IRDiRC OCTOBER-NOVEMBER 2017 UPDATE

The 6th IRDiRC Consortium Assembly meeting

Dr Makoto Suematsu and the Japan Agency for Medical Research and Development (AMED) hosted an IRDiRC Consortium Assembly face-to-face meeting on November 10-11, 2017 in Tokyo, Japan. Over two days, IRDiRC members exchanged on the progresses made by their organizations since the last IRDiRC Conference in Paris, France (February 2017) that contribute towards the Consortium's Mission, and identified key actions for the Scientific and Constituent Committees to collaboratively and collectively move towards the new IRDiRC Goals for 2017-2027.

Additionally, AMED also organized a colloquium to showcase the strengths and to discuss the challenges faced in rare diseases research in Japan. The session opened with an introduction by the Parliamentary Vice Minister of the Ministry of Health, Labor and Welfare (MLHW), Ms Mizuho Onuma, who reiterated the importance of rare diseases research and its impact in improving patients' quality of life. A series of presentations by different representatives followed the welcome address: IRDiRC and AMED on their contributions towards rare diseases research and funded activities; MHLW on the initiatives of the Japanese government for intractable and rare diseases; the Pharmaceuticals and Medical Devices Agency (PMDA) on the efforts in rare disease therapeutic development in Japan; and researchers from the Universities of Keio and Nagoya respectively on Japan's Initiative on Rare and Undiagnosed Diseases (IRUD) and innovative medical device development.

This meeting was an opportunity to welcome IRDiRC new members. In particular, umbrella patient advocacy membership recently expanded with, now, representatives from the USA, Canada, Europe, South Africa, Japan, China, India and Australia. IRDiRC has long recognized the importance of patient voice in its program and activities, and welcomed their valuable input to advance patient-centered rare diseases research. Thanks to in-person as well as teleconference attendance and committed participation of members of the Consortium Assembly, this meeting presented new actions for the Consortium towards its new goals.

photo credit: Japanese Ministry of Health, Labor and Welfare

New IRDiRC members

IRDiRC is pleased to welcome three additional umbrella patient advocacy groups and a company as new members: the Canadian Organization for Rare Disorders (CORD), Rare Diseases South Africa (RDSA), Rare Voices Australia (RVA), and Cydan II.

The Canadian Organization for Rare Disorders (CORD) aims to normalize the access to diagnosis and treatment for patients with rare disease in all regions of Canada. In 2015, CORD proposed Canada's Rare Disease Strategy focusing on the five following actions points: improving early detection and prevention; providing timely, equitable and evidence-informed care; enhancing community support; providing sustainable access to promising therapies; and promoting innovative research.

Founded in 2013, Rare Diseases South Africa (RDSA) set out its mission to support patients and their families facing a diagnosis for a rare condition. However, significant increase of members led RDSA to become a registered non-profit organization, focusing on all aspects of advocacy and support to rare disease patients in South Africa. It undertakes a wide range of activities including fundraisings, patient advocacy, communication over health policy and ongoing clinical trials, and conference organization.

Rare Voices Australia (RVA) was established in 2011 in response to an international symposium called "Awakening Australia to Rare Diseases: Global perspectives on establishing a coordinated approach to a national plan" that was held in Fremantle, Western Australia. The lack of rare disease policy in Australia prompts RVA - in addition to promoting rare disease research, diagnosis and treatment - to set out to develop and contribute to the development of new health policy for rare diseases.

Cydan II was launched in 2013 by a team of experts in drug, clinical and business development. The company dedicates its work to develop drugs for patients with rare diseases, specifically for diseases not yet studied by other companies. Strong of its successes, Cydan recently launched two new biotechs: in 2015 it started Vtesse, developing drugs for Niemann-Pick Disease Type C (NPC) and in 2016 IMARA, committed to developing a treatment for the sickle cells disease.

Information on membership application can be found at Become a Member page.

"IRDiRC Recognized Resources"

Two resources received the "IRDiRC Recognized Resources" label: "Guidelines for diagnostic next-generation sequencing" and "The FAIR Guiding Principles document for scientific data management and stewardship."

"Guidelines for Diagnostic Use of Next-Generation Sequencing (NGS)" lays out 38 statements that support the harmonization and quality assurance of NGS diagnostics. The progress in genome sequencing have made NGS a very popular and widely-used tool in research on human genetics. It completely changed the way genetic diagnostics are performed nowadays. However, the use of new technologies always comes with new challenges in term of technical aspects, data management, results interpretation, ethical regulation and counseling, and these guidelines provide guidance to these aspects.

The Findable, Accessible, Interoperable and Reusable (FAIR) Data Principles address the lack of broadly applicable and harmonized best practices surrounding the publication of scientific data. These clear and precise guidelines – designed and endorsed by a diverse set of stakeholders – emphasize on improving the ability of researchers and automatable machines to find and (re)use data, given appropriate quality standards on data publication. This is particularly important in the context of rare diseases where data are sparser and more distributed than in other health data domains.

Featured articles

The International Rare Diseases Research Consortium: Policies and Guidelines

In rare disease research, data are scattered and the number of patients is often small, making critical the need for collaboration. The IRDiRC Policies and Guidelines were set out to address best practices in term of data/expertise sharing, integration, use of resources in rare diseases research. A change in how science is performed in addition to the involvement of all stakeholders (scientists, clinicians, patients, industries, regulators) is key to achieve efficient international collaboration.

One of the efforts to widely disseminate these guiding principles was achieved through a publication in the *European Journal of Human Genetics*. The Policies and Guidelines, ratified by IRDiRC members for implementation in their rare diseases research program, are structured around 11 major topics: data sharing/standards, ontologies, diagnostics, biomarkers, patient registries, biobanks, natural history, therapeutics, model systems, publication/intellectual property and communication. In addition to developing new initiatives based on these principles, IRDiRC will also continue its efforts in further disseminating the Policies and Guidelines as well as assessing their impact to update them when required.

For details, please read the full article and the IRDiRC Policies and Guidelines document.

Measuring what matters to rare disease patients – reflections on the work by IRDiRC taskforce on patient-centered outcome measures

The aim of clinical trials is to evaluate the effectiveness and safety for patients of a medical intervention, based on comparable results: the outcome measures. Despite guidance documents on outcomes, many trials, on rare diseases in particular, still do not include standardized outcomes. This situation leads to failures in late-stage of orphan drug development or simply difficulties to prove their clinical effectiveness.

The paper published in the *Orphanet Journal of Rare Diseases* is a position statement based on the work and discussions done by the IRDiRC Task Force on Patient-Centered Outcome Measures (PCOM). The authors, Thomas Morel and Stefan Cano, emphasize on PCOMs being the best opportunity to obtain a meaningful and interpretable measure of the patient benefit. While PCOMs are still largely omitted across the medical and research community, in particular for rare diseases, fully embracing PCOMS would lead into a win-win scenario for patients, clinicians, researchers, regulators, health technology assessment and payers. The authors described the benefits brought by PCOMs as following:

• Measurement of what matters to patients
• Guidance of treatment decisions
• Improvement of drug development and reimbursement outcomes
• Contribution to understanding natural history
• Demonstration of clinical effectiveness
• Interpretation of surrogate or composite endpoints

The authors describe methods used in PCOM research with their advantages and constraints as well as the key role often played by patients' organizations in leading patient outcome measurement initiatives. They also discuss how PCOMs can be applied to rare diseases. While it seems unrealistic to develop PCOM specifically to all rare diseases, the careful examination of existing tools and their (re)use is worth considering. Finally, the authors defined 5 principles that should guide the development meaningful PCOMs for rare diseases: Collaboration, Alignment, Integration, Innovation and Communication.

