IRDiRC
INTERNATIONAL RARE DISEASES RESEARCH CONSORTIUM

Meeting report series

Report of the 5th IRDiRC Diagnostics Scientific Committee meeting

Teleconference
2 September 2014

Organization

Organized by: Scientific Secretariat
Teleconference

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REPORT

1. Update from the Executive Committee meeting (Berlin, May 2014)

a. Review of the Diagnostics Scientific Committee Roadmap

The Diagnostics Scientific Committee (DSC) and the Interdisciplinary Scientific Committee (ISC) roadmaps were grouped according to the core objectives of IRDiRC. The Therapies Scientific Committee (TSC) did not develop a similar schematic roadmap in time for the Executive Committee (EC) meeting in May, due to its change of chair. The ISC / DSC roadmap includes the development of standards, tools and position statements assigned to the IRDiRC Working Groups (WG). This roadmap was well received by the EC, who then asked for proposals on how to ensure the development of the tools and standards proposed (short-term funding).

The EC also asked advice on which area of research to fund (long-term funding) as topics of research funding are decided at least one year in advance by funding agencies.

b. 'IRDiRC Recommended' label

The EC agreed to create a label entitled 'IRDiRC Recommended' to highlight tools, standards, and guidelines either generated by IRDiRC activities or identified by IRDiRC as a key resource. The purpose of this label is to encourage the community to work with the same standards, thereby ensuring interoperability.

Process for adoption was defined:

- WG and/or Scientific Committee to produce 1-2 pages of rationale, including list of other most important tools or standards, and contentious issues.
- Consultation of the two other Scientific Committees.
- Submission to the Executive Committee for approval.

Any recommended tools/standards/guidelines will be highlighted on the IRDiRC website. A logo has been designed.

2. Review of each WG progress

a. WG on Genome/Phenome

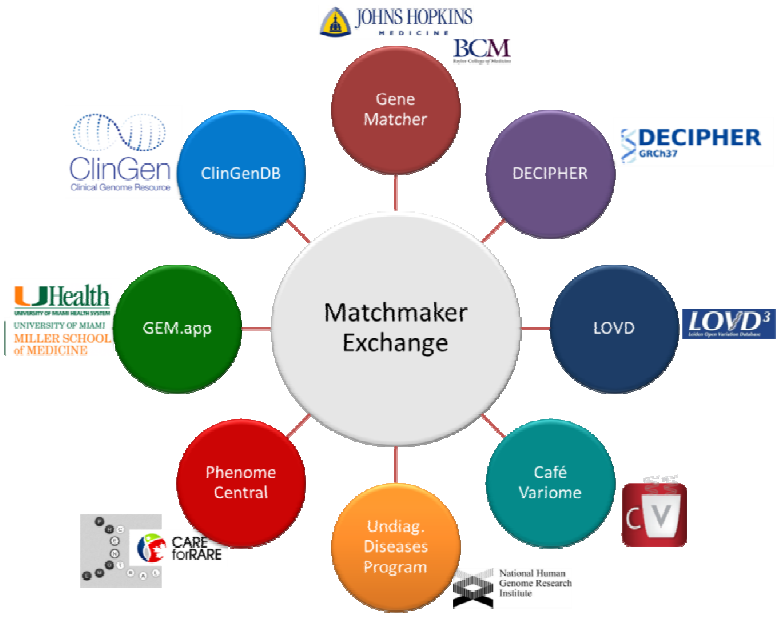
i. API Matchmaker Exchange summary

API Matchmaker Exchange is a collaborative effort to facilitate gene discovery through the matching of cases with similar phenotypic and genotypic profiles (matchmaking) thanks to standardized application programming interfaces (APIs) and standard operating procedures.

It is facilitated by the Global Alliance for Genomics and Health (GA4GH) – organizing teleconference and minutes – and deemed to be driven and supported equally by IRDiRC. Several members of the WG on Genome/Phenome participate in this project.

The diagram below shows databases currently existing that house these types of data. Matchmaker tries to link these databases. As a pilot for the matchmaker concept, the first version of the API allows the resources of GeneMatcher (USA) and PhenomeCentral (Canada) to communicate for data discovery. It is based on a 'data submission' approach: i.e., a match 'requestor' must provide patient data, after which the query principles via which similar patients are identified is decided by the database receiving the request (e.g., gene-based matching, degree of phenotype similarity, mutation types, etc).

Pilot project will start in September, and outcomes will be monitored carefully in the following months. Next steps will be to include GEM.app and possibly DECIPHER. The Undiagnosed Rare Disease Program (intramural) is already linked to PhenomeCentral, and the new extramural program is considering how best to link to these existing resources. The Deciphering Developmental Disorders project (DDD, UK) will transfer data into DECIPHER.



ii. Summary of 3rd and 4th teleconferences

In the last teleconference of this WG, possible areas of focus going forward have been suggested including metadata standardization and minimum content open data conventions. Members of the DSC agreed that the topics suggested should be further discussed by the WG.

a. Regarding metadata standardization, groups interested in this topic (e.g., NeurOmics, IRDiRC, BiomedBridges, pending EU funding proposals) should work together to define some minimum metadata standards. To start, a few workshops would be sufficient to establish the core issues and develop some details – perhaps funded by IRDiRC? Several questions were raised:

- Would it be possible to organize a half-day workshop at the ASHG meeting in San Diego?
- Who should be the chair of such workshop?
- Could IRDiRC fund it?
- How much could the Global Alliance for Genomics and Health be engaged in this project? GA4GH has several rooms reserved at ASHG meeting for a series of satellite meetings occurring. Could they provide a room for a meeting as they have done for Matchmaker Exchange?

b. Minimum content open data conventions address ethical concerns on which data should be protected and which data should not be protected, and which data could be openly and freely accessible (specific genes with specific mutations? phenotype?). A statement on this topic should be drafted by the WG to be finalized by the DSC with the input of the ISC and the TSC.

b. WG on Model Systems

i. Summary of 2nd to 4th teleconferences

The members of this WG have developed a mission statement and two long-term funding proposals which are called “Market Place” and “Disease Relevance Phenotyping”. These two proposals can be put forward to the EC for longer term funding:

- The Market Place will be a system which will facilitate collaboration between clinician researchers discovering new disease genes and basic researchers performing functional studies in model systems.
- The Disease Relevance Phenotyping proposal is more focused on therapeutics and the identification of drug target. For this purpose, it was previously decided that this WG should also report to the TSC.

Commentaire [bc1]: For information, the TSC will discuss the possibility to include a TSC member in this WG on October 6.

The WG on Model Systems also aims to produce a ‘connect’ manual for clinician researchers and model organism researchers, in order to connect them. The DSC approves this initiative and would like the WG to develop a proposal with more details.

The WG on Genome/Phenome and the WG on Model Systems, which have topics in common, should have a teleconference together to discuss how to approach variants of unknown significance using model systems.

c. WG on Ontologies and Rare Disease Prioritization

i. Summary of 2nd and 3rd teleconferences

The WG on Ontologies had its last teleconference in July, when the Phenotype Exchange Standard was discussed. The NIH Undiagnosed Disease Program (UDP), in collaboration with Michael Brudno, aims to

create a data exchange format standard for phenotype data using either HPO or something compatible with HPO. This would also include metadata. To avoid duplication of work, people from NIH Undiagnosed Rare Disease Program, as well as other large scale initiatives dealing with this problem were integrated in the WG on Ontologies. This group drafted a paper about the need for such a Phenotype Exchange Standard, and will also try to involve Africa and Asia to engage the whole community.

The WG on Ontologies will also prepare for the DSC a draft of 'IRDiRC Recommended' standards. HPO and ORDO will be the two recommended ontologies to describe rare diseases and rare disease phenotypes, respectively.

d. WG on Sequencing

i. Next steps

This WG has not met since November 2013. Two teleconferences have been scheduled for September and October:

- In the September's teleconference, they will review the EuroGentest guidelines on NGS use and inform the DSC if they consider that IRDiRC should recommend these guidelines.
- In the October's teleconference, they will explore their other objectives, which are to look at countries which have successfully translated genomic sequencing into clinical care, understand their approach, and which tools and resources they used, etc.

Another topic to work on for this WG would be a pipeline comparison of various informatics platforms for identification of rare variants. RD-Connect would be interested in this and has efforts underway. This topic may also be addressed in the EuroGentest guidelines.

e. WG on Population Controls Variant Datasets

i. Membership

The general objective of this WG is to develop standards for data collection and facilitate the aggregation of anonymized variant frequency data from specific populations. Broad membership is required. Currently, members come from Kuwait, China, Turkey, Spain, Canada, Germany and UK.

ii. Date of first teleconference: 16 September 2014

The first teleconference of this WG will be held on September 16, 2014, in order to discuss what data collections exist, are available and how to gather and use them. To do so, GEUVADIS, a variant server which contains data on several thousand individuals, could be used.

f. Proposal to invite Chairs of WGs to DSC teleconference

Regular teleconferences between the chairs of the WGs and the DSC members might be a better way to communicate. Teleconferences could be scheduled every six-eight weeks asking one or two chairs of the WGs to be on the call.

3. EC request for short-term funding proposals to enable roadmap milestones

The EC asked the Scientific Committees to provide proposals for funding to ensure deliverables of the roadmap to be met.

2 projects of the DSC and 2 projects of the ISC were presented during the last teleconference of the EC.

Funding for the Matchmaker Exchange project (DSC) would go to Canada to evaluate the outcomes of the API's first version, which would provide information for the development of version 2 of the API. This data would be used to set the stage for a 2-day workshop that could be held in Miami in early 2015.

The Communitize HPO project (DSC) brings together Germany, Canada and Australia to help HPO progress. In Berlin they will improve the HPO website. In Toronto they will work on the functionality of PhenoTips. In Australia, they will work on the automatic recognition of HPO terms from text.

The ISC also presented two proposals: a proposal to: (i) develop model consent clauses for rare disease research; and, (ii) a proposal to develop a Data Standards Clearinghouse for Rare Diseases.

The EC found these proposals very interesting but really focused on how to fund them. Two possibilities for funding were addressed:

- A common pot in which the funders would put money in to fund this type of work.
- Interested parties to fund the part of the project that would happen in their country.

The second possibility seems more plausible. Canada and Australia could have some opportunities for funding in the near future. The EC will meet again in September/October to further discuss this topic. If they find a mechanism by which this would work, they will come back to the Scientific Committees with the official process for application.

4. EC request for long-term funding proposals

The EC requested suggestions on specific areas of rare disease research to fund in the coming years (long-term funding), as topics of research funding are decided at least one year in advance by funding agencies.

The DSC will look back at the WGs work to identify gaps in rare disease research and prioritize these in terms of community need with respect to IRDiRC goals for further development into white papers for the EC.

This topic will be in the agenda of the next DSC teleconference.

5. Update on the 2nd IRDiRC Conference, Shenzhen, November 2014

It is expected that 90% of the attendees will be Chinese. 600-800 people are expected to attend. The program is essentially complete with four parallel tracks in the topics of Diagnostics, Interdisciplinary-Technologies, Therapies, and Educational, as well as a one day of training course. The educational track will be in Chinese, and the other tracks will be in English with both Chinese and international speakers.

6. Dates for next teleconference and next face-to-face meeting of the DSC

The next teleconference should be held in early October to discuss long-term funding. Members of the DSC attending the ASHG 2014 meeting which will take place in San Diego on October 18-22, should meet there to continue the discussion as proposals for such funding should be ready for the next meeting of the EC to be held in November in China.

The next face-to-face meeting of the DSC will take place on June 5, 2015, in Glasgow, in conjunction with the European Society of Human Genetics meeting on June 6-9.

7. Publication of an article in Nature Genetics

An article about the IRDiRC roadmap (DSC, ISC and TSC) with details on the tools, standards and guidelines being developed could be published in Nature Genetics as a commentary. The TSC roadmap will be ready in November.