



QUEST - BIH CENTER FOR TRANSFORMING BIOMEDICAL RESEARCH

QUALITY | ETHICS | OPEN SCIENCE | TRANSLATION

Action plan towards Open Science
Open Science Workshop Berlin 22.9.2017

THIS WEEK

EDITORIALS

DRUGS New agreement to tackle pharmaceutical pollution **p.184**

WORLD VIEW Vaccination the best way to measure health care **p.185**



Let's think about cognitive bias

The human brain's habit of finding what it wants to find is a key problem for research. Establishing robust methods to avoid such bias will make results more reproducible.

Ever since I first learned about confirmation bias I've been seeing it everywhere. Some researchers already do this well, so one relatively simple strategy

Reproducibility: Seek out stronger science

• **Monya Baker**

Nature 537, 703–704



DATA SHARING

An open mind on open data

The move to make scientific findings transparent can be a major boon to research, but it can be tricky to embrace the change.

Power failure: why small sample size undermines the reliability of neuroscience

Katherine S. Putman, John D. A. Little

Repetitive flaws

Strict guidelines to improve the reproducibility of experiments are a welcome move.

From next week, scientists who submit grant applications to National Institutes of Health (NIH) will be asked to take more care. As part of an increasing drive to boost the reliability of research, the NIH will require applicants to explain the scientific premise behind their proposals and defend the quality of their experimental designs. They must also account for biological variability, for example, by including both male and female mice in planned experiments and describe how they will authenticate experimental materials such as cell lines and antibodies.

These demands are timely, sensible and, if researchers have followed the advice of their scientific societies, will sound familiar. Over the past year, a string of organizations have published their statements and guidelines to boost the reproducibility of research.

Collectively, the message is: show your work, and don't fool yourself with unreliable measurements or shoddy data. Instead, establish

from the Federation of American Societies for Experimental Biology, for example, or the American Society for Cell Biology. The importance of everything is not studied. Infrastructure. The American Society has had a long history of creating community works, and fur

Raise standards for preclinical cancer research

C. Glenn Begley and Lee M. Ellis propose how methods, publications and incentives must change if patients are to benefit.

Fewer numbers, better science

Scientific quality is hard to define, and numbers are easy to look at. But bibliometrics are warping science — encouraging quantity over quality. Leaders at two research institutions describe how they do things differently.



There are at least six things in this picture that quality assurance managers would try to improve. Can you spot them?

QUALITY TIME

IT MAY NOT BE SEXY, BUT QUALITY ASSURANCE IS BECOMING A CRUCIAL PART OF LAB LIFE.

BY MONYA BAKER

WORKPLACE CLIMATE

Metrics for ethics

Focus on perceived working conditions could help graduate schools to train responsible researchers.

THIS WEEK

EDITORIALS

POSTDOCS More pay but fewer jobs on the way **p.438**

WORLD VIEW Treat antibiotic resistance as an ecological crisis **p.439**



DRONES Tiny flying robots with power to stick around **p.441**

Reality check on reproducibility

A survey of Nature results. Research NATURE | NEWS

Muddled meanings hamper efforts to fix reproducibility crisis

Researchers tease out different definitions

THE LANCET

"85% of health research is wasted."

Research: increasing value, reducing waste

Acknowledging and Overcoming Nonreproducibility in Basic and Preclinical Research

Science for nonreproducibility in basic and pre-clinical research vs 0.71 (95% CI),

biomedical research from diverse

COMMENT

nature International weekly journal of science

Home | News & Comment | Research | Careers & Jobs | Current Issue | Archive | Audio & Video

News & Comment | News | 2016 | May | Article

NATURE | NEWS

Missing mice: gaps in data plague animal research

Reports of hundreds of biomedical experiments lack essential information.



Hide results to seek the truth

More fields should, like particle physics, adopt blind analysis to thwart bias, urge Robert MacCoun and Saul Perlmutter.

Believe it or not: how much we rely on published data on power

Low statistical power in biomedical science: a review of three human research domains

Scientific method: Statistical errors

P values, the 'gold standard' of statistical validity, are not as reliable as we assume.

ROYAL SOCIETY OPEN SCIENCE

rsos.royalsocietypublishing.org

Research



Confidence in preclinical research

For decades, model organisms have provided an important reductionist approach for understanding

making strides in their efforts to understand and for the complexity of the microbiome in rodent models

DUE DILIGENCE, OVERDUE

Results of rigorous animal tests by the Amyotrophic Lateral Sclerosis Therapy Development Institute (ALSTDI) are less promising than those published. All these compounds have disappointed in human testing.

Perrin S (2014) Nature 407:423-426

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.

QUEST Approach

- **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’.

QUEST Approach (continued)

- **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



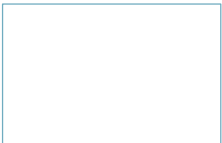
Dr. Miriam Kip

Indicators & Incentives officer ('Good evaluation practice')



Dr. Ulf Toelch

Education, Training – Quality of research



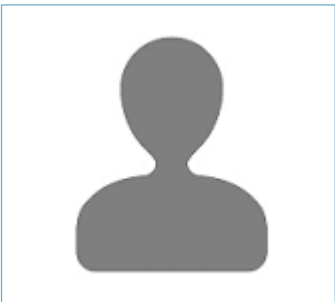
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IT administrator: digital research infrastructures, repositories, electronic lab notebook

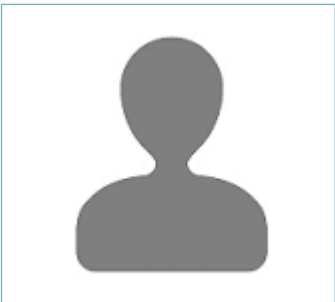
QUEST Research Groups



**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 Kimmelman (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

Lisa Liebenau



QUEST OA FUND



Projektantrag

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.-Ing. Dr. Sabine Kunst, Präsidentin,
Humboldt-Universität zu Berlin, Unter den Linden 6, 10099 Berlin

Ansprechpartner:

Prof. Dr. Axel Radlach Pries, Dekan
Charité – Universitätsmedizin Berlin, Charitéplatz 1, 10117 Berlin



The screenshot shows the website for the BIH Open Access Publication Fund. The page title is "BIH OPEN ACCESS PUBLICATION FUND". The main content area includes a heading "BIH OPEN ACCESS PUBLICATION FUND" and a sub-heading "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." Below this, it states "The costs for your Open Access publication can be paid by the QUEST Center if the following formal criteria are met:" followed by a list of five criteria:

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@bihealth.de

On the right side, there are two callout boxes:

- 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 Liebenau
Referentin für Open Science
Open-Access-Beauftragte BIH und Charité
openscience@bihealth.de

The top navigation bar includes "INSTITUTE RESEARCH ACADEMY NEWS" and "QUEST Center" is highlighted in the main menu.

Initiatives (continued...)

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.

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.

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

F1000Research

F1000Research 2016, 5:2 Last updated: 25 JUL 2016



OPINION ARTICLE

A pocket guide to electronic laboratory notebooks in the academic life sciences [version 1; referees: 4 approved]

Ulrich Dirnagl¹⁻⁵, Ingo Przesdzing¹

[F1000Research 2016, 5:2](#) (doi: [10.12688/f1000research.7628.1](https://doi.org/10.12688/f1000research.7628.1))

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MAKE MORE OUT OF YOUR RESEARCH

labfolder is the easiest way to document your research and to organize your protocols and data. Whether you want to use your smartphone to take notes, have all your data organized in one place, or collaborate with colleagues - labfolder is an essential part of your laboratory equipment that helps you to accelerate your research!

Ingo Przesdzing



Develop and deploy structured quality management, e.g. LabCritical Incidence Reporting



COMMUNITY PAGE

A Laboratory Critical Incident and Error Reporting System for Experimental Biomedicine

Ulrich Dirnagl^{1,2,3,4,5*}, Ingo Przesdzing¹, Claudia Kurreck¹, Sebastian Major¹



PLOS Biology | DOI:10.1371/journal.pbio.2000705 December 1, 2016

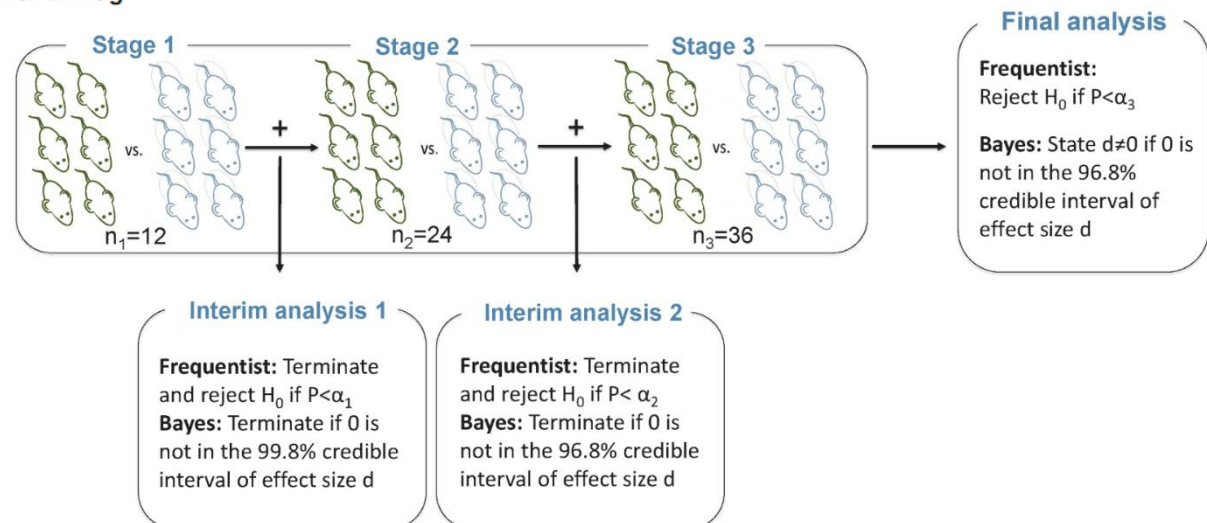


Develop and implement novel (& more efficient) study designs

PERSPECTIVE

Increasing efficiency of preclinical research by group sequential designs

Konrad Neumann¹, Ulrike Grittner^{1,2}, Sophie K. Piper^{1,2,3}, Andre Rex^{2,4}, Oscar Florez-Vargas⁵, George Karystianis⁶, Alice Schneider^{1,2}, Ian Wellwood^{2,7}, Bob Siegerink^{2,8}, John P. A. Ioannidis⁹, Jonathan Kimmelman¹⁰, Ulrich Dirnagl^{2,3,4,8,11,12}



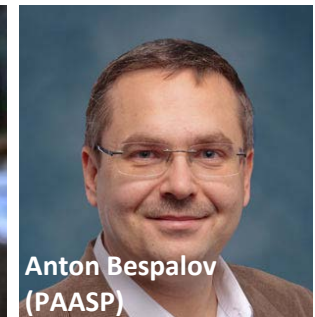
IMI Project - Data quality in preclinical research development

European Quality In Preclinical Data (EQIPD)

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

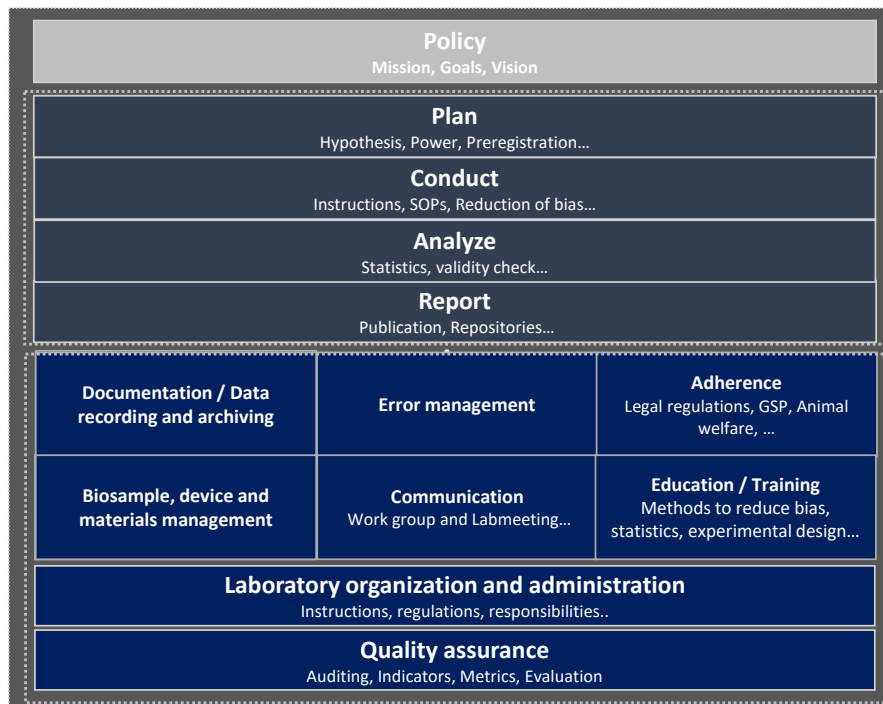
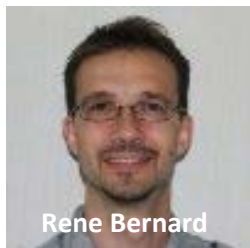
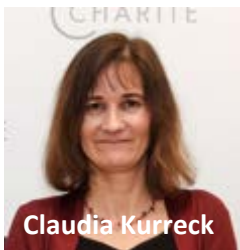


- 18 applicants (coordinated by M.Macleod/E.Sena U Edinburgh)
 - 10 Universities (Germany, Netherlands, Switzerland, UK)
 - 6 SMEs
 - 1 scientific society
 - 1 PMO



PREMIER - Predictiveness and Robustness through Modular Improvement of Experimental Research

Structured quality assurance *from and for* academic preclinical biomedicine - Establishment and proof of concept



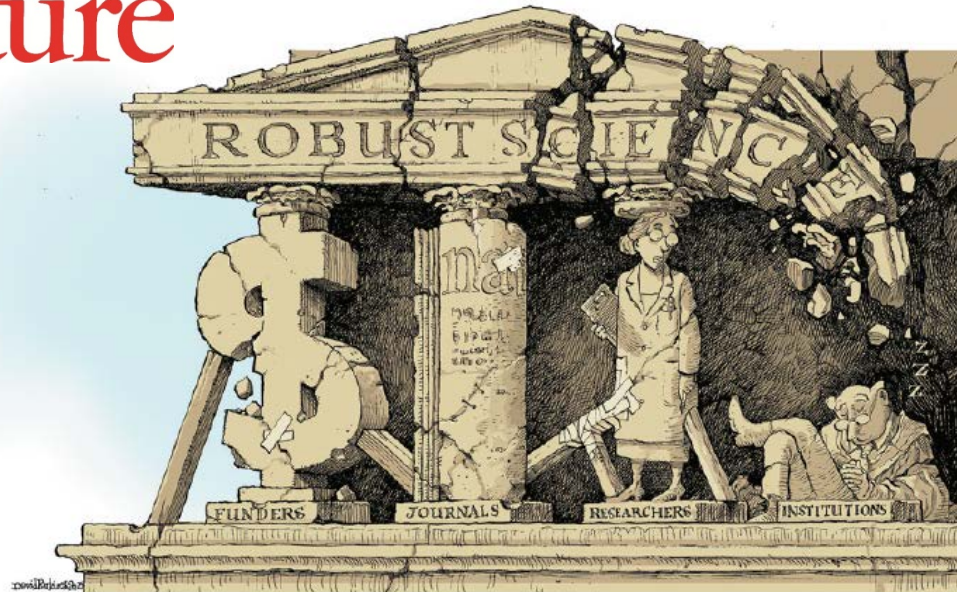
The research process

Supporting processes

Funded by

Develop and deploy good institutional practice (incl. novel incentives and rewards)

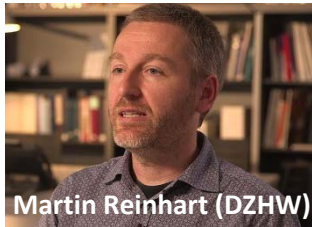
nature



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



McGill



THE UNIVERSITY
of EDINBURGH

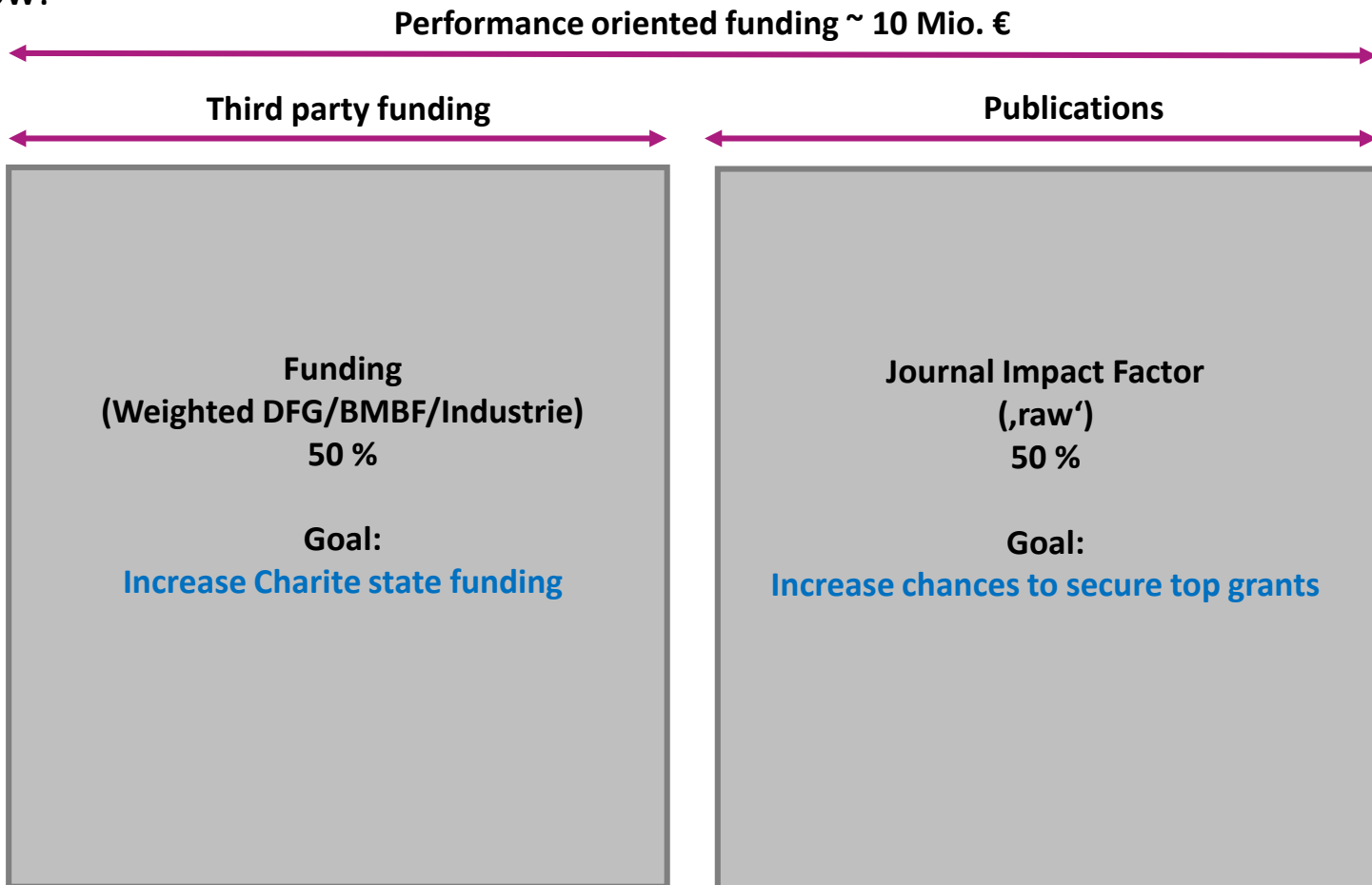
International Survey on Organizational Research Climate und Research Practice

Part 4 Items regarding publication practices

<u>I.4a</u>	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
<u>I.4b</u>	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
<u>I.4c</u>	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
<u>I.4d</u>	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

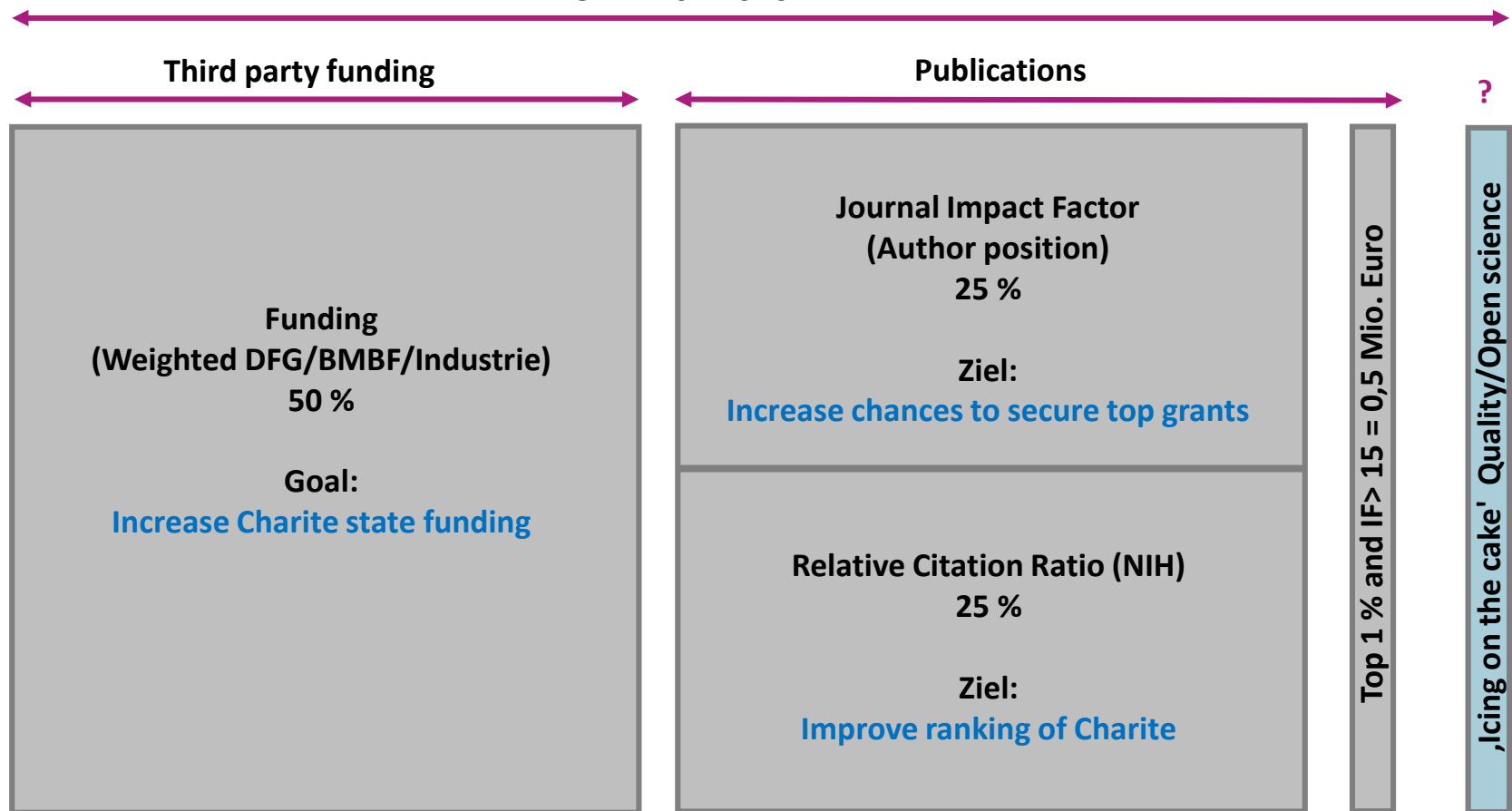
until now:



Novel indicators for performance oriented funding

from 2018:

LOM ~ 10 Mio. €





Miriam Kip





Axel Pries


QUEST Opening | BIH x Charité application service x

Sicher | <https://career.charite.de/am/?site=home&lang=eng>

Apps PMed LEO Webst Synon JCBFM Forum ExpNeuropedia OpenProject QUEST QUEST SP Ex.Neu Tel. Weitere Lesezeichen

Professorship Application Service




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Applicants-Management Charité

Currently Vacant Professorships

Description of Professorship	calls	notes	date due
W3 Universitätsprofessur für Hämatologie und Onkologie m. S. Lymphome/Multiples Myelom	call for applications	application notes	28.09.2017
W3 Universitätsprofessur für Hämatologie und Onkologie m. S. Medizinische/Internistische Onkologie	call for applications	application notes	28.09.2017
Further vacancies at Charité	Job offers		



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 Charité 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?**

...

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.

...

Remaining characters: 1000

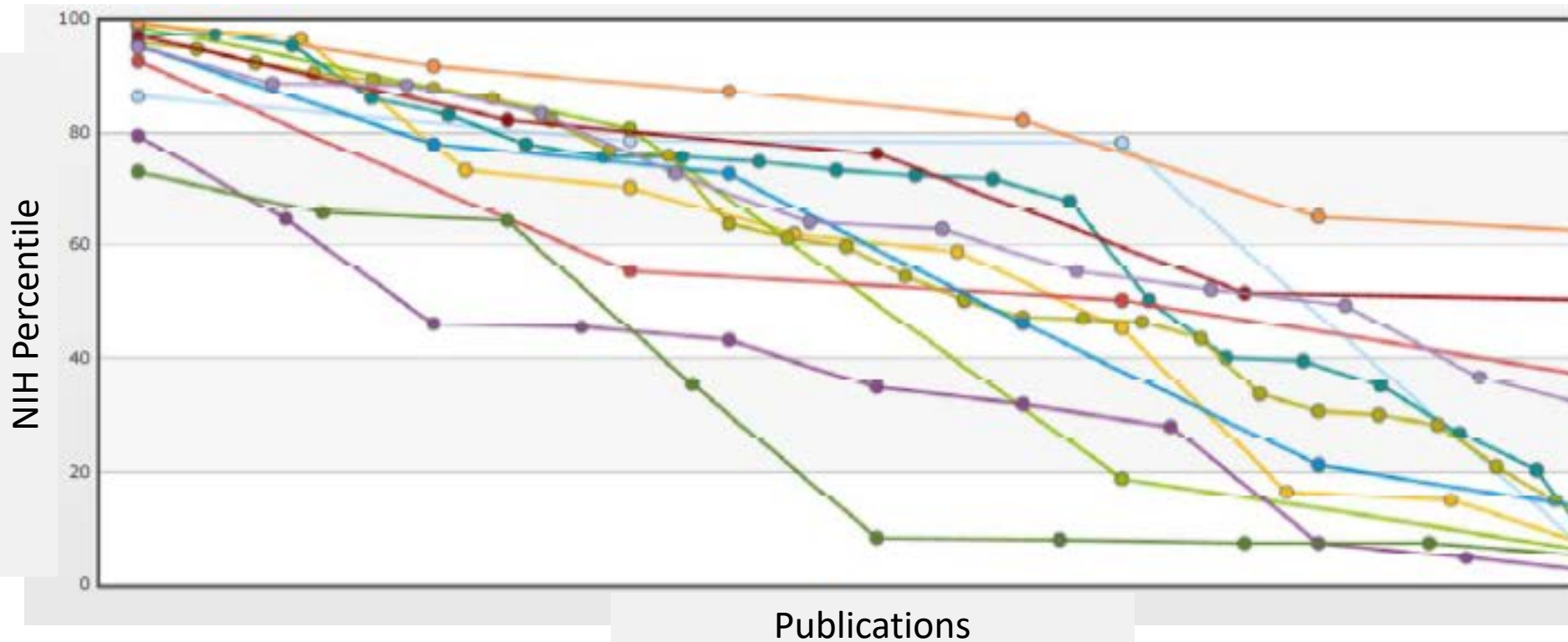
relevant patents

[patent number]

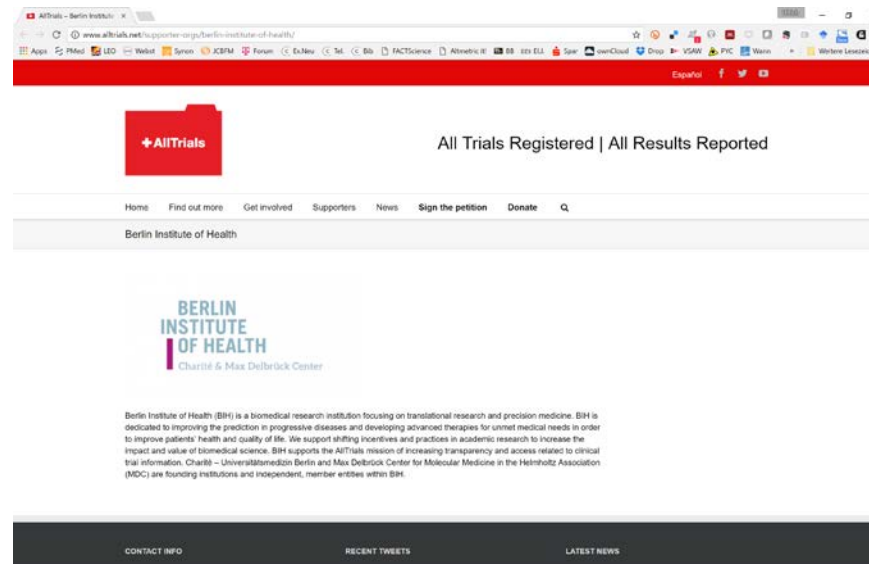
[Description]



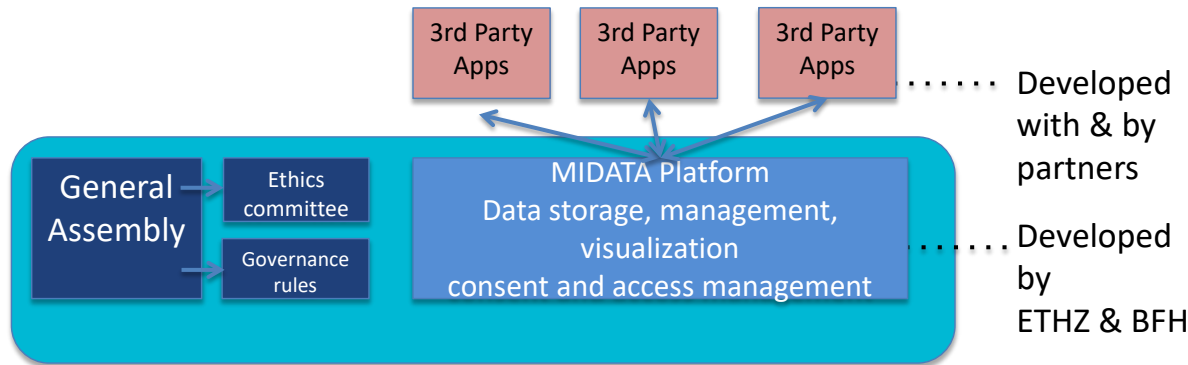
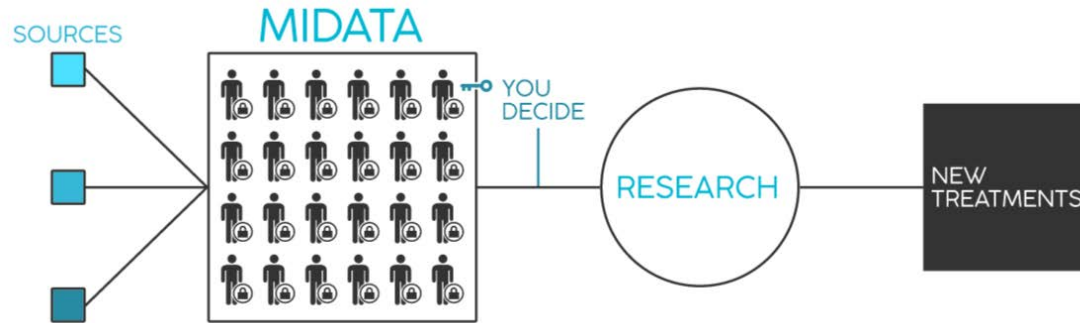
Novel perspective on publication records



Tracking (and safeguarding) the publication of clinical trials



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



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.

<http://www.volkswagenstiftung.de/hktranslationalneuroscience>

FEBRUARY 14 - 16, 2018 / HANOVER, GERMANY

LOST IN THE MAZE? NAVIGATING EVIDENCE AND ETHICS IN TRANSLATIONAL NEUROSCIENCE

HERRENHAUSEN CONFERENCE

ORGANIZED BY

Prof. Dr. Ulrich Dirnagl, Charité Berlin
and Berlin Institute of Health
Prof. Mark Yarborough, UC Davis

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MORE INFORMATION

www.volkswagenstiftung.de/hktranslationalneuroscience



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), **Malcom Macleod** (University of Edinburgh/UK), **Frank Miedema** (University Medical Center Utrecht/The Netherlands), **Jeffrey Mogil** (McGill University/Canada), **Ubaka Ogbogu** (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 Pharmaceuticals/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 publishing'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**

**QUEST
CENTER**

Transforming Biomedical Research
Berlin Institute of Health

Registration and program:

<http://bit.ly/questopening>