Workshop Schedule
Making Sense of Clinical Translation: Ethical, Regulatory and Policy Challenges for Europe and the United States
Fondation Brocher, Hermance, Switzerland

Organized by Erik Aarden (University of Vienna, Austria), Alessandro Blasimme (INSERM, France), Dustin Holloway (Harvard Medical School, United States), Luca Marelli (European School of Molecular Medicine & University of Milan, Italy)

May 17

Evening Dinner

Introduction by/of the organizers (Luca Marelli, European School of Molecular Medicine, Italy))
Introductions by Participants

May 18

Welcome and Introductions

8.45-9:15 - *Introductory Remarks by the Organizing Committee (Erik Aarden, University of Vienna, Austria))*
Introductory Remarks by Angela Simone (Fondazione Giannino Bassetti)

Morning Session: Expanding Access/Remaking Risk

9:15-10:45 - Keynote Speaker & Discussion:

- Hans-Georg Eichler (European Medicines Agency, United Kingdom)
  From Adaptive Licensing to Adaptive Pathways: Delivering a Flexible Life-Span Approach to Bring New Drugs to Patients.

10:45-11:15 - Coffee Break

11:15-13:15 - Panel & Discussion: Chair: Rachel Douglas-Jones (IT University of Copenhagen, Denmark)

- Alessandro Blasimme (INSERM, France)
  Evidence, uncertainty and the new ethics of adaptation.
- Nadine Levin (University of California Los Angeles, United States)
  What's Being Translated in "Translational Research"?
- Effy Vayena (University of Zürich, Switzerland)
  TBA
- Christian Haddad (University of Vienna, Austria)
  Enacting the promise of stem cell therapy: visions, imaginaries, and struggles over biomedical innovation

13:15-14:30 - Lunch Break

Afternoon Session: Re-imagining National Priorities

14:30-16:00 - Keynote Speaker & Discussion:

- Sheila Jasanoff (Harvard University, United States)
  Citizens and Subjects in the Politics of Translation

16:00-16:30 - Coffee Break

16:30-18:30 - Panel & Discussion: Chair: Ulrike Felt (University of Vienna, Austria)

- Luca Marelli (European School of Molecular Medicine, Italy)
  Performing translations in iPCS-based Innovation
- Kalina Kamenova (University of Alberta, Canada)
  Forecasting timelines for stem cell therapies: News media portrayal of clinical translation.
- Robert Meckin (University of Sheffield, United Kingdom)
  A translational science? Performing synthetic biology as a bridge between fundamental, applied and industrial research.
- Michael Morrison (University of Oxford, United Kingdom)
  Re-imagining Supra-national priorities: The case of the Innovative Medicines Initiative

Evening Dinner

18:45 Address by the organizers (Erik Aarden, University of Vienna, Austria)
19:00 Dinner

<u>May 19</u>

Morning Session: Accelerating Translation - What's Next?

9:00-10:30 - Keynote Speaker & Discussion:

- Paolo Bianco (University of Rome 'La Sapienza', Italy)
  How a wrong economic model of "translation" generates pseudoscience, misbeliefs, disruption of regulation, and societal damage.

10:30-11:00 - Coffee Break

11:00-13:00 - Panel & Discussion: Chair: Pierre Delvenne (Universite de Liege, Belgium)

- Willy Lensch (Harvard University, United States)
  TBA
- Annelien Bredenoord (Utrecht University, The Netherlands)
  Value(s), risk and translational research.
- Mark Robinson (DePaul University, United States)
  Can Non-Innovation Constitute Responsible Innovation? A Reflection on Responsible Research and Innovation in Light of the Emergence of Clinical Translational Research and Medicine.
- Vincent Pidoux (ULB, Belgium)
  The acceleration of what? Or how psychiatry hasn't taken the translational turn yet (though strives to).

13:00-14:00 - Lunch Break

Afternoon Session: Wrap-up & Concluding Remarks

14:00-15:30 - Final keynote & Discussion: Chair: Alessandro Blasimme (INSERM, France)

- Andrew Webster (University of York, United Kingdom)
- Concluding Remarks from the Organizers

Abstracts

Hans-Georg Eichler (European Medicines Agency, United Kingdom)
From Adaptive Licensing to Adaptive Pathways: Delivering a Flexible Life-Span Approach to Bring New Drugs to Patients .

The concept of adaptive licensing (AL) has met with considerable interest. Yet some remain sceptical about its feasibility. Others argue that the focus and name of AL should be broadened. Against this background of ongoing debate, we examine the environmental changes that will likely make adaptive pathways the preferred approach in the future. The key drivers include: growing patient demand for timely access to promising therapies, emerging science leading to fragmentation of treatment populations, rising payer influence on product accessibility, and pressure on pharma/investors to ensure sustainability of drug development. We also discuss a number of environmental changes that will enable an adaptive paradigm. A life-span approach to bringing innovation to patients is expected to help address the perceived access vs. evidence trade-off, help de-risk drug development, and lead to better outcomes for patients.

Nadine Levin (University of California Los Angeles, United States)
What's Being Translated in "Translational Research"?

This paper examines the challenges and politics surrounding the generation, interpretation, and dissemination of data in translation research. It examines translational research as it is occurring in the field of metabolomics, the post-genomic study of the molecules and processes that make up metabolism. Drawing on case studies of translational metabolomics research at the laboratory-clinic interface, I argue that "translation" is characterized by (often) problematic attempts to create, shape, and move data between the realms – conceptual and physical – of laboratory research and clinical practice.

My discussion of metabolomics is anchored in ethnographic research at the Computational and Systems Medicine (CSM) Laboratory at Imperial College London, which hosts several dedicated translational research centres—including the UK Government funded National Phenome Centre—in which laboratory researchers and clinician-researchers collaboratively carry out epidemiological studies and develop personalized medical interventions. The CSM makes an excellent locale for examining the dynamics and challenges of translational research, as well as the performative aspects of and values embedded within the act of "translation."

Drawing on case studies of molecular imaging and surgical technologies, I discuss how challenges arise in moving data between the laboratory and the clinic, because laboratory and clinical researchers have different ideas about what constitutes data, and about what value data might have, in biomedical interventions. I then move to a case study of efforts—in conjunction with the European Bioinformatics Institute (EBI)—to develop open databases and infrastructures for the large datasets generated at the National Phenome Centre. I discuss the challenges of doing Open Science across metabolomics laboratories: the challenges of obtaining, harmonizing, and using data

from different projects, in the field of metabolomics which has struggled to develop standards and infrastructures for heterogeneous and complex data.
Given this array of challenges, this paper asks: what is and isn't being translated, and why? How are the laboratory and the clinical brought together in unclear and contested ways? What politics are being done within translational research, as data is emphasized over clinical judgment and patient care?

Kalina Kamenova (University of Alberta, Canada)
Forecasting timelines for stem cell therapies: News media portrayal of clinical translation.

Since the early years of discovery, media reporting of stem cell research has focused largely on its promise and ethical issues arising from the destruction of human embryos in stem cell derivation. The media coverage, however, has recently shifted from the ethics and politics of stem cells to stories about clinical translation. This study examines the portrayal of stem cell clinical trials in major newspapers in Canada, the United States, and the United Kingdom from 1 January 2010 to 31 December 2013. The Factiva database was used to collect news stories about stem cell therapy translation in major daily newspapers in Canada, the United States, and the United Kingdom. The search generated 153 articles that mentioned 55 clinical studies with locations in Canada, the United States, the United Kingdom, Netherlands, Belgium, Spain, Japan, and China. A content analysis was conducted to establish how clinical trials were represented in terms of disease, stem cell type and product, trial phase, timelines, and study location. The results were further cross-referenced with data from clinical trials registries and study protocols were compared with the information presented in the press. The analysis established discrepancies between media narratives on clinical trials and the registries, particularly regarding the timelines for completing the studies and the introduction of new therapies. Media stories tended to exaggerate the clinical "readiness" of stem cell treatments and often contained inaccuracies in representing the nature and protocols of the studies. Mass media can play a significant role in framing the public discourse on emerging technologies and such highly optimistic predictions for stem cell therapies can contribute to unrealistic public expectations regarding the speed of clinical translation.

Robert Meckin (University of Sheffield, United Kingdom)
A translational science? Performing synthetic biology as a bridge between fundamental, applied and industrial research.

The talk begins with a brief history of translation in UK bioscience arguing that "translation" has changed and begun appearing in wider forums than in oncology where it first appeared including various medical and biotechnological research. The talk then introduces synthetic biology (SB) – an approach to doing biology where practitioners are applying design principles as they aim to engineer new organisms and improve existing organisms along with standardising the biological parts and devices needed for such a project. In other words, one of their stated goals is to make engineering life easier. Synthetic biology is also referred to as a 'translational science'.

The paper discusses findings from observations, interviews and documents from a range of laboratories, organisations and events in the UK. By using post-ANT notions of enactment, translating synthetic biology is understood as a complex of practices, rather than as a discursive device. What appears to bind these practices together, in part, is a linear structure to the relationship between 'discovery' and 'applied' science. Synthetic biology is performed as an object which can bridge a 'translational gap' because it processes the findings from academic disciplines and has the potential to turn them into commercial and industrial applications. The paper closes suggesting that such a performance is just one way "translation" could be performed, and that its current enactment has implications for democratic science and technology.

Michael Morrison (University of Oxford, United Kingdom)
Re-imagining Supra-national priorities: The case of the Innovative Medicines Initiative

The European Medicines Initiative (IMI) is a public-private partnership between the European Union and the European pharmaceutical industry association (Efpia) to fund a series of large scale pre-competitive research collaborations in the life sciences. The first phase of IMI (2008 – 2013) focused on the translation of novel technology platforms such as genomics and stem cells into tools to reinvigorate traditional small molecule drug discovery, while the second phase (2014-2024) turns more directly to the translation of European scientific knowledge into new medicinal products. This talk will draw out the imaginaries of a specifically European set of interests in economic growth, international competitiveness and unmet health needs which underpin the IMI concept. Issues of the allocation of resources and distribution of benefits will be considered in terms of the public-private financing of IMI projects and the nature of the anticipated economic and medicinal benefits. Particular attention will be paid to the envisioned role of patients and patient groups with respect to engagement and advocacy through the IMI program in general and through the IMI European patient academy (EUPATI) more specifically. Finally I will reflect on my own involvement with the IMI phase 1 project StemBANCC – stem cells for drug discovery.

Paolo Bianco (University of Rome 'La Sapienza', Italy)
How a wrong economic model of "translation" generates pseudoscience, misbeliefs, disruption of regulation, and societal damage.

The Stamina affair in Italy has represented not only a major threat to the regulatory framework for advanced cell therapies across Europe, but also a crystal clear paradigm of how the current economic model of translation has produced a direct alignment of the dissemination of misbeliefs both within the scientific community and in society. Within the scientific community, a biased and scientifically ungrounded description of an object of the natural world (so-called "mesenchymal stem cells") has taken over the accurate scientific description of the same object (identity, assays, properties, potential significance for medicine). Outside of the scientific community, a rush to inappropriate or premature clinical trials largely for commercial purposes has matched the outright marketing of unproven therapies, of which the Stamina affair is a special case. One of the contributing factors in generating this scenario is a specific model of "translation" of sciene into applicative and marketable items. The economic layout of this model,

adopted worldwide in policy making and research funding schemes allows for the direct use of public research funding for business development. One of the most visible impacts of this complex array of events has been on the regulatory framework, seen as to be in essence abrogated in order to allow direct marketing of technically unproven cell therapies. This resonates with a specific view of medicine as a mere free market-shaped human activity, in which the buying and selling of "therapies" replaces the cognitive exchange and the moral act inherent to medicine since pre-Christian civilizations. This approach is virtually identical conceptually in the Stamina model and in current proposals for revision of regulatory frameworks around the world.

Mark Robinson (DePaul University, United States)
Can Non-Innovation Constitute Responsible Innovation? A Reflection on Responsible Research and Innovation in Light of the Emergence of Clinical Translational Research and Medicine.

The marked growth of clinical translation and the translational sciences in the West has brought with it an opportunity to again reflect broadly on the ethics of research. In many ways, the confident moral associations accorded onto clinical translation – improving health for populations; leveraging science for the global good; turning the world's scientific innovation structures and their outputs back towards society – are reminiscent of the claims that also emerge out of the paradigm that is responsible research and innovation, especially as the notion of responsibility compels stakeholders towards designing a more societially desirable, sustainable, and public-facing research pathway. And yet, both clinical translation and Responsible Research and Innovation (RRI) share a temporal paradox: Both RRI and clinical translation are largely already path-dependent, similarly animated by determinative presuppositions about the morality and utility of particular investigational pathways. In the case of RRI, there is an assumption that an ethical development pathway actually exists. Does RRI allow for non-innovation? Are those involved in RRI, especially in context of private industry, able to call for the abandonment of a project in the name of responsibility?

The political economy of clinical translation is inextricable from the meeting of twin forces: including market-oriented demands made of state-funded bioscience research as well as an neoliberal ethical trajectory in which bioentrepreneurship becomes understood as a primary pretext for – and means of-- ethical scientific action. As such, clinical translation must necessarily advance certain scientific research ideas and foreclose others. What implications emerge from this shift towards "translational thinking?" Which intellectual predeterminations are ready-built into translational approaches? Informed by recent ethnographic research about several translational neuroscience sites in northern California and the effects of the translational shift, this paper takes clinical translation as an opportunity to reflect upon the presuppositions that inform Responsible Research and Innovation and it attendant ethical and social implications.

Vincent Pidoux (Universite Libre de Bruxelles, Belgium)
The acceleration of what? Or how psychiatry hasn't taken the translational turn yet (though strives to).

My comment will address the question of whether talking of "translational turn" in the field of mental health means anything (and for whom), and if so, how it works (or "performs"), and for whom it is a matter of concern. My aim also points to the question of whether the notion of "translation" has to be analysed by considering the specificity of disciplines and the alliances/compatibilities these latter build with other disciplines to foster inter/trans-disciplinarity and successful clinical translation.

I will stress the fact that, in psychiatry, translational research is much more desired and promised than a full-fledged reality. I will question the way brain research to clinical psychopathology translation has been advertised along with the challenge of bringing "precision medicine" to psychiatry (Insel, Cuthbert, 2015), notably as part of the US NIMH Research Domain Criteria (RDoC) Project. The RDoC project is an attempt to re-design mental disorders as brain disorders, which is a prerequisite for the "translational turn project" in psychiatry. I will argue that mixed claims/intentions/promises/solutions/problems of the realignement of the normal and the pathological, of the animal models and the human conditions, of the brain functioning and the mental dysfunctioning, imply the transformation of clinical categories, and training, in the name of neurobiological research innovation, acceleration, and productivity.