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IRDiRC: looking toward the next ten years in rare diseases research

INFRAFRONTIER-IMPC Stakeholder Meeting
Athens, 14 November 2017

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Genetics, Canadian Institutes of
Health Research
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Research Consortium (IRDiRC)

Initial goals: universal diagnostics and 200 new therapies

Published online 4 April 2011 | *Nature* 472, 17 (2011) |
doi:10.1038/472017a

News

Rare-disease project has global ambitions

Consortium aims for hundreds of new therapies by 2020.

[Allison 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.



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IRDiRC – basic principles

- ▶ Co-operation at international level to stimulate, better coordinate & maximise output of rare disease research efforts around the world



- ▶ Teams up public and private organisations investing in rare diseases research
- ▶ Research funders can join & work together
- ▶ Each organisation funds research its own way
- ▶ Funded projects adhere to a common framework



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Australia

- Western Australian Department of Health



Canada

- Canadian Institutes for Health Research
- Genome Canada



China

- Beijing Genomics Institute
- Chinese Rare Disease Research Consortium
- WuXi Apptec



EU

- European Commission



Finland

- Academy of Finland



France

- French Association against Myopathies
- Agence National de la Recherche



Georgia

- Children's New Hospital Management Group



Germany

- Federal Ministry of Education and Research



Italy

- Italian Higher Institute of Health
- Telethon Foundation
- Chiesi Farmaceutica



International Consortium

- E-RARE 3 Consortium



Japan

- Japan Agency for Medical Research and Development
- National Institutes of Biomedical Innovation, Health, and Nutrition



Republic of Korea

- Korean National Institute of Health



Netherlands

- The Netherlands Organization for Health Research and Development



Kingdom of Saudi Arabia

- Saudi Human Genome Project



Spain

- National Institute of Health Carlos III



UK

- National Institute for Health Research



USA

- Food and Drug Administration Orphan Products Grants Program

- Isis Pharmaceuticals

- National Human Genome Research Institute (NIH)

- National Center for Advancing Translational Sciences (NIH)

- National Cancer Institute (NIH)

- National Eye Institute (NIH)

- National Institute of Neurological Disorders and Stroke (NIH)

- National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIH)

- National Institute of Child Health and Human Development (NIH)

- NKT Therapeutics

- Office of Rare Diseases (NIH)

- PTC Therapeutics

- Sanford Research Institute

- International Pharma Companies

- Genzyme (Sanofi)

- Novartis

- Pfizer

- Shire

Today over 40 members from 17 countries

Progress toward IRDiRC's goals for rare disease research

(source: www.irdirc.org)

- Diagnostics (goal: most rare diseases by 2020)
 - Nearly 4,100 rare diseases for which there is a genetic test available, as compared with 2,200 in 2010.
- Therapies (goal: 200 new therapies by 2020)
 - Achieved! 222 as of end 2016.



IRDiRC's own role in achieving the 200 therapies goal is difficult to measure

- Some therapies were developed by IRDiRC's industry members.
- Some likely resulted from publicly-funded drug discovery studies.
- However, the therapeutic development pipeline is lengthy and many new therapies result from initiatives that predate IRDiRC.
- Many developers of therapies are not members of IRDiRC yet all new FDA and/or EMA approvals are counted.
- No therapies other than FDA/EMA-approved drugs or devices were counted.

Diagnostic projects funded by IRDiRC members

- Have been the major factor in the discovery of ~1,900 new rare disease genes.
- Have led to the optimization of next-generation sequence pipelines in a clinical setting.
- Have increased the diagnosis rate for patients with unknown disorders from ~10% to 30-50%.
- Have established diagnostic pipelines that can be, and have been in some jurisdictions, translated out of research programs and into normal clinical practice.

RD diagnosis today—still work to do

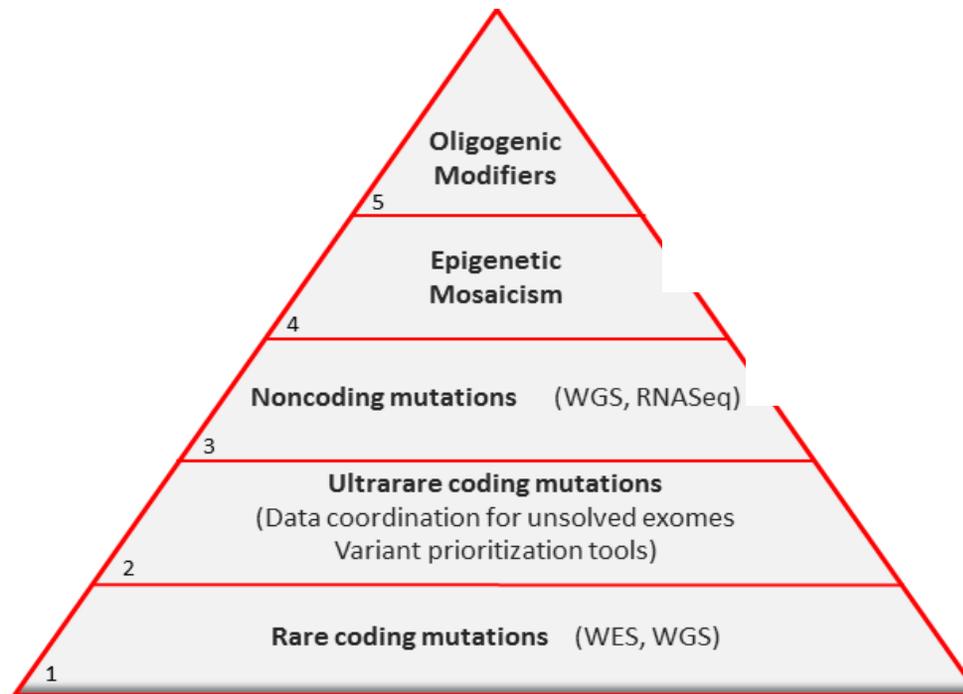
- Genomics technology exists to diagnose many rare diseases that affect most rare disease patients.
- This technology is being transferred from research programs to healthcare but implementation in healthcare is spotty—serious inequities among and within jurisdictions remain to be addressed.
- Many genetic diseases still elude diagnosis by genomics—substantial discovery research is still needed to improve diagnostic yield.



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Complexity of disease mechanism



*Identification and interpretation of non-coding mutations
and other more complex disease mechanisms*

from K. Boycott

IRDiRC Goals, by 2027

- ▶ All patients coming to medical attention with a suspected rare disease will be diagnosed within one year if their disorder is known in the medical literature; all currently undiagnosable individuals will enter a globally coordinated diagnostic and research pipeline

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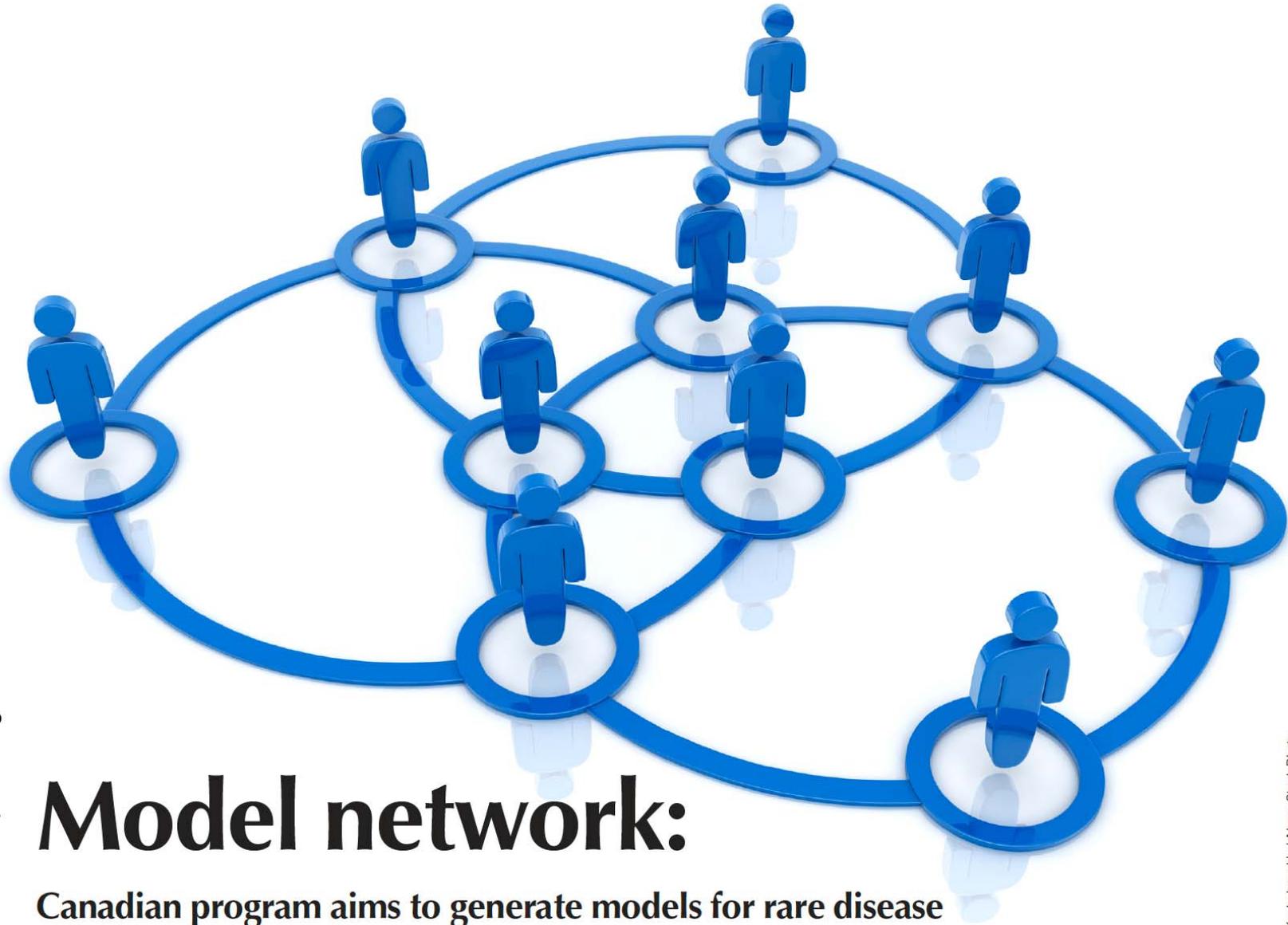
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- ▶ 1000 new therapies for rare diseases will be approved, the majority of which will focus on diseases without approved options

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- ▶ Methodologies will be developed to assess the impact of diagnoses and therapies on rare diseases patients

How can IMPC align?

- ▶ Prioritizing RD-relevant mouse models, animal models are specifically mentioned in *European Joint Program in Rare Diseases*.
- ▶ Proactive seeding of collaborations with clinical researchers, building on the example of the Rare Diseases Models and Mechanisms initiative.
- ▶ Possibly interacting with IRDiRC to develop a priority list of rare diseases to be de-risked through public efforts to enable therapeutic development.



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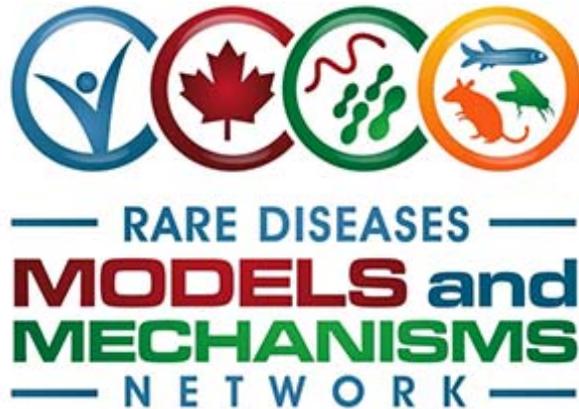
Model network:

Canadian program aims to generate models for rare disease

By Katherine Ellen Foley

Nature Medicine 2015 21: 1242-3

Vladislav Kochelaevskiy / Alamy Stock Photo



Progress Nov 2014 through Apr 2017



QUICK STATISTICS

- ✓ Genes Added: 5906
- ✓ Number of researchers registered: 441
- ✓ Number of researchers registered with genes: 281
- ✓ Number of genes added unique: 5098
- ✓ Number of Catalyst Grants Awarded: 47

FUNDERS



Fondation du Grand Défi Pierre Lavoie (FGDPL)



dravet.ca



Undiagnosed Diseases Program



Discoveries for life





Progress Nov 2014 through
Apr 2017



Some diseases thus far addressed: epileptic encephalopathy, hyposialylation disease, bone dysplasia, ciliopathy, novel dysmorphology, sudden cardiac death, vitreoretinopathy, hydranencephaly, seizure syndrome, novel disease related to Angelman's syndrome, novel blood disorder

3 papers thus far published (*Human Mutation*, *Nature Genetics*, *J. Electrocardiol.*), 2 others submitted, 11 conference presentations.

2444 visits to RDMM website in 2016.



Moving toward RDMM phase 2

International partnerships

- Continue existing partnership with US Undiagnosed Disease Network (NIH, Baylor)
- Develop a Canadian-European-Australian RDMM network
 - EC H2020 application submitted (Riess, Brunner, Lochmüller) on solving unsolved rare diseases. This would fund something similar to RDMM in Europe.
 - Plan would be to enable Canada-Europe matches, as well as Canada-Canada and Europe-Europe. For Canada-Europe teams the location of the model organism lab would determine who funds it.
 - Australian Genomics Health Alliance pursuing similar activities, would partner in a similar manner.



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Thank you for your attention.