QUEST - BIH CENTER FOR TRANSFORMING BIOMEDICAL RESEARCH

QUALITY | ETHICS | OPEN SCIENCE | TRANSLATION

Action plan towards Open Science
Open Science Workshop Berlin 22.9.2017
DUE DILIGENCE, OVERDUE
Results of rigorous animal tests by the Amyotrophic Lateral Sclerosis Therapy Development Institute (ALS TDI) are less promising than those published. All these compounds have disappointed in human testing.

Challenges in academic biomedicine (selection)

**Methodology**
- Concerns about reliability and reproducibility.
- Weaknesses in planning, conducting, analysing, and reporting.
- Underutilized sharing, evaluation, and synthesis of high quality evidence.
- Nonpublication of results.
- Conflicts of interest (...among others)

**Ethics and policy**
- Focus on robust evidence of clinical promise as well as safety to hold the first tests of drugs in humans to a higher standard.
- Despair of patients means they often fail to consider the major risks intrinsic to early clinical trials of novel modalities such as stem cell interventions and gene therapy. (...among others)

**Research governance**
- Economic pressures and current reward structures can antagonize methodological robustness and rigor, as well as stimulate overinterpretation of results.
QUEST Mission Statement

... to increase the value of biomedical research at BIH and beyond.
• **Open Science**: improve the accessibility and transparency of BIH research and its results through Open access and Open data.

• **Quality assurance**: promote compliance of preclinical and clinical research with standards and guidelines on design, conduct, analysis and reporting.

• **Education**: develop and implement training and teaching resources on experimental and study design, methods to reduce bias, new modes of publishing, open science, etc.

• **Meta-Research**: identify opportunities for improving research practice and obtain evidence for the impact of its activities through ‘research on research’.
• **Rewards and incentives**: develop, implement, and assess the impact of novel indicators incentives and metrics to improve the current funding, reward and career system in academic research.

• **Research for and with the public**: foster public outreach and public involvement in BIH research (Citizen science / Participatory health research).

• **Bioethics of translation**: implement innovative, scientifically informed policies and training modules for research quality and human protections.

• **Think tank**: act as advisors to stakeholders in biomedicine from funders to politics.
QUEST Team

Dr. Stephanie Ohlraun
Administrative Head: Overall coordination and budgets

Lisa Liebenau
Open Science Officer: open access representative BIH/Charité, publication officer

Dr. Nico Riedel
Data Scientist: Data and text mining, social network- and bibliometric analyses

Dr. Miriam Kip
Indicators & Incentives officer ('Good evaluation practice')

Dr. Ulf Toelch
Education, Training – Quality of research

NN
IT administrator: digital research infrastructures, repositories, electronic lab notebook
Prof. Dr. Ulrich Dirnagl, BIH-Chair and QUEST Founding Director
Research Group ‘Transforming biomedical research’

BIH-Professor (NN)
Research Group ‘Bioethics of translation’

Junior group leader (NN)
Research Group ‘Improving value of preclinical research through meta-research’
BIH Professorship ‘Bioethics of Translation’

Jonathan Kimmelmann (call)
Associate Professor in the Biomedical Ethics Unit, Social Studies of Medicine, McGill University, Montreal

Daniel Strech (loco secundo)
Institute for History, Ethics and Philosophy of Medicine, Hannover Medical School
QUEST Scientific Advisory Panel

Gerd Antes  
Cochrane Deutschland, Freiburg, Germany

Alastair Buchan  
University of Oxford, Medical School und Medical Sciences Division, Oxford, UK

Katherine Button  
University of Bath, Department of Psychology, Bath, UK

John P.A. Ioannidis  
Stanford University, School of Medicine, School of Humanities and Sciences, Meta-Research Innovation Center, Stanford, USA

Emily Sena  
University of Edinburgh, Centre for Clinical Brain Sciences, Edinburgh, UK
Examples of ongoing projects
Open science policy - FAIR use of data
Counseling / Education / Training
Einrichtung eines Publikationsfonds für die Charité – Universitätsmedizin Berlin und Verstetigung der Finanzierung von Open-Access-Publikationen

Förderlinie: Wissenschaftliche Literatur- und Informationssysteme
Förderprogramm: Open Access Publizieren
Teil B Beschreibung des Vorhabens

Antragsteller:
Univ.-Prof. Dr. Peter-André Alt, Präsident
Freie Universität Berlin, Kaiserswerther Str. 16-18, 14195 Berlin
Prof. Dr. med. Sabine Kunst, Präsidentin, Humboldt Universität zu Berlin, Unter den Linden 6, 10099 Berlin
Ansprechpartner:
Prof. Dr. Axel Radlach, Dekan
Charité – Universitätsmedizin Berlin, Charitéplatz 1, 10117 Berlin

BIH OPEN ACCESS PUBLICATION FUND

To promote the publication in open access journals, the QUEST – BIH Center for Transforming Biomedical Research offers the payment of Open Access fees for a total of up to 15 publications. The applications are processed according to the order in which they are received.

The costs for your Open Access publication can be paid by the QUEST Center if the following formal criteria are met:

1. The publication has already been accepted by the publisher.
2. The first, last or corresponding author of the publication is professor or "Privatdozent" at the Charité, leading researcher at the MDC or published with the BIH affiliation.
3. The journal in which you have published is listed in the DOAJ Directory of Open Access Journals and is not a so-called hybrid journal.
4. Your article is licensed under a Creative Commons license (preferably CC by) and can be used without restrictions.
5. The publisher’s invoice is addressed to the BIH.

Please apply the payment of your Open Access fee here: BIH Portal

Questions can be addressed to: openscience@bihhealth.de

Unsure whether you are eligible to apply?
Just send us your open access paper and we will check the fulfillment of the criteria for you.

Contact
Lisa Uebeau
Referentin für Open Science
Open-Access-Beratung BIH und Charité
openscience@bihhealth.de
The QUEST 1,000 € Preregistration Award

*Preregister your preclinical studies challenge – increase the credibility of your results and get early credit for your ideas!*

The QUEST Center supports the preregistration of planned preclinical studies. Preregistration increases the credibility of results, the conclusions based on them, and secures the originality of ideas and hypotheses before experiments have been performed.

QUEST is offering **15 awards of 1,000 €** to first/last/corresponding BIH, MDC or Charité authors of preclinical research papers containing preregistered (basic or translational, not clinical) studies.

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The QUEST 1,000 € NULL results and Replication study Award

*Publish your NULL results – Fight the negative publication bias!*

*Publish your Replication Study – Fight the replication crises!*

The QUEST Center supports the publication of results which do not support the initial hypothesis, so called NULL results, sometimes unfairly labelled as ‘negative studies’. We also want to promote the publication of studies with the explicit attempt to replicate own results or the results of others.

QUEST is offering **15 awards of 1,000 €** each to first/last/corresponding BIH, MDC or Charité authors of research papers in which the main result is a NULL or ‘negative’, or in which the replication of own results or the results of others is attempted. Basic, translational as well as clinical studies are eligible.

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The QUEST 1,000 € Open Data Award

*Make your data FAIR - Findable, Accessible, Interoperable, and Re-usable!*

The QUEST Center strives to make relevant research data findable, accessible, interoperable and re-useable (‘FAIR’).

QUEST is offering **15 awards of 1,000 €** each to first/last/corresponding BIH, MDC or Charité authors of research papers which have unconditionally shared their original data by citing them in the references of the paper via the persistent identifier of an open repository containing the annotated data. Basic, translational as well as clinical studies are eligible.
Develop and deploy structured quality management, e.g. roll out Electronic Laboratory Notebook
Develop and deploy structured quality management, e.g. LabCritical Incidence Reporting
Develop and implement novel (& more efficient) study designs

Increasing efficiency of preclinical research by group sequential designs

Konrad Neumann\textsuperscript{1e}, Ulrike Grittner\textsuperscript{1,2e}, Sophie K. Piper\textsuperscript{1,2,3}, Andre Rex\textsuperscript{2,4}, Oscar Florez-Vargas\textsuperscript{5}, George Karystianis\textsuperscript{5}, Alice Schneider\textsuperscript{1,2}, Ian Wellwood\textsuperscript{2,7}, Bob Siegerink\textsuperscript{5,8}, John P. A. Ioannidis\textsuperscript{9}, Jonathan Kimmelman\textsuperscript{10}, Ulrich Dmann\textsuperscript{2,3,4,6,11,12}

Final analysis

\textbf{Frequentist:} Reject $H_0$ if $P < \alpha_3$

\textbf{Bayes:} State $d \neq 0$ if 0 is not in the 96.8\% credible interval of effect size $d$

Interim analysis 1

\textbf{Frequentist:} Terminate and reject $H_0$ if $P < \alpha_1$

\textbf{Bayes:} Terminate if 0 is not in the 99.8\% credible interval of effect size $d$

Interim analysis 2

\textbf{Frequentist:} Terminate and reject $H_0$ if $P < \alpha_2$

\textbf{Bayes:} Terminate if 0 is not in the 96.8\% credible interval of effect size $d$
IMI Project - Data quality in preclinical research development

European Quality In Preclinical Data (EQIPD)

- 11 industry partners (Coordinated by T. Steckler, Janssen)

- 18 applicants (coordinated by M. Macleod/E. Sena U Edinburgh)
  - 10 Universities (Germany, Netherlands, Switzerland, UK)
  - 6 SMEs
  - 1 scientific society
  - 1 PMO
Structured quality assurance *from and for* academic preclinical biomedicine - Establishment and proof of concept

### The research process

<table>
<thead>
<tr>
<th>Policy</th>
<th>Plan</th>
<th>Conduct</th>
<th>Analyze</th>
<th>Report</th>
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<tbody>
<tr>
<td>Mission, Goals, Vision</td>
<td>Hypothesis, Power, Preregistration...</td>
<td>Instructions, SOPs, Reduction of bias...</td>
<td>Statistics, validity check...</td>
<td>Publication, Repositories...</td>
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### Supporting processes

- **Documentation / Data recording and archiving**
- **Error management**
- **Adherence** Legal regulations, GSP, Animal welfare, ...
- **Biosample, device and materials management**
- **Communication** Work group and Labmeeting...  
- **Education / Training** Methods to reduce bias, statistics, experimental design...
- **Laboratory organization and administration** Instructions, regulations, responsibilities...
- **Quality assurance** Auditing, Indicators, Metrics, Evaluation

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**Funded by**: VolkswagenStiftung
Develop and deploy good institutional practice (incl. novel incentives and rewards)

Institutions must do their part for reproducibility

Tie funding to verified good institutional practice, and robust science will shoot up the agenda, say C. Glenn Begley, Alastair M. Buchan and Ulrich Dirnagl.
International Survey on Organizational Research Climate und Research Practice
### Part 4 Items regarding publication practices

<table>
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<tr>
<th>Item</th>
<th>Description</th>
<th>Options</th>
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</thead>
</table>
| I.4a | How committed are researchers in your immediate research environment to apply open access in their publication practice? | (1) Not at All  
(2) Somewhat  
(3) Moderately  
(4) Very  
(5) Completely  
(9) No Basis for Judging |
| I.4b | How committed are researchers in your immediate research environment to apply open data principles when publishing research results? | (1) Not at All  
(2) Somewhat  
(3) Moderately  
(4) Very  
(5) Completely  
(9) No Basis for Judging |
| I.4c | How committed are the senior administrators at your institution (Charité / MDC) (e.g., deans, executive board, scientific directorate) to apply open access in their publication practice? | (1) Not at All  
(2) Somewhat  
(3) Moderately  
(4) Very  
(5) Completely  
(9) No Basis for Judging |
| I.4d | How committed are the senior administrators at your university institution (Charité / MDC) (e.g., deans, chancellors, executive board, scientific directorate vice presidents) to apply open data principles when publishing research results? | (1) Not at All  
(2) Somewhat  
(3) Moderately  
(4) Very  
(5) Completely  
(9) No Basis for Judging |
Novel indicators for performance oriented funding

until now:

Performance oriented funding ~ 10 Mio. €

Third party funding

- Funding (Weighted DFG/BMBF/Industrie) 50 %
  - Goal: Increase Charite state funding

Publications

- Journal Impact Factor ('raw') 50 %
  - Goal: Increase chances to secure top grants
Novel indicators for performance oriented funding

from 2018:

LOM ~ 10 Mio. €

Third party funding

Funding
(Weighted DFG/BMBF/Industrie)
50 %

Goal:
Increase Charite state funding

Publications

Journal Impact Factor
(Author position)
25 %

Ziel:
Increase chances to secure top grants

Relative Citation Ratio (NIH)
25 %

Ziel:
Improve ranking of Charite

Top 1 % and IF> 15 = 0,5 Mio. Euro

‘Icing on the cake’ Quality/Open science
### Description of Professorship

<table>
<thead>
<tr>
<th>Description of Professorship</th>
<th>Calls</th>
<th>notes</th>
<th>date due</th>
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<tr>
<td>W3 Universitatsprofessor für Hämatologie und Onkologie m. S. Lymphome/Multiple Myelom</td>
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<tr>
<td>W3 Universitatsprofessor für Hämatologie und Onkologie m. S. Medizinische/Internistische Onkologie</td>
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<tr>
<td>Further vacancies at Charité</td>
<td>call for applications</td>
<td>application notes</td>
<td>28.09.2017</td>
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### Dates

- 28.09.2017
Main Focus: Science
- e.g. Apoptosis

Main Focus: Clinic
- e.g. Clinical Psychotherapy

Please describe in short what you believe is your scientific contribution in your scientific field.

[scientific contribution]

Remaining characters: 1000

What do you consider to be the 5 most important papers you have published? Please briefly justify this selection and mention your respective contribution. How were the work accepted in the scientific field, what impact did they have on the advancement of knowledge or the clinical practice (therapies, guidelines)?

[Pubmed-ID] OR [DOI]

[Description of first publication] [Own share of the first publication]

The Charte attaches great importance to transparent, replicable research and supports the objectives of Open Science (Open Access, Open Data). This includes the registration of studies in registries (clinicaltrials.gov, DRKS, etc.), the preregistration of studies, and the publication of negative and zero results. How have you been pursuing these goals so far and what are your plans for the future?

... [Narrative]

Remaining characters: 1000

Charité is interested in team science and collaborations. Please describe in short most important collaboration projects within recent five years.

- e.g. Karolinska Inst.

[Description]

Please describe in short your interactions with relevant actors in biomedicine, e.g. industry, patient care, policy panel, etc.

... [Narrative]

Remaining characters: 1000

[relevant patents]

[prefatent number]

[Description]
Novel perspective on publication records

![Graph showing NIH Percentile vs. Publications]
Tracking (and safeguarding) the publication of clinical trials

Nico Riedel

Daniel Strech (MHH)
Outreach to the public and participatory research (MIDATA) - pilot with BELOVE

MIDATA Platform
Data storage, management, visualization, consent and access management

3rd Party Apps

3rd Party Apps

3rd Party Apps

Developed with & by partners

Developed by ETHZ & BFH

General Assembly

Ethics committee

Governance rules

Ernst Hafen (ETH Zürich)

Kati Jegzentis

Sein Schmidt
Policy: E.g. counseling FDA on QM in 'unregulated' biomedical research

Quality Management for Academic Labs: Burden or Boon?

Ulrich Dirnagl, Ph.D.

Date: May 31, 2017, 10-11:30AM
FDA White Oak Campus
Building 2, Room 2051 and Webinar
Lost in the Maze? Navigating Evidence and Ethics in Translational Neurosciences

The Herrenhausen Conference on February 14-16, 2018 in Hannover focuses on major scientific and ethical challenges of novel neurological interventions and how they can be overcome. Participants will explore how critically needed trials of new treatment modalities can be launched safely and conducted ethically.
Alison Abbott (Nature Publishing Group/USA), Enrica Alteri (European Medicines Agency/UK), Christopher Baum (Hannover Medical School/Germany), Julie Belluz (Vox.com/USA), Annelien Bredenoord (Utrecht University/The Netherlands), Virginie Bros-Facer (Eurordis/France), Dominique Brossard (University of Wisconsin-Madison/USA), Leena Bruckner-Tuderman (Albert-Ludwigs-University of Freiburg and Deutsche Forschungsgemeinschaft/Germany), Alex Capron (University of Southern California/USA), Timothy Caulfield (University of Alberta/Canada), Iain Chalmers (James Lind Initiative/UK), Isabelle Clavier (Sanofi/France), Katherine Cowan (James Lind Alliance/UK), Ulrich Dirnagl (Charité Berlin and Berlin Institute of Health/Germany), Jodi Halpern (University of California Berkeley /USA), Henrike Hartmann (Volkswagen Foundation/Germany), Insoo Hyun (Case Western Reserve University/USA), John Ioannidis (Stanford University/USA), Katie Jackson (Help 4 HD International), Nanette Joyce (University of California Davis/USA), Scott Kim (National Institutes of Health/USA), Jonathan Kimmelman (McGill University/Canada), Paul Knoepfler (University of California Davis/USA), Wilhelm Krull (Volkswagen Foundation/Germany), Malcolm Macleod (University of Edinburgh/UK), Frank Miedema (University Medical Center Utrecht/The Netherlands), Jeffrey Mogil (McGill University/Canada), Ubaka Ogbohu (University of Alberta/Canada), Sarah Perrault (University of California Davis/USA), Laurent Pradier (Sanofi/France), Axel Radlach Pries (Charité Berlin/Germany), Bernard Ravina (Voyager Therapeutics/USA), Emily Sena (University of Edinburgh/UK), Shai Silberberg (National Institutes of Health/USA), Daniel Strech (Hannover Medical School/Germany), Thomas Streckler (Janssen Pharmaceutics/Belgium), Vicki Wheelock (University of California Davis/USA), Hanno Würbel (University of Bern/Switzerland), Mark Yarborough (University of California Davis/USA) and others.
The OPENING of the QUEST Center for Transforming Biomedical Research
November 16/17, 2017, Berlin

Program – November 16, 2017

Venue: Charité Campus Mitte, Charitéplatz 1, 10117 Berlin
Address on Campus: Hörsaalruine, Virchowweg 17

6:30-7:00 pm  Registration

7:00-7:15 pm  OPENING REMARKS by Martin LOHSE (Berlin Institute of Health, Max Delbrück Center for Molecular Medicine) and Axel Radlach PRIES (Berlin Institute of Health, Charité - Universitätsmedizin Berlin)

7:15-8:15 pm  KEYNOTE LECTURE by David MOHER
The quest for better behavior in science
Ottawa Hospital Research Institute; School of Epidemiology and Public Health, University of Ottawa, Canada

8:15-10:00 pm  CHEESE, WINE & MUSIC

Registration and program: http://bit.ly/questopening
Program – November 17, 2017

Venue: Festsaal der Humboldt Graduate School, Luisenstraße 56, 10115 Berlin

8:45-9:15 am Registration & Coffee

9:15-9:30 am WELCOME REMARKS by Ulrich DIRNAGL (Berlin Institute of Health, Charité - Universitätsmedizin Berlin)

9:30-11:00 am TALKS by Ivan ORANSKY, Ernst HAFEN and Trish GROVES

Ivan ORANSKY
Retractions, post-publication peer review, and fraud: scientific publishine’s Wild West

Ernst HAFEN
Genome meets iPhone – citizen-controlled use of personal data for research
Department of Biology, Institute of Molecular Systems Biology, ETH Zürich, Switzerland

Trish GROVES
Open Science: why it's much more than simply data sharing (and why that's not simple)
The BMJ, UK

11:00-11:30 am Coffee break

11:30 am-1:00 pm TALKS by Londa SCHIEBINGER, Daniel STRECH and Frank MIEDEMA

Londa SCHIEBINGER
Gendered innovations in health and medicine
History Department, Stanford University, USA

Daniel STRECH
Effective and efficient bioethics of translation! How to?
Institute for History, Ethics and Philosophy of Medicine, Hannover Medical School, Germany

Frank MIEDEMA
New incentives and rewards for better science: the dean's perspective
University Medical Center Utrecht, Netherlands

1:00-1:30 pm GENERAL DISCUSSION and CLOSING REMARKS

Registration and program: