NATIONALT GENOM CENTER

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Minutes

1. meeting in DNGC's international advisory board

Date: October 6th, 15.00-17.00 (CET)
Location: Teams (Link is in the Outlook invitation)

Agenda

Item	App. time	Activity
1/10	15.00	Welcome and round of presentations v/Bettina Lundgren
2/10	15.10	Presentation of DNGC and the Danish strategy on Personalised Medicine v/Bettina Lundgren
3/10	15.20	Presentation of the data journey v/ Camilla Borchorst
4/10	15.30	Presentation of DNGC's pipelines and bioinformatics v/Ole Lund
5/10	15.40	Presentation of DNGC's research infrastructure and research access v/ Ali Syed and Lene Cividanes
6/10	15.55	Presentation of the twelve patient groups selected for whole genome sequencing v/ Peter Johansen
7/10	16.05	Review of the terms of reference, including the role and mandate of the DNGC's international advisory board for research and infrastructure, review of policy of impartiality, review of rules of procedure v/Christian Dubois *Appendix 1: Terms of Reference: DNGC's International Advisory Board* *Appendix 2: Policy of Impartiality* *Appendix 3: Rules of Procedure: DNGC's International Advisory Board*
8/10	16.10	Election of chairmanship v/Bettina Lundgren
9/10	16.20	Discussion on key challenges in the development of Precision Medicine and future perspectives v/Bettina Lundgren **Questions for members:** 1. Based on the initiatives you have been involved in, what is an example of a best practice or a suc-

		cess story from implementing precision medicine initiatives on either a regional, national or international level, we can learn from? 2. In your experience, what is the key challenges in developing and implementing precision medicine initiatives?
10/10	16.55	Concluding remarks and next meeting v/Elected chair

Participants
Tim Hubbard, Professor, Kings College London
Richard Rosenquist Brandell, Professor/senior physician, Karolinska Institute
Valtteri Wirta, Dr., Ph.d., Karolinska Institute
Heidi Rehm, Ph.D, Chief Genomics Officer, Broad Insitute
Dag Erik Undlien, Professor, M.D., PhD, Oslo University Hospital
Russ Altman, Professor, Stanford University
Jean- François Deleuze, Ph.d., Head of CNRGH
Aarno Palotie, M.D., Ph.d, Institute for Molecular Medicine Finland
Ruben Kok, Ph.d., Director Dutch Techcentre for Life Science

DNGC's Secretary
Bettina Lundgren, Director, DNGC
Peter Johansen, Chief Consultant Health Care team, DNGC
Camilla Borchorst, Chief Operating Officer, DNGC
Christian Dubois, Chief of Staff, DNGC
Ole Lund, Chief Bioinformatics officer, DNGC
Ali Syed, HPC Platform, DNGC
Cathrine Jespersen, Chief of the National Whole Genome Sequencing Center, DNGC
Lene Cividanes, Head of Research, Clinic and International Relations, DNGC
Ivana Bogicevic, Policy officer, Research, Clinic and International Relations, DNGC

Minutes

1/10 Welcome and round of presentations / Bettina Lundgren

- Bettina Lundgren opened the meeting and thanked everyone for accepting the invitation to participate in DNGC's international advisory board.
- All advisory board members gave a short presentation of themselves.
- Lene Cividanes announced that the appointment of at least one member is still pending. DNGC would like to see more female members on the board. Lene Cividanes encouraged members of the DNGC's international advisory board to send proposals to Lene Cividanes or Ivana Bogicevic from the DNGC's secretariat.

2/10 Presentation of DNGC and the Danish strategy on Personalised Medicine /Bettina Lundgren

Bettina Lundgren gave a short presentation of the DNGC and the Danish strategy on Personalised Medicine:

- The Danish strategy was initiated in 2017 by the Danish government and Danish regions who oversee the public healthcare system.
- The Danish strategy focuses on the diagnosis and treatment of patients and creating research infrastructures to support further development of personalised medicine.
- Current strategy runs until 2022.
- The DNGC is an institution under the Ministry of Health.
- The DNGC has its financial foundation through financing from the state, existing regional funds, and the Novo Nordisk Foundation.
- The grant from the Novo Nordisk Foundation is allocated to building the necessary infrastructure to perform genome sequencing and securely store information.
- The goal is to have conducted 60.000 WGS distributed across the selected patient groups by summer 2024.
- Denmark has a strong tradition for registration of data in health registries and biobanks.
- DNGC is currently experiencing a broad support amongst Danish citizens.

- Funding for the DNGC from 2024 and onwards was discussed. The DNGC is currently in dialogue with the Danish Ministry of Health and the Danish regions regarding funding.

3/10 Presentation of the data journey / Camilla Borchorst

Camilla Borchorst gave a short presentation of the data journey, including

- The DNGC's core objectives are to create and implement:
  - National infrastructures for standardized, uniform, and efficient whole genome sequencing (WGS) in patient treatment.
  - User-friendly and efficient general reporting of genetic analysis to the national genome database.
  - Secure access to genetic data for clinicians and researchers.
  - Access to relevant interpretation tools, pipelines, and applications for clinicians and researchers.
  - Access to the supercomputer's capacity and storage via NGC's private cloud solution.
- The goal during the last two years has been to build the proper infrastructure to reach the 2024 goal of 60.000 WGS from patients.
- According to Danish law, it is mandatory to report comprehensive genetic analysis to the DNGC, both from research and clinic. At the moment the DNGC is still in the process of deciding on how much metadata should be included in the reported data.
- The vision is that the DNGC should offer at least 6 services:
  - WGS Service
  - Clinical Services
  - Research Services
  - General reporting Service

        - NGC Private Cloud
        - NGC Analytic platform
    - The focus at the moment is WGS and Clinical Services.
    - The future vision is to both offer researchers access to a private NGC Cloud and different analytical platforms.

- Main points from the discussion following the presentation were:
    - Members from the advisory board raised the importance of building a variant database or other knowledge databases in the future.
    - Members from the advisory board raised the importance of creating secure platforms for data linkage in the future.

4/10 Presentation of DNGC's pipelines and bioinformatics /Ole Lund

Ole Lund presented the DNGC's pipeline, including:

- The 60.000 WGS are clinical samples, not population genetics.
- DNGC provides the data and the infrastructure for data to be returned in real time to clinicians in hospitals who are responsible for the interpretation.
- Raw data is stored in the national genome database.
- Future vision is to build a classified and non-classified variant database, based on data from the interpretation in hospitals.
- Data is locally stored in the DNGC's own supercomputer.
- Turnaround time is 10 days.
- Focus for the next 6 months is to build a pipeline for somatic samples.

- Main points from the discussion following the presentation were:
    - It is important to reflect continuously on the ethical implications of return of results and secondary findings.
    - Different technologies for identifying samples were discussed.

5/10 Presentation of DNGC's research infrastructure and research access / Ali Syed and Lene Cividanes

Ali Syed presented the national supercomputer and research infrastructure, including:

- The supercomputer is "green" - 70 pct. of the computer's servers are cooled with 40C hot water, and the heat from this is recycled to heat the surrounding buildings.
- The supercomputer is designed especially for Life Science. It can handle large amounts of data both in a secure, flexible and precise manner.
- The supercomputer has latest generation Intel **17,000 CPUs** and **Nvidia V100 GPUs** corresponding to approx. 4,200 powerful PCs.
- The supercomputer is based on "security by design" and provided as a service.
- The data life cycle has been an integral part of the design process.
- The supercomputer is built with inspiration from the "embassy model". There is a cloud infrastructure on top of the HPC. This allows researchers to rent a cloud where they can control data and process data based on their specific needs.

Lene Cividanes presented research access to the national genome database and research infrastructure, including:

- The NGC offers four different models:
  - An empty cloud.
  - A cloud with tool and pipelines for analysis.
  - A cloud with (read) access to the national genome database.
  - A collaboration with DNGC where new analytical tools or research pipelines can be developed.
- Researchers must apply for access both to a NGC Cloud and to data from the national genome database.
- Access to the national genome database is read only.
- To gain access researchers and the research project must be affiliated with a certified Danish research institution, and gain all necessary ethical and legal approvals.
- Private companies may only gain access as part of a collaboration with a research project affiliated with a certified Danish research institution.
- The DNGC has bilateral partnerships with Genomic Medicine Sweden, Genomics of England and the French plan for Genomic Medicine.
- The DNGC is part of the 1+Million Genomes project and Global Alliance for Health.
- The DNGC is in the process of initiating a project on creating a Danish reference genome as part of the European reference genome (1 Million Genomes).

6/10 Presentation of the twelve patient groups selected for whole genome sequencing /Peter Johansen

Peter Johansen gave a presentation of the patient groups and how they are chosen, including:

- Overall principle: equal access for patients nationally
- In selecting patients, there are three main clinical principles:
  - Significant benefit from access to WGS in the form of gaining (faster) access to better treatment or diagnostics.
  - Existing clinical experience in comprehensive genetic testing for the specific patient group.
  - Existing environment for providing WGS or comprehensive genetic analyses with the possibility of extending the use nationally.
- Other principles include:
  - Socio-economic consideration.
  - Broad effect: THE DNGC should offer whole genome sequencing to a wide range of patient groups.
- Selecting patient groups is a long process, including:
  - A nomination phase
  - Academic Evaluation
  - Academic and multidisciplinary qualification
  - Decision
  - Establishment of national specialist networks
- During the first nomination phase, the DNGC received 72 applications. 34 went through to second step. Applications were consolidated into 12 overall patient groups.
- Rare diseases in children and young people under 18 years was started as a pilot project.
- The next four groups to be consolidated are:

  - Haematological cancer
  - Rare diseases in adults over 18 years
  - Neurogenetic patients
  - Fetal medicine

- Main points from the discussion following the presentation were:
  - DNGC was advised to gain an overview on how many patients or citizens were currently opting out.
  - Advisory board members suggested that the DNGC collects data on e.g. diagnostic rates on the selected patient groups in order to measure whether WGS does create the expected benefit for patients.
  - Advisory board members suggested that the DNGC ensures that linking genomic data with other data from Danish biobanks and registries becomes possible in the future.
  - It was discussed that it is important to ensure that data is findable, accessible, interoperable, and reusable.
  - The DNGC has two ways of receiving data:
    - From the clinic: WGS is conducted at one of the two national WGS facilities, as part of patient treatment.
    - From research, where WGS takes places as part of a research project.

      Both types of data are stored in the national genome database. Both types of data can be made available to research, if researchers have the correct ethical approvals, are affiliated with a certified Danish research institution, and consent has been obtained.

      The DNGC has the opportunity to extend storage capacity if necessary.

  - Members in the advisory board suggested that the DNGC provides the possibility for real world data linkage in the future.
  - The DNGC was advised to ensure that national standards for interpretation and diagnosis are created, and ensure alignment across national laboratories and clinics.
  - Members in the advisory board raised the importance of developing pipelines and infrastructures for research in pharmacogenetics in the future.

7/10 Review of the terms of reference, including the role and mandate of the DNGC's international advisory board for research and infrastructure, review of policy of impartiality, review of rules of procedure / Christian Dubois
Appendix 1: Terms of Reference: DNGC's International Advisory Board

Appendix 2: Policy of Impartiality
Appendix 3: Rules of Procedure: DNGC's International Advisory Board

Christian Dubois presented the terms of reference and the role of the advisory board, including:

  - External, impartial and critical collaborator for the DNGC.
  - Advise the DNGC about relevant international experiences, knowledge and tendencies within the field of personalised medicine.
  - Assist with reviews of reporting, implementation and exploration of development opportunities as well as international cooperation opportunities.
  - Advise about the development of the DNGC's technological infrastructure (HPC).
  - On the basis of international experience advise on ethical and legal issues.
- The declarations of impartiality will be made available on the DNGC's webpage.
- There were no remarks to the proposed rules of procedure. Christian Dubois concluded, that the proposed rules of procedure were approved.
- A question was raised regarding how meetings will take place. The DNGC answered that the majority of meetings will be held online. However, there is possibility for arranging in person meetings. These will be planned in due time.

8/10 Election of chairmanship /Bettina Lundgren

- Tim Hubbard offered to take on the position as chair.
- Richard Rosenquist Brandell offered to take on the position as vice chair.
- There were no objections.
- The chairmanship was elected.

9/10 Discussion on key challenges in the development of Precision Medicine and future perspectives /Bettina Lundgren

Questions for discussion that was sent out prior to the meeting:

1. Based on the initiatives you have been involved in, what is an example of a best practice or a success story from implementing precision medicine initiatives on either a regional, national or international level, we can learn from?
2. In your experience, what is the key challenges in developing and implementing precision medicine initiatives?

Main points from the discussion were:

- The success of both national and transnational genomic initiatives requires public engagement and transparency.
- Engagement should be proactive and include both patients, citizens, and professionals in the healthcare sector.
- It is important to reflect on how to return value to citizens and patients who participate in genomic research.
- The DNGC was advised to look into how to make pharmacogenetic information available in the public healthcare system and part of patient treatment.

- It is important to proactively secure the right expertise and work force to perform the interpretation of WGS and other comprehensive genetic tests.
- It is important to design pipelines, interfaces, and tools facilitating interpretation, in close dialogue with end-users, who are responsible for the interpretation.
- Pipelines, interfaces, and tools developed to facilitate interpretation, should also aim to secure standardization in interpretation practices across the nation.
- It is important that the DNGC create a central database that also stores information on interpretations, which clinicians can access.
- It is important to create infrastructures for sharing knowledge across national laboratories, e.g. through shared databases such as a variant database.
    - It was suggested that such infrastructures should be administered centrally.
    - Australia and Canada were highlighted as two examples that has successfully managed to create infrastructures for sharing data and knowledge across national diagnostic laboratories.
- The DNGC was advised to create a national overview of current hospital laboratories performing comprehensive or smaller genetic testing.
- The DNGC was advised to add the development of centralized and automated re-analysis services to their future visions.
- The DNGC was advised to ensure, that there is a close dialogue with end-users, such as clinicians or laboratory technicians, when developing new pipelines or services.
- The DNGC was advised to explore how to reduce turn-around time e.g. through different software systems.
- The DNGC was advised to ensure that data is presented in a way that support clinicians in interpreting data.

The main points raised during the discussion, will serve as inspiration to the DNGC's work with outlining future strategies and visions.