WORKSHOP ON GENOME EDITING & PRENATAL TESTING

Organised by the CUHK Centre for Bioethics

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Lecture Theatre 6, 2/F, Cheng Yu Tung Building

The Chinese University of Hong Kong, Shatin

List of Abstracts

Dr. Alexandre Erler

"Genome Editing at the Intersection of Prevention and Enhancement: Can Fixing Also Mean Optimizing?"

A widespread view, reflected in a recent report on human genome editing (HGE) by the US National Academies of Sciences, Engineering, and Medicine, states that uses of HGE for purposes of enhancement, as contrasted with treatment and prevention, are ethically more problematic than the latter, therapeutic uses, and that this has significant implications for regulation. For instance, according to the US report, clinical trials of HGE for non-therapeutic purposes should not be authorized, at least at the present time. Building on recently published work, I will argue that some prospective uses of HGE, which defy the traditional dichotomy between prevention and enhancement, present a challenge for this regulatory approach. Examples include George Church's project to forestall aging-associated diseases by controlling gene expression, with the goal of reversing the aging process; and the possibility of editing out a pathological gene sequence to replace it not just with a "normal" variant, but with an "optimal" one.

I will consider some ways of stating the treatment—prevention—enhancement distinction that would avoid the challenge in question, and will argue that they have counterintuitive implications. I will also raise doubts about the viability of using the idea of a genetic variant being "prevalent in the population" as a criterion of sufficient safety for HGE, as the authors of the US report do. To conclude, I shall argue that while such prospective uses of HGE – and particularly those involving early-stage interventions – do raise legitimate safety concerns,

the magnitude of the risks associated with such uses needs to be assessed on a case by case basis, as their sheer nature as enhancements does not automatically entail an unfavourable risk/benefit ratio, in light of their therapeutic (and other) benefits.

Dr. Stephen Lam

"Current Practices and Ethical Issues of Reproductive Genetics"

The term Eugenics has a bad reputation because of the atrocities and sufferings that had been operated on various populations under its name in the past century. Literally the term 'eugenics' means 'good birth', as coined by Francis Galton, the founder of the 'Eugenics Movement'. The objectives of Eugenics, as stated by some, are threefold, to improve the quality of the population, to prevent suffering, and to reduce the financial cost of the whole society in caring for the disabled. It refers to the "technique and policies that allow for the reproduction of people with the 'desired' attributes and reduce the reproduction of those with the 'undesired' attributes". Some argues that both the definition and objectives of Eugenics sound reasonable, and together with Galton's opposition to coercion as a means towards Eugenics, the whole concept appears to be acceptable. Yet, after the catastrophic implementation of what is now called 'Classical Eugenics' in the past century, the term 'Eugenics'is seldom found in usual medical discussions. However, the actual fact is that a contemporary form of Eugenics is being implemented on a large scale. Through our current use of reproductive technology, 'Contemporary Eugenics'is practised in the form of non-invasive prenatal testing, prenatal diagnosis, preimplantation genetic diagnosis and screening, and possibly, in the not too distant future, in the form of gene editing. This paper will discuss the practical and ethical issues involved in our current practices in reproductive genetics.

Prof. Ruipeng Lei

"Balancing Benefits and Burdens in Precision Medicine"

The author will first analyze the concept of Precision Medicine and argue that the term "precision" would be relative because the probabilistic nature of medicine cannot be eliminated. Then the China's project of Precision Medicine which is sponsored by Ministry of Science and Technology will be briefly described. The author will question the project because it is not scientifically and ethically justified to invest billions of Chinese dollars in precision medicine. In China it is urgently needed to establish a system of accessible, available, affordable and high-quality primary care, but precision medicine, even though successful, may be provided affordably only in tertiary care. Which allocation of resources is more cost-effective, investing in precision medicine or in primary care? It is an issue that

remains to be solved. Secondly the author will raise the issue of equitable access to precision medicine, including who controls the access to the results of precision medicine research, the decision of using the results is made by individuals, physicians and hospitals or the government, whether the costs of precision medicine will be covered by socialized health insurance: if yes, whether the health insurance system will be financially bankrupt, if no, does it mean the poor will be excluded from the beneficiaries of precision medicine. It is a tough issue that how to equitably allocate the benefits and burdens among the citizens or taxpayers, the benefits is allocated according to need or to buying power, whether the inequitable access to precision medicine will jeopardize existing social injustice and broaden the divide between the poor and the rich. All of these issues are waiting for a solution.

Prof. Tak-Yeung Leung

"Genome Editing: Potential Use in Prenatal Treatment?"

(Pending)

Prof. Hon-Lam Li

"What We Owe to Those Who Cannot Afford the Cost of Genetic Enhancement: A Contractualist View"

This paper argues for the following: (1) Sports analogies are inappropriate to, and hence do not bear on, the issue of genetic enhancement. Various kinds of genetic enhancement, in particular cognitive enhancement, has far-reaching importance to opportunities (and other positional goods) that roughly represent a zero-sum game (e.g., whether one can get admitted to university or get a decent job) and hence the issue of fairness becomes relevant. (Enhancements that relate to non-positional goods, such as longevity, may be less problematic.) (2) Certain objections are taken up and replied. (3) This paper then argues that if utilitarianism were correct, it may be easier to justify genetic enhancement. It is argued that contractualism, rather than utilitarianism, is the more plausible moral theory, and hence that fairness as well as consequences are both relevant. (4) The possibility of a right to a "basic package" of genetic enhancement for every citizen is explored. This paper argues that this middle ground may be more plausible or acceptable than those that permit genetic enhancement without any restriction, or on the other hand those that disallow the technology at all costs.

Dr. Tamra Lysaght

"Building Trustworthy Governance for Sharing Genome Data in Singapore"

Singapore is one of many nations investing substantial resources into initiatives promoting human genomics and precision medicine. The aim of these initiatives is to generate tailored health interventions for individuals and specific patient populations based on their underlying clinical, socio-demographic and genetic profiles. Essential to their success will be the facilitation of data flows from multiple sources between researchers, healthcare providers and health consumers. However, sharing data between researchers and practitioners at different institutions raises not only practical questions of data management and storage, but also ethical ones concerning the rights and interests of the individuals whose information is being transferred. This is particularly true for genetic information.

In this paper, I discuss ongoing empirical and normative research into governance regimes for sharing genome data in Singapore. As Singapore currently lacks any non-discrimination legislation, the possibility of genetic discrimination if information is shared insecurely both raises risks for data providers, and can potentially engender mistrust in precision medicine initiatives. Data may be anonymised, but increasingly the complexity and richness of these data makes long-term anonymization questionable. Ineffective governance may exacerbate the possibility of re-identification, and breaches may undermine wider public trust in the institutions responsible for protecting the data. Many questions have also been raised around the type and quality of consent that should be obtained for sharing genome data amongst institutions both domestically and abroad. I address these concerns and conclude with some recommendations that have been emerging from our research findings for trustworthy governance of genome data sharing in Singapore.

Dr. Catherine Mills

"Integrating NIPT in Australia"

Non-invasive prenatal testing technology has been commercially available in Australia since about 2008. Since that time the technology has become increasingly embedded in the prenatal testing regime, with increasing uptake reducing costs to consumers. However, as yet, there has been little public discussion beyond expert circles of whether NIPT should be routinely offered to pregnant women, or whether it should be subsidized in ways similar to ultrasound testing, or what consent procedures are required for people offered this. Further, there has been no research done in the Australian context that ascertains who is using NIPT, why they do so (or why other reproducers don't), nor assessing the information provision, consent procedures and consumer understanding involved. This paper canvasses some of

the issues involved in the provision of NIPT screening in the Australian system of public and private prenatal care, and discusses ethical issues around consent and choice, testing for foetal sex, and access to prenatal screening.

Dr. Vardit Ravitsky

"Ethical and Social Implications of the Shifting Landscape of Prenatal Testing"

The introduction of cell-free Fetal DNA testing, or Non-Invasive Prenatal Testing (NIPT), is gradually changing the landscape of prenatal testing. By providing results that are more reliable than serum screening, earlier in the pregnancy and without increased risk of miscrriage, NIPT represents great benefits. It reduces the number of invasive diagnostic tests, consequently reducing fetal losses. It also allows women more time for decision-making. NIPT is currently shifting from a second-tier screening test offered only for high-risk pregnancies, to a first-tier screening test for all pregnant women. It may, at some point, be recognized as a diagnostic test for certain conditions. The probable routinization of NIPT raises numerous ethical and social challenges.

The talk will address challenges related to: 1/ obtaining informed consent for a non-invasive screening test that poses no increased risk of miscarrage, in light of ongoing challenges surrounding consent for 'traditional' serum screening; 2/ a possible increase in detection of trisomy 21, leading to increased termination rate and as a result increased stigmatization of families raising children with special needs; 3/ the cost of NIPT as a barrier to access (since it is not publicly funded in most countries) and associated concerns about equity; 4/ the global spread of NIPT and the unique cultural challenges associated with its offer in countries with different healthcare systems and different legal frameworks (related to pregnancy termination on one hand, and support for children with special needs on the other).

The talk will conclude with a focus on expanded use of NIPT, from trisomies and specific genetic conditions, all the way to whole genome sequenceing. The decision regarding what conditions to screen for is not only clinically challenging, but also ethically sensitive, as it depends on personal and social values. These challenges will be discussed based on the bioethics literature, using examples from a Canadian national study (http://pegasus-pegase.ca/) that explored the implications of introducing NIPT into the Canadian healthcare system.

Prof. Pang-Chui Shaw

"Gene Editing: History and Development"

Genome editing refers to the alteration of DNA of an organism by changing the nucleotides in the genome. This involves breaking the double-stranded strand DNA and joining them together after deleting part of it or inserting a desired sequence. Current gene-editing approaches utilize nucleases of three main categories to produce double-strand breaks (DSBs) – zinc-finger nucleases (ZFN), transcription activator-like effector nucleases (TALEN), and clustered regularly interspaced short palindromic repeats (CRISPR). DSBs can be repaired through natural DNA-repairing mechanisms. Non-homologous end joining (NHEJ) would result in gene disruption. Desired genome changes can be achieved by homology-driven repair (HDR) in the presence of donor homologous DNA sequences. In recent years, the field of genome editing has been vitalized by the huge influx of CRISPR research activities due to the efficiency and robustness of the technique. Despite technical difficulties such as the creation of 'off-target' changes to genome and mosaicism, genome editing activities have become routine in the laboratory and scientists are eager to develop it in clinical applications, for instance turning-off disease-causing point mutations. Publications on gene editing in human embryos have emerged. These include the study of embryo development and the correction of different mutations.

Prof. Robert Sparrow

"Would Genome Editing Harm or Benefit the Person Born As A Result?"

Ever since the publication of Derek Parfit's influential Reasons and Persons bioethicists have tended to distinguish between two different ways in which reproductive technologies may have implications for the welfare of future persons. Interventions may harm or benefit particular, identifiable, individuals. Such interventions are "person affecting": it makes sense to ask what the individual's life would have been like had the intervention not occurred. However, another sort of interventions determine which individual, of a number of possible individuals, comes into existence. Such interventions are "identity affecting": when we ask whether they harm or benefit the individual who is born, we struggle to generate the relevant comparison because had the intervention not occurred a different individual would have been born instead. This latter set of cases raises the famous "non-identity problem". For the past several decades bioethical debate has proceeded on the assumption that direct genetic modification of human embryos would be person affecting. However, bizarrely, now that such gene editing is a realistic scientific possibility, cracks are beginning to appear in this consensus. In this presentation, I will offer some thoughts on the substantive matter of

whether genome editing would be person affecting and how this might matter for its ethics, and some speculations as to why bioethicists are revisiting this question at this particular historical juncture.

Mr. Hugh Whittall

"Genome Editing and Bioethics: Thinking About Applications in Human Reproduction"

Genome editing, especially with the CRISPR-Cas9 system, has been developing rapidly in recent years, offering a powerful set of tools with many potential applications in plants, animals, humans and microbes. The speed, versatility, accuracy and, importantly, affordability of the technology has meant that it has been widely seen as a 'gamechanger' in applied genomics.

In 2016 the Nuffield Council on Bioethics published a broad review of the ethical implications of genome editing, setting out some of the likely areas of application, and the moral perspectives that might be brought to bear in considering them. These included questions of science as a moral enterprise; of moral norms and human rights; welfare and risk; social justice; governance and democracy; and others. It also identified a number of areas in which it felt that urgent and detailed consideration should be prioritized. These included, in particular, areas relating to human reproduction, and to livestock for food production.

A further enquiry by the Council is currently underway looking specifically at genome editing in the context of human reproduction – where interventions would lead to changes that would affect the human germline. In principle, genome editing could be used to avoid serious inherited disorders, but it could also be used for interventions that might be regarded as 'enhancement'. The Council's report will examine the ethical considerations and governance arrangements that will be specifically relevant in the context of human reproductive uses.

This presentation will set out some of the Council's early work in looking at genome editing in a research context, and will outline some of the areas of concern and the ethical considerations that will inform its forthcoming publication on human reproductive applications.

Speakers' Biographies

Dr. Alexandre Erler

Alexandre Erler is a philosopher studying the ethical implications of new technologies with transformative potential, including but not limited to human enhancement technologies (e.g. genetic interventions and direct interventions into the brain). He also works in other areas like the philosophy of psychiatry. He completed a doctorate in Philosophy at the University of Oxford in 2013. Between 2013 and 2017 he was a postdoctoral researcher at the University of Montreal and then at the American College of Thessaloniki. At present he is a Research Assistant Professor in Philosophy and Bioethics at the Chinese University of Hong Kong. He has written on various issues within the ethics of human enhancement, including its potential impact on human identity and authenticity. He has also addressed ethical issues surrounding mental disorders like ADHD. His work has been published in journals such as Bioethics, AJOB Neuroscience, the American Journal of Bioethics, Neuroethics, the Journal of Medical Ethics and the Journal of Applied Philosophy.

Dr. Stephen Lam

Stephen Lam is a Fellow of Hong Kong College of Paediatricians, Fellow of Royal College of Physicians (Edinburgh), and Fellow of Hong Kong Academy of Medicine. He was the Consultant Clinical Geneticist, and Head of Clinical Genetic Service, Department of Health, Hong Kong (1990-2015). He is an Honorary Professor of the Faculty of Medicine in the Chinese University of Hong Kong since 2012. He was the founding Chairman of the Hong Kong Society of Medical Genetics in 1987; Past President of the Asia Pacific Society of Human Genetics (2011-12), and the International Federation of Human Genetic Societies (2012-14). He has published more than 100 articles and edited two books. He serves as editor of several international journals. Since July 2016, he is the Director of Clinical Genetics Service and Honorary Consultant in Clinical Genetics in the Hong Kong Sanatorium and Hospital in Hong Kong.

Prof. Ruipeng Lei

Ruipeng Lei is Chair of Department of Philosophy, and Executive Director of Center for Bioethics, Huazhong University of Science and Technology. She is the board member of Chinese Society for Bioethics, Associate President of Asian Bioethics Association (2011-2015), research fellow of International Biomedical and Health Research Ethics Program at

Harvard School of Public Health and member of The International Network on Feminist Approaches to Bioethics. Her research focuses on ethical and policy issues raised by emerging technologies e.g. synthetic biology, as well as philosophical reflections and ethical analysis on xenotransplantation, synthetic biology and biobanks.

Prof. Tak-Yeung Leung

Professor Tak-Yeung Leung is the Chairman of the Department of Obstetrics and Gynaecology of The Chinese University of Hong Kong, as well as the Director of the Maternal Fetal Medicine of the same unit. His special interest is in perinatal medicine especially fetal hypoxia, shoulder dystocia, preterm delivery, and external cephalic version. His works also include prenatal diagnosis using aCGH and NIPT, and fetal therapy such as laser for twin-twin transfusion syndrome and radiofrequency for selective fetocide. He has published more than 270 papers in international peer reviewed journals and his H-index is 30. He is also the Scientific editor of British Journal of Obstetrics and Gynaecology (BJOG since 2016), and editorial board member of other international journals such as American Journal of Perinatology, Pediatric Research (Fetus & Pregnancy Section) and Journal of Maternal Fetal and Neonatal Medicine.

Professor Leung is currently the Senior Vice President of Hong Kong College of Obstetricians and Gynaecologists. He has strong international and Asian-Pacific connection with appointment in several international professional bodies including: Member of FIGO Preterm Working group (2016 – present), Expert Panel for the revision of the FIGO intrapartum fetal monitoring guidelines (2014 – present), Chairman of the Prenatal Maternal Screening Special Interest Group of International Society for Prenatal Diagnosis (2009 – 2013), Foundation Board member of Global Obstetric Network (GONet; 2009 – 2013), Foundation Secretary of The Chinese Fetal Medicine Foundation.

Prof. Hon-Lam Li

Hon-Lam Li is Professor in the Department of Philosophy, and Deputy Director at the Centre for Bioethics, Chinese University of Hong Kong. He has published papers in practical ethics (including bioethics), ethics, political philosophy, and philosophy of law. His current project is contractualism and its implications to various moral issues.

Prof. Dennis Lo

Dennis Lo is the Li Ka Shing Professor of Medicine and Professor of Chemical Pathology of The Chinese University of Hong Kong. He obtained his undergraduate medical training from the University of Cambridge and his Doctor of Medicine and Doctor of Philosophy degrees from the University of Oxford. He discovered the presence of cell-free fetal DNA in maternal plasma in 1997 and has translated this discovery into a new platform for non-invasive prenatal testing which is now used globally. He has received numerous awards and honours for his research, including elections to the Royal Society and the US National Academy of Sciences, and awards of the Future Science Prize in 2016 and the King Faisal International Prize in 2014.

Dr. Tamra Lysaght

My research interests lie broadly around the sociopolitical, ethical and regulatory issues surrounding stem cell innovation, regenerative medicines, precision medicine, genomics and reproductive technologies. I have expertise in empirical bioethics and experience in using both qualitative and quantitative research methods to inform normative questions pertaining to emergent biotechnologies and the biomedical sciences. I have worked on policy issues with the Committee for Ethics, Law and Society of the Human Genome Organisation, the Technical Working Group on Ethics at the World Health Organization, the Singapore Ministry of Health and Bioethics Advisory Committee. I am currently an Assistant Professor and Phase Director of the Health Ethics, Law and Professionalism (HeLP) Programme at the Centre for Biomedical Ethics, National University of Singapore. I hold multiple grants on projects examining the ethics and regulation of innovative stem cell-based therapies, genome editing and Big Data, and have research interests in governance issues surrounding the return of incidental findings and data sharing in precision medicine.

Dr. Catherine Mills

Catherine Mills is Associate Professor of Bioethics and an Australian Research Council Future Fellow in the Monash Bioethics Centre, Monash University. Her work focuses on ethical issues that arise in human reproduction, especially relating to prenatal testing and other reproductive technologies, and ideas about maternal responsibility. She is the author of numerous journal articles and chapters, as well as 3 sole authored books, most recently Biopolitics (2017, Routledge).

Dr. Vardit Ravitsky

Vardit Ravitsky, PhD, is Associate Professor at the Bioethics Programs at the Department of Social and Preventive Medicine of the School of Public Health, University of Montreal. She is Director of the Ethics and Health Branch of the Center for Research in Ethics. Ravitsky is an elected Board member and Treasurer of the International Association of Bioethics (IAB). She is a member of the Canadian Institutes of Health Research (CIHR) Standing Committee on Ethics and of the CIHR's Institute Advisory Board on Research Excellence, Policy and Ethics. Ravitsky is member of the Quebec Reproduction Network (RQR) and the Canadian Fertility and Andrology Society (CFAS). Previously, she was faculty at the School of Medicine at the University of Pennsylvania.

Prof. Ravitsky's research focuses on reproductive ethics and the ethics of genetic and genomics research. Her research interests in bioethics also include research ethics and health policy. She is particularly interested in the various ways in which cultural frameworks shape public debate and public policy in bioethics. She published over 100 articles, book chapters and commentaries on bioethical issues, and is lead-editor of "The Penn Center Guide to Bioethics".

Prof. Pang-Chui Shaw

Professor Pang-Chui Shaw obtained his Ph.D degree from Imperial College, University of London, UK. He is now Professor and Director of Biochemistry Programme, School of Life Sciences of the Chinese University of Hong Kong. Professor Shaw teaches molecular biology, molecular biotechnology and bioethics to Biochemistry and life sciences students. He has served as the Chairman of the Hong Kong Bioethics Association and now the Chairman of the Endangered Species Advisory Committee of the Agriculture, Fisheries and Conservation Department of the Hong Kong SAR. His research focuses on the authentication, quality control and pharmacological studies of Chinese medicinal material. He has published 230 refereed articles, three books and obtained four USA and four Chinese patents.

Prof. Robert Sparrow

Professor Rob Sparrow is a researcher and lecturer in the Philosophy Program, a Chief Investigator in the Australian Research Council Centre of Excellence for Electromaterials Science, and an Adjunct Professor in the Monash Bioethics Centre, at Monash University, where he works on ethical issues raised by new technologies. His research interests include the ethics of artificial organs, aged care robotics, preimplantation genetic diagnosis, xenotransplantation, and human enhancement.

Mr. Hugh Whittall

Hugh Whittall is the Director of the Nuffield Council on Bioethics, whose task is to identify and report on ethical questions raised by new developments in biological and medical research. Recent reports have covered areas including neurotechnology, emerging biotechnologies, children and clinical research, biodata and genome editing.

Hugh was previously at the Department of Health, where he was involved with the preparation of the Human Tissue Act 2004 and the setting up of the Human Tissue Authority. He was also involved in end-of-life issues and transplantation policy.

Prior to that Hugh spent three years at the European Commission in Brussels, involved in the funding and promotion of bioethics research, and he was for several years Deputy Chief Executive of the Human Fertilisation and Embryology Authority.