For details, please read the full article and the PCOM Task Force's report

Spotlights on IRDiRC Member Organizations

• The IRDiRC commentary "International Cooperation to Enable the Diagnosis of All Rare and Genetic Diseases" was cited by the *American Journal of Human Genetics* in its special issue of "The Best of 2016-

2017"

• An interview of Dr Austin by *BioCentury Innovations* puts IRDiRC's new goals into perspective

• A perspective article by Sharon Terry about IRDiRC's new vision and goals was published in *Genetic Testing and Molecular Biomarkers*

• The theme of the International Rare Disease Day 2018, organized by EURORDIS-Rare Diseases Europe, is "Research", with a particular focus on the role of rare disease patients in this field

• The European Commission's Joint Research Centre (DG JRC), together with DG SANTÉ, is developing the EU Rare Diseases Registries Platform; the Set of Common Data Elements for RD Registration, which is a first step towards interoperability of registries in Europe, was recently released

• Nominations for NORD's 2018 Rare Impact Awards are now open

• The European Commission and the European Medicine Agency (EMA) published a document questions and answers related to the United Kingdom's withdrawal from the European Union with regard to the medicinal products for human

• European Commission launches its Horizon 2020 Health Research Programme 2018-2020 including the Rare Disease European Joint Programme (EJP) Cofund

• European Commission has presented to the European Parliament and the Council a report about the progress on children's medicines

• EURORDIS-Rare Diseases Europe launched the Parliamentary Advocates for Rare Diseases, a network of European and national members of parliament advocating to improve the lives of people living with a rare disease

• The French Foundation for Rare Diseases appointed Dr Daniel Scherman as its new Director

• Government of Western Australia: People urged to share selfies for science to gain insight in rare diseases

• Shire's Adynovi® obtained EU Market Authorization for adults and adolescents with Hemophilia A

Rare Diseases Research Highlights

• The Global Alliance for Genomics and Health (GA4GH) initiated formal collaborations with 15 international genomic data initiatives as 2017 Driver Projects, including the Matchmaker Exchange Project

• The EMA published a report illustrating how collaboration between regulators and healthcare payers could create synergies facing the challenges in the field of pricing and reimbursement decisions at a national and regional level

• On October 10th, Orphanet celebrated its 20 years anniversary and welcomed at the same time Japan as its 41st member country

• An article published in *Clinical Therapeutics* identifies how social media impacts orphan drug development in three ways: from assisting the study of orphan diseases, to playing a vital role in the clinical trial process, and increasing awareness of rare diseases

• The International Repository Locator (IRL) is an initiative by ISBER to help investigators locate biospecimen and data repositories by developing a directory of repository information that can be searched online

• The EMA is moving to Amsterdam, the Netherlands

• A recent article published in *Nature* demonstrates how researchers regenerate the skin of a patient suffering from junctional epidermolysis bullosa using transgenic keratinocyte cultures

• An article published in the *Journal of Human Genetics* describes how interdisciplinary collaboration between various services can contribute to the success of next-generation sequencing (NGS) diagnostics

• An article published in *Genetics in Medicine* describes how periodic re-analysis of clinical whole-exome sequencing data can increase diagnosis rate

• A study published in *Drug Discovery Today* shows that computational drug repositioning has been successfully applied to the development of treatments and thus be beneficial in the rare diseases field

• RD-Connect renamed two of its platforms: the genomic platform becomes the Genome-Phenome Analysis Platform and the registries and biobanks directory previously called ID-Cards becomes the Registry & Biobank Finder

Events

• The RE(ACT) Congress, co-organized by the Blackswan Foundation and E-Rare ERA-NET will take place on March 7-10, 2018 in Bologna, Italy. Abstract deadline: **December 15, 2017**
• The Genomics of Rare Diseases (GRD) Conference 2018, organized by the Wellcome Genome Campus, will take place on March 26-28, 2018 in Cambridge, UK. Abstract deadline: **January 30, 2018**
• The European Conference on Rare Diseases & Orphan Products (ECRD), organized by EURORDIS-Rare Diseases Europe, co-organized with Develop Innovate Advance (DIA) and Orphanet, is taking place in Vienna, Austria on May 10-12, 2018: Abstract deadline: **January 31, 2018**

IRDiRC-Related Funding Calls

The FDA has launched a call entitled "Clinical Studies of Safety and Effectiveness of Orphan Products Research Project Grant". This funding opportunity announcement is to support the clinical development of products for use in rare diseases or conditions where no current therapy exists or where the product being developed will be superior to the existing therapy. FDA provides grants for clinical studies on safety and/or effectiveness that will either result in, or substantially contribute to, market approval of these products. Application deadline: **February 7, 2018**.

The NIH has launched a call entitled " Clinical Trial Readiness for Rare Neurological and Neuromuscular Diseases". This funding opportunity announcement is to support clinical studies that will fill gaps in the design of upcoming clinical trials in rare neurological or neuromuscular diseases by validating clinical outcome measures or biomarkers, or by characterizing cohorts of relevant patients. Through the support of trial readiness studies, NINDS expects to accelerate the initiation of clinical trials for rare diseases and to increase the likelihood of success in those trials. Application deadline: **February 15, 2018** and **August 17, 2018**.

The European Commission launched a call entitled "Pilot Programme on a Clinical Compound Bank for Repurposing: Rare/Orphan diseases". The overall objective of this pilot programme is to take one of the previously deprioritised clinical compounds and investigate their therapeutic potential in new clinical indications in the area of Rare/orphan diseases. Application deadline: **February 28, 2018**.

The European Commission launched a call entitled "Rare Disease European Joint Programme (EJP) Cofund". The overall objective is to create a research and innovation pipeline "from bench to bedside" ensuring rapid translation of research results into clinical applications and uptake in healthcare for the benefit of patients. The specific objectives of the program are to improve integration, efficacy, production and social impact of research on rare diseases through the development, demonstration and promotion of sharing of research and clinical data, materials, processes, knowledge and know-how, and to implement and further develop an efficient model of financial support for research on rare diseases including basic, clinical, epidemiological, social, economic, and health service research. Application deadline: **April 18, 2018**.

For more IRDiRC-related calls, please consult this page.

New IRDiRC documents

• Funders Constituent Committee – report of the 2nd Funders Constituent Committee meeting – July 12, 2017, Teleconference
• Funders Constituent Committee – report of the 3rd Funders Constituent Committee meeting – September 28, Teleconference
• Patient Advocates Constituent Committee – report of the 2nd Patient Advocates Constituent Scientific Committee meeting – October 12, 2017, Teleconference
• Diagnostic Scientific Committee – report of the12th Diagnostic Scientific Committee meeting – October 12, 2017, Teleconference

• Interdisciplinary Scientific Committee – report of the 19th Interdisciplinary Scientific Committee meeting – September 18, 2017, Teleconference
• Interdisciplinary Scientific Committee – report of the 20th Interdisciplinary Scientific Committee meeting – November 6, 2017, Teleconference
• Therapies Scientific Committee – report of the 13th Therapies Scientific Committee meeting – October 26, 2017, Teleconference

Upcoming Teleconferences and Meetings

• December 4, 2017 – Solving the Unsolved Task Force - Teleconference
• December 6, 2017 - Operating Committee – Teleconference
• March 25, 2018 – Solving the Unsolved Task Force - Workshop

If you are presenting in a meeting or a conference, and you would like to include some information about IRDiRC, standard slides are available on the IRDiRC private website; additional slides can be made available upon request.

Please also email the Scientific Secretariat when and where you will be presenting, so we can keep track of "IRDiRC presence at conferences."

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For more information on IRDiRC and its activities, please visit the IRDiRC website. Stay up to date with news regarding IRDiRC and the rare diseases research community by following @IRDiRC on Twitter.