DANISH NATIONAL GENOME CENTER

Minutes

4th Meeting in the DNGC's international advisory board

Date: April 25, 2024, 13.00-16.00 (CET)
Location: Hybrid meeting (at DNGC/Copenhagen and online)

Agenda

Item	App. time	Topic
1/7	13.00	**Welcome and introduction** /Tim Hubbard
2/7	13.10	**Status Danish National Genome Center today and tomorrow** /Bettina Lundgren
3/7	13.25	**Current trends and tendencies in genomics and personalised medicine** /All
4/7	13.50	**DNGC's participation and role in EU projects and international collaborations** /Lene Cividanes and Tobias Petersen
5/7	14.40	**Access to data in the Danish national genome database opening spring 2024** /Astrid Munk Pedersen
6/7	15.20	**Health economics and economic evaluation of WGS** /Lene Cividanes
7/7	15.50	**Thank you and next steps** /Tim Hubbard and Bettina Lundgren

Participants
Tim Hubbard, Director, Elixir (Chair)
Heidi Rehm, PhD, Broad Insitute
Valtteri Wirta, Dr., PhD., Karolinska Institute
Richard Rosenquist Brandell, Professor, Karolinska Institute (Vice Chair) (online)
Dag Erik Undlien, Professor, M.D., PhD, Oslo University Hospital (online)
Aarno Palotie, M.D., PhD, Institute for Molecular Medicine Finland (online)
Ruben Kok, PhD, Director, Dutch Techcentre for Life Science (online)
Kym Boycott, Clinical geneticist, University of Ottawa (online)
Jean- François Deleuze, PhD, Head of CNRGH (online)

DNGC's Secretariat
Bettina Lundgren, CEO, DNGC
Lene Cividanes, Head of Research and International Relations, DNGC
Christiane Karle (secretary), Academic officer, Research and International Relations, DNGC

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1/7 Welcome and introduction /Tim Hubbard (Chair)

Tim Hubbard welcomed everyone and introduced the program shortly.

2/7 Status Danish National Genome Center today and tomorrow /Bettina Lundgren

Bettina Lundgren presented a short status of DNGC. Currently, the National Database contains 28,240 genome samples. The samples are collected from all 17 patient groups.

DNGC is in the process of evaluating the clinical effect of whole genome sequencing (WGS) in the patient groups. Interviews with clinicians and use cases highlight positive experiences, including faster and more accurate diagnosis, closer collaboration, and increased knowledge.

Currently, DNGC is negotiating with the Danish regions about governance and financing after 2024, as the funding from the Novo Nordisk Foundation is ending mid-2024. There are many larger (cross-organizational) projects in pipeline, as DNGC is now opening the Danish National Genome Database in May, and planning to establish an HPC cooperation (health data lakehouse) in collaboration with other health agencies and partners.

DNGC's annual report for 2023 has been launched and can be downloaded here.

After Bettina's presentation, the following was discussed:

- The board advised, that DNGC should focus on retrieving phenotypes in order to make the WGS data more valuable for researchers. Currently, researchers are able to link WGS data with other registries through a personal identifier (CPR-number) and combine data.
- Patient safety and scalability are two major arguments in order to scope a project linking genetic data with phenotype.
- In the negotiations with the regions, DNGC was encouraged to emphasize the need for a unified and standardized model across regions. DNGC must stress the strength of having a national center for data sharing and embrace that DNGC is more than a "standard" IT infrastructure, but centered nationally and on a law basis. It was discussed, that DNGC should focus on convening the "ground level" people (clinicians, bioinformaticians, and users of platform) in discussions on which solutions on the platform.
- DNGC must "pick its battles" and decide, what is the "core" thing to be shared and standardized (e.g. unified datasets) across the country, and that all regions should adapt to. Develop simple use cases that show "quick wins", and then save some areas for innovation purposes and let regions decide if they want to focus on specific areas etc.
- In Sweden, the 21 regions have implemented WGS as a standard of care within pediatric cancer, amongst others. This has contributed to calculating health economic outputs of data. Data has been useful for showing regions the "diagnostic yield" of WGS.

3/7 Current trends and tendencies in genomics and personalised medicine /All

Under this agenda item, it was shortly discussed that participation in EHDS and GDI will in the long run foster access to more opportunities and data. DNGC should use European projects as a guideline for how to share data within regions.

It was discussed, that more researchers are looking at genes not implicating disease and figuring out how to engage in rare disease space. This also implies for a connection between clinic and research, to encourage researcher to look at unidentified cases.

4/7 DNGC's participation and role in EU projects and international collaborations /Lene Cividanes and Tobias Petersen

Lene Cividanes presented DNGC's participation in international collaborations, including the bilateral agreements with Genomic Medicine Sweden, French National Alliance for Life Sciences and Health and Genomics England.

Tobias Petersen presented DNGC's approach to Genomic Data Infrastructure (GDI), including how DNGC is planning to take GDI products to production and reach operational goals. DNGC is facing challenges regarding integration, specifically that the proposed authentication and authorization framework do not comply with DNGC's compliance requirements, and that the clinical expectations of the infrastructure conflicts with the research-focused outset.

Afterwards there was a discussion about DNGC's participation in EHDS, as this will open for opportunities for both primary and secondary use of data. DNGC must focus on helping local organizations comply to upcoming regulations. Heidi Rehm encouraged DNGC to engage further in the working groups under GA4GH.

5/7 Access to data in the Danish national genome database opening spring 2024 /Astrid Munk Pedersen

DNGC's National Genome Database is opening for research access in May. In order to gain access to the database, researchers must have an approval from the research ethics committee, a data processing agreement with DNGC and be associated with a Danish research institute. Access to the data is given through a secure processing environment, and it is possible to combine the accessed genetic data with own data or data from other registries.

Afterwards the following was discussed:

- To increase use of data and to ensure data minimization, DNCG should consider creating aggregated datasets with public access. DNCG could also consider asking researchers to make their datasets public after performing analyses on large amount of data or when using a specific tool. This is to ensure that the same analyses on the same data are not performed multiple times. The benefit for the researchers could be a price reduction.

- There must be an attention to how to treat research results within rare diseases with only a few patient cases. There is a general standard in several contexts advocating for not publishing, if there are less than five cases.
- There was a discussion on the tools researchers should be able to bring to the platform (e.g. Medlab, R studio, Python). It is recommended to have a portfolio of tools build in the system, but also to let researchers be able to bring their own so the portfolio is scaleable.
- Heidi mentioned, that they have built a network of mentors for use of their bioinformatical platform as part of the All of Us Research Program, e.g. medical students, postdocs, to provide scientific support.
- DNGC was advised to consider how to position DNGC as a stakeholder in the field targeting researchers, e.g. establish link between researchers and research funders for use of the infrastructure.

6/7 Health economics and economic evaluation of WGS /Lene Cividanes

DNGC is coordinating HEOR working group in 1+MG and collaborating with European countries responding to CSA. There is a need for clinical evidence and economic models in order to legitimize decisions on a political level. The working group is fostering exchanges and developing an overview of health economic models to measure the impact of WGS.

Afterwards the following was discussed:

- DNGC is negotiating with the Ministry of Health whether funding should be a unified model across the country, or if regions should decide funding themselves. There is an emphasis on equality, that the WGS offer should be the same across the country.
- Heidi suggested a strategy with upfront systematic reviews to gather an evidence base that can be incorporated into clinical guidelines. E.g. the American college of medical genetics has developed evidence-based reviews into current guidelines which has an impact on which tests are covered by insurance companies. Due to the heterogeneity within the field, it is necessary to group patients according to i.e. age or disease-groups, and important to collaborate internationally and across medical areas.
- Different parameters for evaluating effect were discussed, e.g. clinical effect, economy/financial effect, technological perspectives (i.e. diagnostic utility, simplified lab-flow), patient perspectives etc. The pros and cons of different models for evaluating effect was discussed briefly, e.g. micro- vs. macroeconomic models or health economic models such as HTA. Importantly, the models/parameters must address the questions asked by the funding bodies.

Following links were shared as part of the discussion:
The cost-effectiveness of whole genome sequencing in neurodevelopmental disorders - PubMed (nih.gov)
Invitae - Invitae Enters into Agreement with Labcorp for Sale of Business
Invitation for Public Comment: WHO principles for human genome access, use and sharing

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7/7 Thank you and next steps /Tim Hubbard and Bettina Lundgren

Tim Hubbard and Bettina Lundgren closed the meeting and thanked everyone for the many good inputs from the sessions.