psychdpc

Psychiatric Diagnostic and Prevention Consortium

Project Handbook

February 2012

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PARTNERS IN PsychDPC

Number	Name	Short name	Team Leaders	Country
1	deCODE genetics	deCODE	Hreinn Stefansson	Iceland
2	King's College London	KCL	David Collier	UK
3	Ludwig-Maximillians University	LMU	Dan Rujescu	Germany
4	Region Hovedstaden	IBP	Thomas Werge	Denmark
5	University of Oslo	UOslo	Ole A. Andreassen	Norway

PROJECT OBJECTIVES

To develop a framework for research into genetic and genomic epidemiology that will strengthen the collaboration among European researchers working on schizophrenia. The specific aims for this project are:

1) To apply novel approaches to uncover more susceptibility variants for schizophrenia,

2) To study the phenotypic stamp conferred by variants conferring high risk,

3) To generate an interactive genotype:phenotype database for clinicians and researchers,

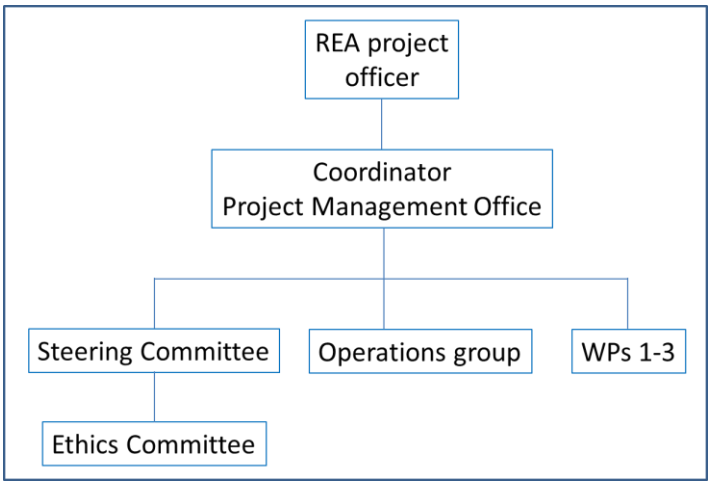
4) To launch diagnostic products

5) To generate algorithms for risk assessments.

MANAGEMENT STRUCTURE AND PROCEDURES

PROJECT MANAGEMENT ORGANIZATION

The management of the consortium is governed by the **Consortium Agreement**. Project coordination and management of PsychDPC is in two different committees; the *Project Steering Committee* (decision making) and the *Operations Group* (operations). The project's coordinator will also establish *Ethics group*.



PROJECT STEERING COMMITTEE

The **Project Steering Committee** will be composed of the partners' scientific team leaders and will be chaired by the Project Coordinator. The Committee shall be in charge of the project and its overall coordination. The Project Steering Committee will meet annually. Its main tasks include to:

- oversee the implementation of the project in accordance with the Consortium Agreement and the contract
- guide the project's scientific progress
- ensure the necessary harmonization across participating centers
- ensure appropriate attention to ethical, gender equality and intellectual property issues
- arbitrate and resolve any conflicts between participants

The **Project Coordinator** shall be responsible for:

- chairing the Steering Committee, and taking all actions to enable proper decision making;
- ensuring effective operation of the project, the project web site, quality assurance and quality control procedures;
- submitting all required progress reports, deliverables and financial statements to the REA;
- receiving funds from REA and transferring of payments of funds to participants' respective financial officers as per the provisional budget agreed by the consortium.

The **Project Coordinator** as the chair of the Project Steering Committee is the intermediary between the Research Executive Agency (REA) and the Consortium as well as the supervisor of the overall progress and scientific and technical progress of the project.

Operating rules - The **Project Coordinator** as the chair of the Project Steering Committee

- convene the Project Steering Committee in the month that follows the beginning of the project and annually the following years unless the interest of the project may require additional meetings. The chairman will also arrange TC or Skype meeting with 2-3 month intervals
- enable the decision making procedures (convocation, agenda, minutes, quorum and voting rules) according to the Contract and the Consortium Agreement;
- quality control all external communications of the project including publication of scientific papers, stakeholder and public dissemination, press releases, and monitor corrective actions. Quality control will include insuring the authorship of scientific papers is properly assigned, reviewing and prioritizing proposals for papers and tracking production with a web based system.
- quality control the ethical compliance of the project, act on the recommendations of the Ethics Group and monitor corrective actions.

The Steering Committee is the interface to the public and directly in charge of fostering and reviewing activities undertaken in the context of science and society and information to citizens.

OPERATIONS GROUP

The **Operations Group** will be composed of the project's work package leaders and others who have significant research roles in the project. It will be chaired by the Project Coordinator. The Group shall ensure the project's operations under the guidance of the Steering Committee. Members of the Operation group will in part be the steering committee members and other consortium members. Its main tasks include to:

- address and document risks which may impair the progress towards the objectives of the work packages and suggest strategies to anticipate and minimize these risks;
- implement training of seconded personnel
- monitor the work towards the milestones and deliverables of each work package.
- control the execution of the work packages on a regular basis with regards to the statement of work annexed to the contract and monitor corrective actions;
- prepare all significant modifications of the work plan and planned expenses and inform the Steering Committee.
- implement dissemination and training initiatives.

ETHICS GROUP

To ensure the proper handling of ethical issues, an **Ethics Group** will be established. It will be composed of two expert advisors on ethics that are not involved in the consortium. The Ethics Group will participate in regular Periodic Steering Committee meetings when relevant information for their task will be presented. Its main activities are to

i. monitor the project to ensure that all current legislation relating to genetic analysis of humans as well as data protection are complied with and

ii. monitor risks arising from changes in external legislation and rules. The Group is consensual and will not vote.

The Ethics Group shall:

- Identify Ethical Issues in general and in particular vis a vis children with regards to relevant National, European and International Directives, Recommendations and laws and make proposals to the Project Steering Committee accordingly;
- Ensure appropriate review by local and national ethical committees and consider the special justification required for genetic analysis of humans and data protection;
- Check publications to ensure that they comply with data protection and ethical principles.

Ingunn Hansdottir will review the project

PROJECT MANAGEMENT OFFICE

The coordinator of the project will be assisted by the deCODE Project Management Office. The office, with three full time positions, coordinates the work of the company's support units (financial, IT, public relations, IPR and legal affairs) and relevant scientific departments in order to secure the correct and efficient running of the company's various grants and contracts. The office will monitor the timely production of the project's deliverables. Iris Hronn Gudjonsdottir, iris.gudjonsdottir@decode.is, will be responsible for PsychDPC

BUDGET

TOTAL COST AND EC CONTRIBUTION

Total contribution per participant

	Living	Mobility	TOK	Management	OH	Total
deCODE	492.350 €	96.272 €	140.400 €	88.994 €	81.801 €	899.817 €
KCL	83.534 €	16.963 €	27.000 €	15.677 €	14.317 €	157.491 €
LMU	100.737 €	19.778 €	37.800 €	18.460 €	17.677 €	194.452 €
IBP	172.161 €	27.879 €	37.800 €	27.732 €	26.557 €	292.129 €
UOSLO	128.583 €	25.246 €	37.800 €	22.344 €	21.397 €	235.370 €
	977.365 €	186.138 €	280.800 €	173.207 €	161.749 €	**1.779.259 €**

REPORTING PERIODS

P1: from month 1 to month 24 (1.1.2012 – 31.12.2014)

P2: from month 25 to month 48 (1.1.2014 – 31.12.2015)

REPORTING AND MEETING TIMELINES

1.1.2012	1	Period 1	
1.2.2012	2		Kick off meeting at deCODE & ethics approval
1.3.2012	3		
1.4.2012	4		
1.5.2012	5		
1.6.2012	6		
1.7.2012	7		
1.8.2012	8		
1.9.2012	9		
1.10.2012	10		
1.11.2012	11		
1.12.2012	12		
1.1.2013	13		Progress report
1.2.2013	14		
1.3.2013	15		
1.4.2013	16		
1.5.2013	17		
1.6.2013	18		
1.7.2013	19	Period 2	
1.8.2013	20		
1.9.2013	21		
1.10.2013	22		
1.11.2013	23		
1.12.2013	24		Progress report
1.1.2014	25		
1.2.2014	26		Meeting: mid-term review & risk prediction models
1.3.2014	27		Periodic report
1.4.2014	28		
1.5.2014	29		
1.6.2014	30		
1.7.2014	31		
1.8.2014	32		
1.9.2014	33		
1.10.2014	34		
1.11.2014	35		
1.12.2014	36		
1.1.2015	37		Progress report
1.2.2015	38		
1.3.2015	39		
1.4.2015	40		
1.5.2015	41		
1.6.2015	42		
1.7.2015	43		
1.8.2015	44		
1.9.2015	45		
1.10.2015	46		Meeting: diagnostics and translations of findings at King's College
1.11.2015	47		
1.12.2015	48		Conference open to researchers
1.1.2016			
1.2.2016			Periodic report / Final report

