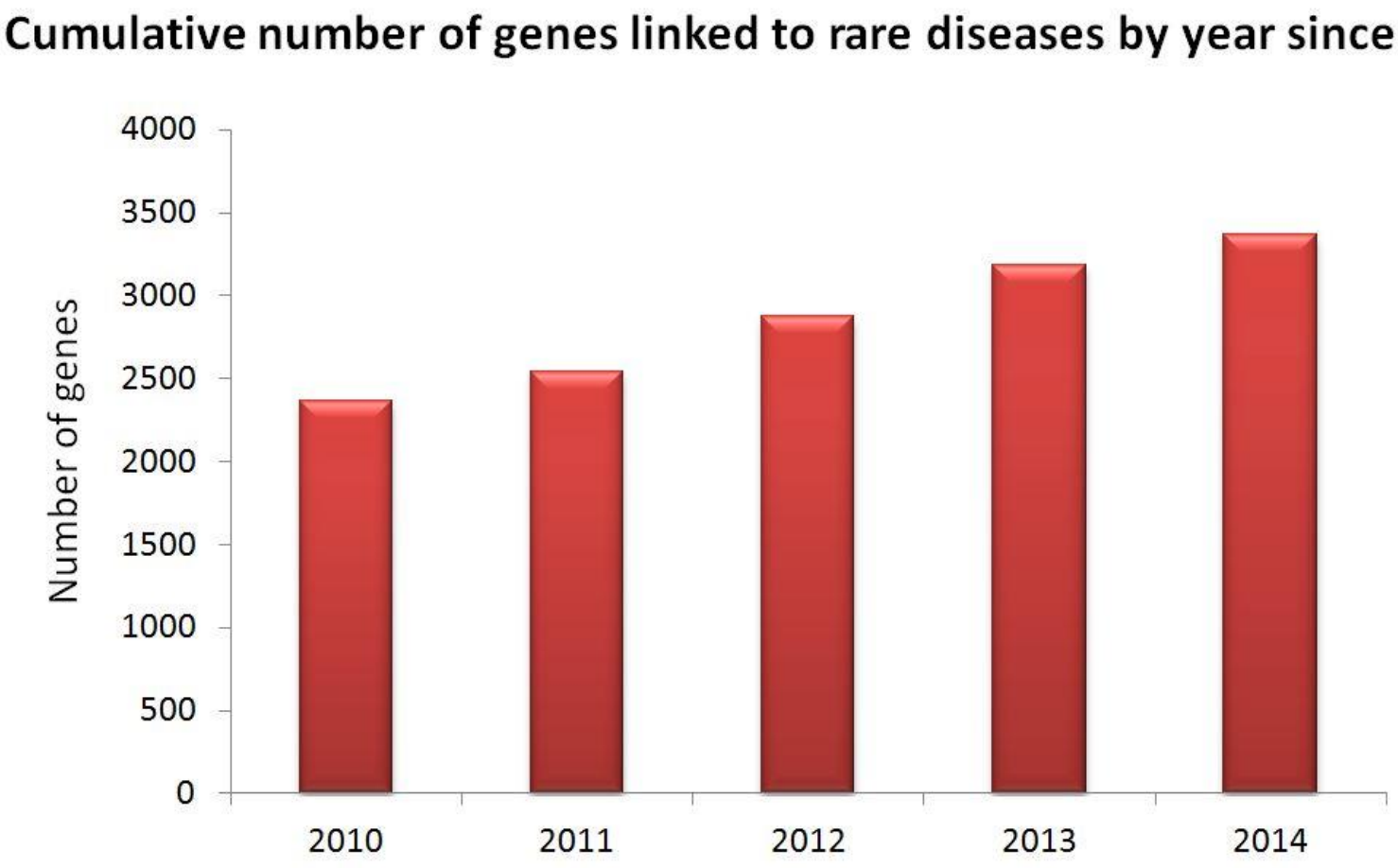
Number of identified Genes causing Rare Diseases



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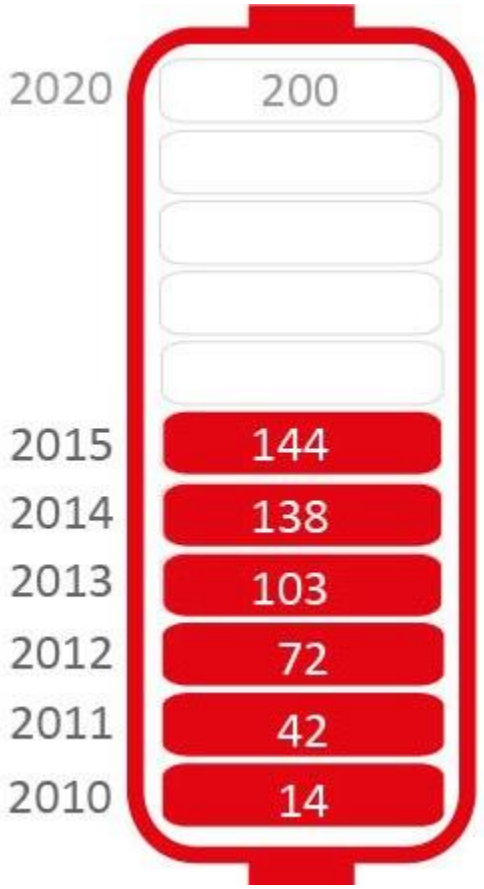
New Orphan Drugs marketed since 2010 in the USA or Europe

- **Monthly updated data are captured into a cumulative and cross-linked table**

Total number of Indications	Year	US	Europe	Total	Cumulative
	2010	12	2	14	14
	2011	24	4	28	42
	2012	25	5	30	72
	2013	28	2	30	102
	2014	30	6	36	138
	2015	4	2	6	144

- **The total is reported into the IRDiRC counter**



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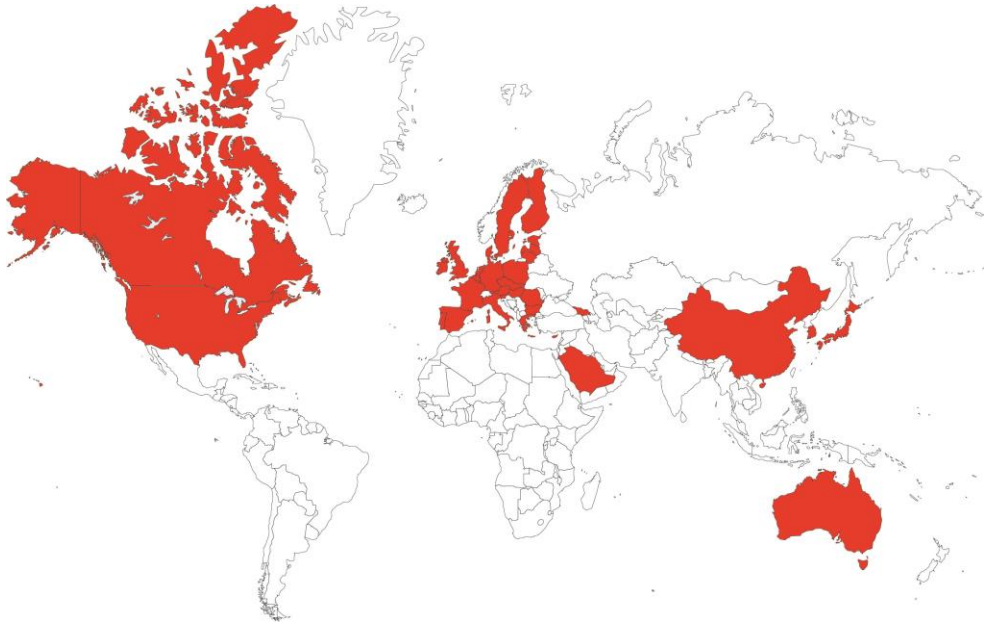
Expansion of the Consortium

Formally launched in 2012

Funding organizations from:

- Asia & Middle East
- Australia
- Europe
- North America



Present commitment exceeds

$1B worldwide

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Adoption of Principles applying to Research activities

- Sharing and collaborative work in RD research
- Scientific standards, requirements and regulations in RD research
- Participation by patients and / or their representatives in research

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2014 Action Plan: Adopt and Promote Standards for Interoperability / Data sharing

- **Launch of ICHPT: International consortium of Human Phenotype Terminologies**
  - Set of 2,300 terms which should be included in any terminology used to describe phenotypic features
  - Recommendation to use HPO and ORDO
  - (Human Phenome Ontology and Orphanet Rare Disease Ontology)

- **Launch of IRDiRC recommended**
  - to promote platforms, tools, guidelines
  - Contributing to IRDiRC goals

2015 Action Plan to boost Therapy Development

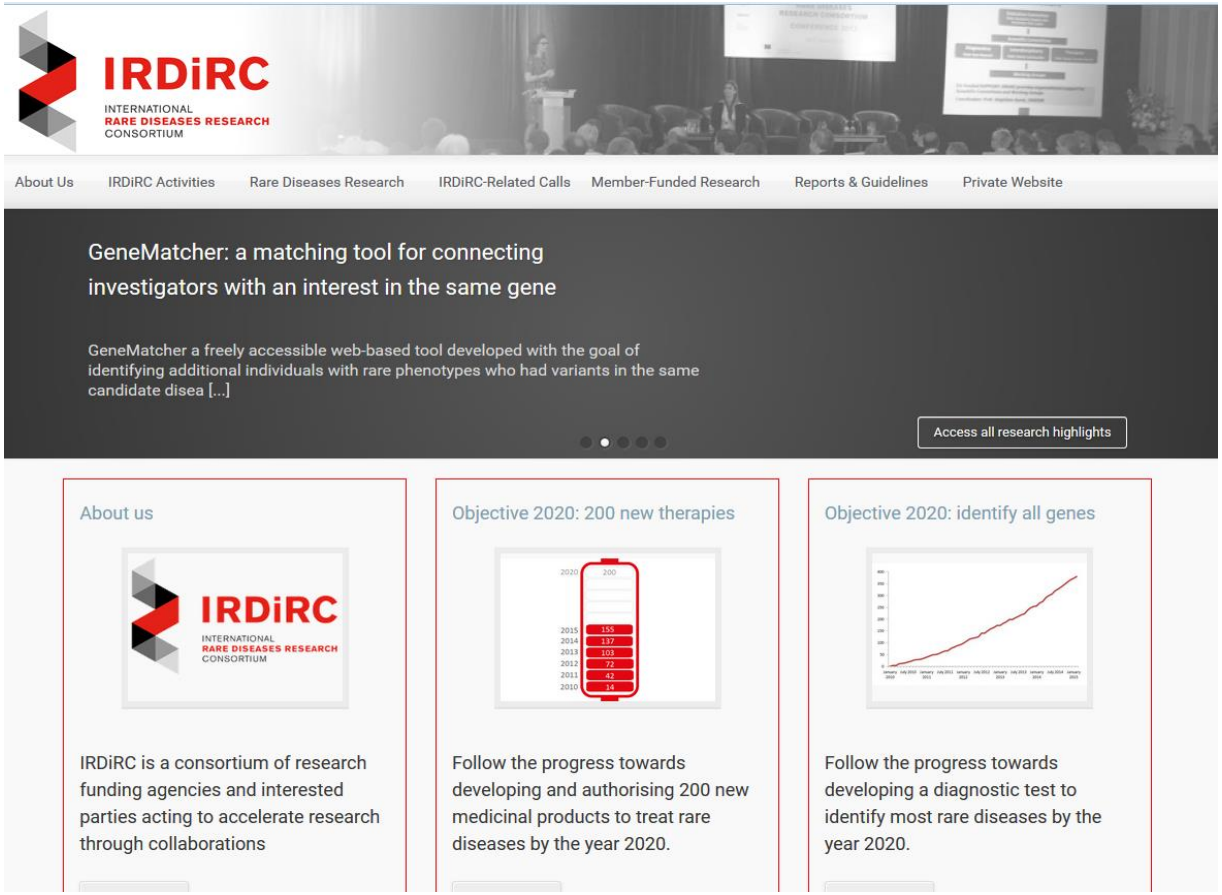
- **Patient-Centered Outcome Measures (PCOM)**
  - To improve quality of trials and allow assessment of the medical added-value of new therapies
    - Report on initiatives worldwide already available and items for action
    - Workshop in Paris on 30 November 2015
    - Review the documents / post recommendations

- **Small population clinical trials (SPCT)**
  - To agree with Regulators on acceptable alternative methods
    - Report on state of play of science and regulatory recommendations
    - Workshop in London at EMA, first trimester 2016

Selected Key Topics for 2015/2016

- **Matchmaker Exchange (MME)**
  - Facilitate matching of unsolved genome/exome sequence cases, based on similar phenotypics/genotypic profiles
    - Workshop in Baltimore on 6 October 2015
- **Machine readable consent (MRC)**
  - To access electronically patient consent to share data and improve research participation
    - Workshop in Paris on 9-10 November 2015
- **Data mining and repurposing (DMR)**
  - to identify new therapeutic targets and to repurpose drugs
    - Members identified / express your interest
    - Process not yet launched/ Workshop planned for T2 or T3 2016

All documents are accessible at www.irdirc.org



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Thank you for your attention

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