DELIVERABLES

Del.no	Deliverable name	WP no	Lead beneficiary	Delivery month
D4.1	Project handbook	4	deCODE	1
D4.2	Consortium Agreement	4	deCODE	1
D4.3	Meetings of Steering Committee and Operational Group	4	deCODE	1
D8	Project Website	4	deCODE	3
D1	Meta-analysis of genetic risk factors in schizophrenia - Publication	1	UOslo/ deCODE	24
D2	Phenotype-genotype database generated – Report	1	UOslo/ deCODE	24
D3	Meta-analysis of neuropsychological phenotypes – Publication	2	KCL/ deCODE	36
D4	Phenotype-genotype database updated with early-stage risk model – Report	2	KCL/ deCODE	36
D5	Phenotype-genotype database updated with complete risk model – Report	3	KCL/ deCODE	48
D6	Diagnostic product for psychiatric disorders launched by industrial partner – Publication	3	KCL/ deCODE	48
D7	Periodic reports including a report from the Ethics Committee, Progress and Final Report to be submitted to the EU project officer.	4	deCODE	
D9	Link with patient groups and the general public trough open days and newsletter (report)	5	deCODE	36
D10	Training	5	deCODE	36
D10	Meeting on the introduction of genetic counseling in psychiatry – Event at the end of the project	5	deCODE	48
D11	Marketing of the diagnostic platform to the general public and health care professionals through meetings and open days (report)	5	deCODE	48
D12	Presentation of key findings in public talks, TV-talks and articles in newspapers about the results of the project and how these results could be relevant to the general public	5	deCODE	48

WORKPACKAGE LIST / OVERVIEW

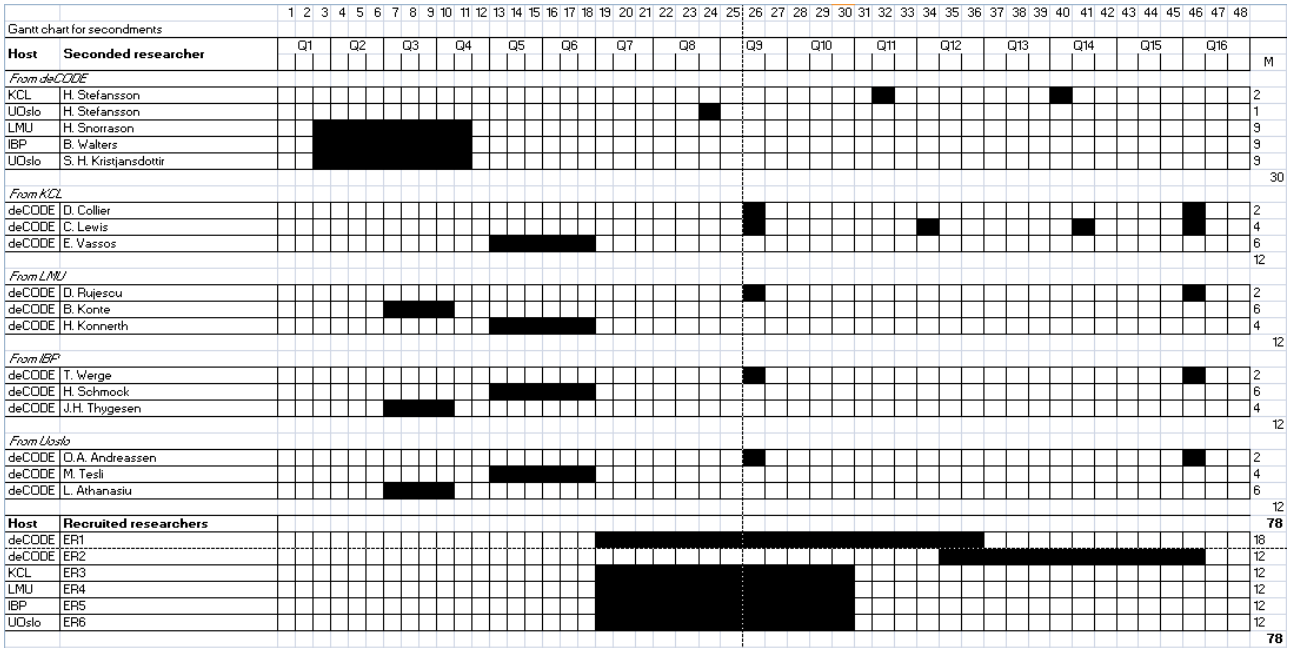
Work package	Work package title	Lead Beneficiary	Start month	End month
WP1	Identification of genomic variants conferring high and moderate risk of schizophrenia	UOslo/ deCODE	M1	M24
WP2	Deep phenotypic characterisation	KCL/ deCODE	M13	M36
WP3	Characterization of significant loci and search for causative variants or genes	KCL/ deCODE	M31	M48
WP4	Management Consortium Agreement Project Handbook Project Website Management of project finances Management of legal and ethical issues Management of project reporting	deCODE	M1	M48
WP 5	Dissemination and outreach Project factsheet Dissemination plan Publication of results	deCODE	M1	M48

LIST AND SCHEDULE OF MILESTONES

Milestone no	Milestone name	WPs* * no's.	Lead beneficiary short name	Delivery date	Comments
M1	Identification of new genetic risk variants for schizophrenia	WP1	deCODE	M18	Manuscript submitted for publication
M2	Consensus on neuropsychiatric variables for phenotype-genotype database	WP2	LMU	M20	Report released and validated by a clinical panel
M3	Identification of genetic variants affecting neuropsychological phenotypes	WP2	deCODE	M30	Manuscript submitted for publication
M4	Identification of genetic variants affecting brain structure	WP2	UOslo	M42	Manuscript submitted for publication
M5	Population based estimates of risk	WP2	IBP	M42	Manuscript

	conferred by high risk variants				submitted for publication
M6	Risk prediction model for schizophrenia	WP3	KCL	M42	Software released and validated by a user group
M7	Diagnostic product	WP3	deCODE	M46	Marketed product

GANNT CHART FOR SECONDMENTS



TRANSFER OF KNOWLEDGE

Fellow No	Recruiting participant	Seconded from participant	Who	Type of contract	Category	Planned start date	Date	Duration
1	deCODE	KCL	David Collier	B	ER>10	26	1.2.2014	2
2	deCODE	KCL	C. Lewis	A	ER>10	26	1.2.2014	4
3	deCODE	KCL	E. Wassos	A	ER<10	13	1.1.2013	6
4	deCODE	LMU	D. Rujescu	B	ER>10	26	1.2.2014	2
5	deCODE	LMU	B. Konte	A	ER<10	7	1.7.2012	4
6	deCODE	LMU	H. Konnerth	A	ER<10	13	1.1.2013	6
7	deCODE	IBP	T. Werge	B	ER>10	26	1.2.2014	2
8	deCODE	IBP	H. Schmock	A	ERS	13	1.1.2013	6
9	deCODE	IBP	J. Thygesen	A	ERS	7	1.7.2012	4
10	deCODE	UOSLO	O.A. Andreassen	B	ER>10	26	1.2.2014	2
11	deCODE	UOSLO	M. Tesli	A	ER<10	13	1.1.2013	6
12	deCODE	UOSLO	L. Athanasiu	A	ER<10	7	1.7.2012	4
13	deCODE	recruitment	TBD	A	ER<10	19	1.7.2013	18
14	deCODE	recruitment	TBD	A	ER>10	35	1.11.2014	12

15	KCL	deCODE	H. Stefansson	B	ER>10	24	1.12.2013	3
16	KCL	recruitment	TBD	A	ER<10	19	1.7.2013	12
17	LMU	deCODE	TBD	A	ER<10	3	1.3.2012	9
18	LMU	recruitment	TBD	A	ER<10	19	1.7.2013	12
19	IBP	deCODE	TBD	A	ER>10	3	1.3.2012	9
20	IBP	recruitment	TBD	A	ER<10	19	1.7.2013	12
21	UOSLO	deCODE	TBD	A	ER<10	3	1.3.2012	9
22	UOSLO	recruitment	TBD	A	ER<10	19	1.7.2013	12

PARTNERS RESPONSIBILITY AND MAIN STAFF

PARTNER 1 (CO-ORDINATOR); DECODE GENETICS

http://www.decode.com

Role:
deCODE has a longstanding track record as one of the leading authorities on human genetics worldwide. The Icelandic population sample stored at deCODE, combining a complete genealogical database with genotypes from tens of thousands of individuals, offers a unique opportunity to derive long phased haplotypes and parental origin of alleles; these properties will shed new light on already identified disease variants. Through its immense size (n_100,000), the Icelandic population sample also provides power to identify phenotypic characteristics among carriers of rare disease-associated variants.

Knowledge transferred from deCODE: 1) Software and algorithms for analysing phase and parental origin of genotype data (LRP). 2) High risk variants associated with schizophrenia uncovered by whole genome sequencing effort at deCODE 3) Expertise in imputing sequence variants into existing chip typed datasets. 4) Neuropsychological phenotypes associated with CNVs 5) Software's for obtaining anthropometric phenotypes.

Secondsments:

Hreinn Stefansson, PhD, Head of CNS division

Heimir Snorrason, BSc, research scientist

Sólveig Kristjánsdóttir, BSc, research scientist

Bragi Walters, BSc, research scientist

PARTNER 2; KING'S COLLEGE

http://www.kcl.ac.uk/

Role:
King's College operates one of the larger centres in Europe for genetic testing, counselling and research, in the Division of Genetics and Molecular Medicine and the NHS Genetics Centre. The KCL group has put effort into assessing whether 'high risk' pathogenic CNVs might be useful in a clinical genetic or diagnostic setting[34].

Knowledge transferred from KCL: 1) Algorithms combining genetic, familial and environmental factors into a comprehensive risk assessment. 2) Development of guidelines and practical training in genetic counselling.

Secondsments:

David Collier, PhD, Professor and Head of Section of Neuropsychiatric Genetics

E. Wassos, PhD, research scientist

Cathryn Lewis, PhD, Professor

PARTNER 3; LUDWIG-MAXIMILIANS UNIVERSITATET MUENCHEN

Role:
Ludwig Maximilians Universitatet has built up a vast database holding results of various neurocognitive tests and other measures contributing to a comprehensive clinical, electrophysiological and cognitive characterisation of psychiatric patients. At current this database includes data from more than 4,000 individuals with genome wide data comprising patients affected with schizophrenia and other neurodevelopmental disorders as well as population controls.

Knowledge transferred from LMU: 1) Generation of neurocognitive data to provide deeper insight into phenotypic features characterising specific disease-associated genetic variants

Secondsments:

Dan Rujescu, PhD, Head of Molecular and Clinical Neurobiology

B. Konte, PhD, research scientist

H. Konnerth, PhD, research scientist

PARTNER 4; REGION HOVEDSTADEN

Role:
Region Hovedstaden is home of the Danish Psychiatric Biobank, and is furthermore the national reference centre in Denmark for genomic analysis and genetic counselling with particular focus on its application in child PsychDPC Page 15 of 44 and adolescent psychiatry. IBP has built a comprehensive database containing information on all admittances to child and adolescent psychiatric wards in Denmark – including information on psychiatric disease in close family members of admitted cases over a 35 year period (1969-2004). Researchers at IBP are thus highly experienced in utilising data from national health registries in genetic research and inferring familial patterns in psychiatric disease.

Knowledge transferred from IBP: 1) Identification of psychiatric patients likely to carry rare disease variants (causing genomic syndromes) through analysis of health records from national registries. 2) Refinement of familial risk assessment in child- and adolescent psychiatry through re-examination of national registries.

Secondsments:

Thomas Werge, PhD, Director of Research

H. Schmock, PhD, research scientist

Johan Hilge Thygesen, PhD, research scientist

PARTNER 5; UNIVERSITETET I OSLO

Role:
Universitetet IOslo holds a high level of expertise in the acquisition and handling of MRI and other neuroimaging data, including Dr Anders M. Dale, who developed automatic quantitative brain imaging software (FreeSurfer). UOslo also has experience with data analysis from different scanners, and has already in place automated procedure to perform statistical analysis (corrections and permutation testing) of brain scans and whole genome data. Further, the partner has extensive experience and expertise in clinical and neuropsychological assessments of psychiatric patients.

Knowledge transferred from UOslo: 1) Protocol for psychiatric MRI data collection across different scanners. 2) Analysis of neuroimaging-genetics data in psychiatric disorders. 3) Evaluation of assessment methods for neurpsychological and clinical phenotypes, and assessment methods.

Secondsments:

Ole A. Andreassen, PhD, Head of Clinical Medicine, TOP study group

M. Tesli, PhD, research scientist

L. Athanasiu, PhD, research scientist

INTELLECTUAL PROPERTY RIGHTS

Intellectual property related to the human genetic discoveries will be protected by filing patent applications. While the IP protection is a strong priority, scientific findings will be rapidly reported in scientific journals.

The Consortium Agreement will deal with IPR in line with EC guidelines as put forward in the relevant EC documents (f. ex. Guide to IP rules for FP7 projects, June 2007; and model contracts), which stipulate that knowledge shall be the property of the contractor carrying out the work leading to that knowledge and that in cases of joint work, the knowledge shall be jointly owned and that contractors shall establish the necessary terms amongst themselves.

The Project Steering Committee shall ensure appropriate handling of IP issues. Care will be taken that all knowledge with potential for intellectual property will indeed be protected. The project coordinator will watch proper protection of innovative knowledge generated during the project by the participants as well as proper handling of IPR. deCODE genetics will provide the other partners with advice and assistance in matters relating to patentable results arising from the study. Care will be taken to protect the knowledge generated during the project.

IP generated through this collaboration will be split between partners based on number of samples in the association analysis. Thus, although the final analysis will take place in Iceland the IP right will be split based on the number of cases analyzed from each partner. Consortium agreement, outlining how the IP will be split, will be distributed and signed before signing the grant agreement.

RECRUITMENT STATEGY

A policy of equal opportunities, in particular between men and women, will be applied. The PsychDPC partners will equally encourage qualified female and male researcher to apply for the positions advertised.

DISSEMINATION OF KNOWLEDGE

Partners shall publish in high impact peer reviewed international journals and addition the results will be regularly communicated to scientific colleagues at meetings of national societies and at international conferences. The partners have a strong track record in this field, and several are actively involved in international scientific organizations (ISPG, ASHG, CINP, ECNP, SCNP). PsychDPC shall in addition host a mini-conference at the end of the project (M48) where the results of the project will be presented and the emerging applications of genetic testing in clinical psychiatry discussed openly in a panel including invited internationally recognized researchers in the field. The project shall also be introduced where feasible through teaching and other classic training activities by the partners (the four academic partners are all regularly involved in lecturing medical students through their university ties, as well as medical staff (nurses, doctors and other caretakers) through their association to psychiatric wards). Acknowledgement of support by the EC will be made in all publications and events. The partners will make the project a vehicle for increased contacts and exchange of information between their organisations.
Acknowledgement of support by the EC shall be made in all publications and events.

Dissemination to the patient community shall be made initially through the collaborating physicians and ultimately to the patient population at large through more general media, including a newsletter to the patients and families who have participated in research, and awareness days for patients, families and carers. The partners shall also explore the dissemination of information by novel methods, such as the UK Wellcome Trust schemes for Researchers in Residence and Junior Café Scientifique, which offer support to all comers, and the National Coordinating Centre for Pubic Engagement website. Several participants are active in dissemination of new research to patient organizations and support groups, and important novel results will also be presented to patient organizations. The project shall also assess the views of patients and their families on genetic testing and the results of this will also be used for dissemination activities through patient organisations.

The projects web page is http://www.psych-dpc.eu/contacts/ where publications, news and other relevant information are available

CONTACT INFORMATION

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KING'S COLLEGE

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PsychDPC BOARDS AND COMMITTEES

Steering committee:
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David A Collier
Dan Rujescu
Thomas Werge
Ole A. Andreassen

Operations Group:
Hreinn Stefansson
David Collier
Ole A. Andreassen

Ethics Group: