# International Commission on the Clinical Use of Human Germline Genome Editing

## Co-chairs

**Kay Davies, Ph.D., DBE FMedSci FRS** is Professor of Genetics in the Department of Physiology, Anatomy and Genetics and Associate Head, Development, Impact and Equality, in the Medical Sciences Division at the University of Oxford. She established the MRC Functional Genomics Unit in 1999 and co-founded the Oxford Centre of Gene Function in 2000. She is Co-Director of the MDUK Oxford Neuromuscular Centre. Her research interests lie in the molecular analysis and development of treatments for human genetic diseases, particularly Duchenne muscular dystrophy (DMD), and the application of genomics for the analysis of neurological disorders and gene–environment interactions. She has published more than 400 papers and won numerous awards for her work. She co-founded Summit Therapeutics and Oxstem. Dr. Davies is a founding Fellow of the Academy of Medical Sciences and was elected a Fellow of the Royal Society in 2003. She was appointed Governor of the Wellcome Trust in 2008 and became Deputy Chair 2013-17. She was made Dame Commander of the British Empire for services to science in 2008.

**Richard P. Lifton, M.D., Ph.D.** is the 11th President of The Rockefeller University. He has used human genetics and genomics to understand fundamental mechanisms underlying a wide range of human diseases. He is well-known for his discovery that mutations with large effect on human blood pressure act by altering renal salt reabsorption, discoveries that have informed dietary guidelines and therapeutic strategies used worldwide to reduce blood pressure, prevent heart attacks and strokes, and for his development and use of exome sequencing for clinical diagnosis and disease gene discovery. Dr. Lifton graduated summa cum laude from Dartmouth College, obtained M.D. and Ph.D. degrees from Stanford University and completed training in Internal Medicine at Brigham and Women's Hospital/Harvard Medical School. Prior to Rockefeller, he was chair of the Department of Genetics and Sterling Professor at Yale University, where he founded the Yale Center for Genome Analysis. He is a member of the National Academy of Sciences and the National Academy of Medicine, and has served on the governing councils of both organizations. He currently serves on the Scientific Advisory Boards of the Simons Foundation for Autism Research and the Chan-Zuckerberg Initiative Biohub, and is a Director of Roche and its subsidiary Genentech. He previously served on the Advisory Council to the NIH Director and co-chaired the NIH Precision Medicine Working Group, which developed the plan for the 'All of Us' Presidential Initiative. He has received numerous awards for his research, including the 2014 Breakthrough Prize in Life Sciences, the 2008 Wiley Prize, and the highest scientific awards of the American Heart Association, the American and International Societies of Nephrology, and the American and International Societies of Hypertension. He has received honorary doctorates from Northwestern University, Mount Sinai School of Medicine and Yale University.

## Members

**Hidenori Akutsu, M.D., Ph.D.** is a director of the Department of Reproductive Medicine at the National Research Institute for Child Health and Development in Tokyo, Japan. He is a member of Expert Panel on Bioethics, Council for Science and Technology Innovation (CSTI) of Japan and a Secretary of the Committee on Genome Editing Technology in Medical Sciences and Clinical Applications of the Science Council of Japan. His research explores mechanisms of preimplantation development and stem cell reprogramming. He has derived human embryonic stem cells in Japan. Akutsu received his M.D. from Hirosaki University and completed his clinical training in obstetrics gynecology at Fukushima Medical University. He completed his Ph.D. at Fukushima Medical University School of Medicine.

**Robert Califf, M.D., MACC, NAM** is the Donald F. Fortin, MD, Professor of Cardiology at Duke University. He is also Professor of Medicine in the Division of Cardiology and remains a practicing cardiologist. Dr. Califf was the Commissioner of Food and Drugs (2016-2017) and Deputy Commissioner for Medical Products and Tobacco (2015-2016). Prior to joining the FDA, Dr. Califf was a professor of medicine and vice chancellor for clinical and translational research at Duke University. He also served as director of the Duke Translational Medicine Institute and founding director of the Duke Clinical Research Institute. A nationally and internationally recognized expert in cardiovascular medicine, health outcomes research, healthcare quality, and clinical research, Dr. Califf has led many clinical trials and has more than 1,200 publications in the peer-reviewed literature. Dr. Califf has served on a number of advisory committees for FDA and NIH. He has led major initiatives aimed at improving methods and infrastructure for clinical research, including the Clinical Trials Transformation Initiative (CTTI), a public-private partnership co-founded by the FDA and Duke.

**Dana Carroll, Ph.D., NAS** is a Distinguished Professor in the Department of Biochemistry at the University of Utah School of Medicine and a member of the Nuclear Control of Cell Growth and Differentiation Program at the Huntsman Cancer Institute. Dr. Carroll's research involves genome engineering using targetable nucleases. His lab pioneered the development of zinc-finger nucleases as gene targeting tools and he continued working with the more recent TALENs and CRISPR/Cas nucleases, with much of the effort focused on optimizing the efficiency of these reagents for targeted mutagenesis and gene replacement. Dr. Carroll's current interests include societal implications of genome editing. He received his Ph.D. from the University of California, Berkeley and did postdoctoral research at the Beatson Institute for Cancer Research in Glasgow, Scotland, and at the Carnegie Institution Department of Embryology in Baltimore.

**Susan Golombok, Ph.D.** is Professor of Family Research and Director of the Centre for Family Research at the University of Cambridge, where she studies the impact of new family forms on child development, specifically families created by assisted reproduction (e.g. IVF). She is an expert in longitudinal studies of children, which is relevant to the Commission's tasks of identifying ways to assess the balance between potential benefits and harms to a child produced by genome editing and identifying and assessing mechanisms for long-term monitoring of children produced by genome editing.

**Andy Greenfield, Ph.D.** has been a Programme Leader at the Medical Research Council's Harwell Institute since 1996 and his lab's research focuses on the molecular genetics of mammalian sexual development. From 2009 to 2018, he was a member of the UK Human Fertilisation and Embryology Authority (HFEA) and he chaired two expert panel reviews of mitochondrial donation techniques in 2014 and 2016. He has spoken on numerous occasions about the science and ethics of genomic technologies and their application in animals and humans. He remains an external advisor to the HFEA Scientific and Clinical Advances Advisory Committee (SCAAC). He is a member of the Nuffield Council on Bioethics and chaired its 2016 working group examining ethical issues arising from the use of genome editing in a range of organisms and contexts. From 2003 to 2007 he served as a member of the Wellcome Trust's Molecules, Genes & Cells Funding Committee. He received his Ph.D. in molecular genetics from St Mary's, Imperial College London and was a post-doctoral fellow at the Institute for Molecular Bioscience, University of Queensland, Australia. He also has an MA in Philosophy from Birkbeck, University of London

**A. Rahman A. Jamal, M.D., Ph.D., MRCP** currently is the Pro Vice Chancellor of the Universiti Kebangsaan Malaysia (UKM) Kuala Lumpur Campus. He is also the founding director of the UKM Medical Molecular Biology Institute (UMBI) at the Universiti Kebangsaan Malaysia (UKM), Kuala Lumpur and a professor of Paediatric Oncology and Haematology, and Molecular Biology. His main research focus is on molecular biology of cancers, other non-communicable diseases, thalassemia and rare diseases. He and his research team have discovered gene signatures associated with the pathogenesis of colorectal cancer (CRC), glioma and leukemias. He has pioneered personalized and precision medicine in UMBI and is now the chairman of the Task Force for Precision Medicine under the auspices of the Academy of Sciences Malaysia. He is the Principal Investigator for The Malaysian Cohort project and is a member of the Asia Cohort Consortium and the International Health Cohort Consortium. He is a member of the Wellcome Trust UK Grant Committee for Longitudinal Population Studies since 2018. He is the chairman of the National Committee for Ethics for Cell Research and Therapy and a member of the National Committee for Clinical Research, both under the Ministry of Health Malaysia. Professor Rahman is currently the Project Director for the UKM Specialist Children's Hospital which will be the first dedicated hospital for paediatric patients in Malaysia. He graduated from UKM in Medicine in 1985 and obtained his MRCP (Paediatrics) from the Royal College of Physicians Ireland in 1991. He was awarded a PhD in Haematology and Molecular Biology in 1996 from University of London, United Kingdom. He also has a Graduate Diploma in Healthcare Leadership and Management from the Singapore Management University (2015)

**Jeffrey Kahn, Ph.D., M.P.H, NAM** is the Andreas C. Dracopoulos Director of the Johns Hopkins Berman Institute of Bioethics, a position he assumed in July 2016. From 2011, he has been the inaugural Robert Henry Levi and Ryda Hecht Levi Professor of Bioethics and Public Policy. He is also Professor in the Dept. of Health Policy and Management of the Johns Hopkins Bloomberg School of Public Health. He works in a variety of areas of bioethics, exploring the intersection of ethics and health/science policy, including human and animal research ethics, public health, and ethical issues in emerging biomedical technologies. Prof. Kahn has served on numerous state and federal advisory panels. He is currently chair of National Academies of Sciences,

Engineering, and Medicine's Board on Health Sciences Policy, and has previously chaired its committee on the Use of Chimpanzees in Biomedical and Behavioral Research (2011); the committee on Ethics Principles and Guidelines for Health Standards for Long Duration and Exploration Spaceflights (2014); and the committee on the Ethical, Social, and Policy Considerations of Mitochondrial Replacement Techniques (2016). He also formerly served as a member of the National Institutes of Health (NIH) Recombinant DNA Advisory Committee. In addition to committee leadership and membership, Prof. Kahn is an elected member of the National Academy of Medicine and an elected Fellow of The Hastings Center. He was also the founding president of the Association of Bioethics Program Directors. Prof. Kahn's publications include three books and over 125 scholarly and research articles. He speaks widely on a range of bioethics topics, in addition to frequent media outreach. From 1998-2002 he wrote the bi-weekly column "Ethics Matters" on CNN.com. Prior to joining the faculty at Johns Hopkins, Prof. Kahn was Maas Family Endowed Professor of Bioethics and Director of the Center for Bioethics at the University of Minnesota.

**Bartha Maria Knoppers, J.D., Ph.D.** (Comparative Medical Law), is a Full Professor, Canada Research Chair in Law and Medicine and Director of the Centre of Genomics and Policy of the Faculty of Medicine at McGill University. She is Chair of the Ethics and Governance Committee of the International Cancer Genome Consortium (2009-2017), as well as the Ethics Advisory Panel of WADA (2015- ). She is Co-Chair of the Regulatory and Ethics Workstream of the Global Alliance for Genomics and Health (2013- ). In 2015-2016, she was a member of the Drafting Group for the Recommendation of the OECD Council on Health Data Governance and gave The Galton Lecture in November 2017. She holds four Doctorates *Honoris Causa* and is a *Fellow* of the American Association for the Advancement of Science (AAAS), the Hastings Center (bioethics), the Canadian Academy Health Sciences (CAHS), and, the Royal Society of Canada. She is also an *Officer* of the Order of Canada and of Quebec, and was awarded the 2019 Henry G. Friesen International Prize in Health Research.

**Eric Lander, Ph.D., NAS, NAM** is president and founding director of the Broad Institute of MIT and Harvard, and is professor of biology at MIT and professor of systems biology at Harvard Medical School. From 2009 to 2017, he served as co-chair of the President's Council of Advisors on Science and Technology for President Barack Obama. A geneticist, molecular biologist, and mathematician, he has played a pioneering role in the reading, understanding, and biomedical application of the human genome. He was a principal leader of the Human Genome Project. He has done pioneering work on human genetic variation, genome evolution, and genome-wide screens to discover the genes essential for biological processes using CRISPR-based genome editing. Dr. Lander has received numerous honors for his work.

**Jinsong Li, Ph.D.** is a Professor at the Shanghai Institute of Biochemistry and Cell Biology (SIBCB) of Chinese Academy of Sciences. He obtained his PhD from Institute of Zoology, Chinese Academy of Sciences, in 2002 and followed by postdoctoral training at Rockefeller University before joining SIBCB in 2007. Somatic reprogramming induced by iPSC and nuclear transfer (NT) technologies has offered exciting promises in basic and applied research. His lab attempts to optimize reprogramming procedures, improve the developmental potential of reprogrammed

cells and reveal the molecular mechanisms involved in somatic reprogramming. In 2012, he reported generation of androgenetic haploid embryonic stem cells (AG-haESCs) that can support full-term embryonic development upon injection into MII oocytes, leading to the generation of semi-cloned (SC) mice. However, frequently observed aberrant development of AG-haESC-derived embryos and very low birth rate of healthy greatly restricts the application. Recently, Dr. Li's lab has shown that AG-haESCs carrying deletions in regions controlling two paternally repressed imprinted genes can efficiently support the generation of SC pups at a rate of 20%. This new technology may be feasible for medium-scale targeted screening at organism level, especially for developmental phenotypes, using the appropriate sgRNA libraries targeting preselected candidate genes. Recently, they showed that mice with different base mutations can be generated in one step through combining "spermatid-like"-cell-based semi-cloned technology and CRISPR-Cas9-mediated base editor system, enabling identification of critical amino acids of DND1 for primordial germ cell (PGC) development. The laboratory is now focusing on the development of primordial germ cells, generation of disease models and large-scale tagging proteins in mice using "spermatid-like" haploid cell-mediated semi-cloned technology.

**Michèle Ramsay, Ph.D**., is Director and Research Chair of Sydney Brenner Institute for Molecular Bioscience (SBIMB) at the University of Witwatersrand, Johannesburg. The SBIMB focuses on the development of new solutions to African health challenges by conducting biomedical molecular and genomic research. Ramsay's research interests include the genetic basis and molecular epidemiology of single gene disorders in South African populations and the role of genetic and epigenetic variation in the molecular aetiology of diseases and traits affected by lifestyle choices. She received her Ph.D. in Human Molecular Genetics from the University of Witwatersrand. She is a member of the Academy of Science of South Africa, and immediate past President of the African Society of Human Genetics and President of the International Federation of Human Genetics Societies.

**Julie Steffann, M.D., Ph.D.** has been a Hospital Practitioner in the Genetic Department of Necker-Enfants Malades Hospital since 2006 and a Professor of Genetics at the Paris Descartes University since 2016. Head of the Preimplantation Genetic Diagnosis laboratory since 2003, she belongs to the "mitochondrial diseases" team at UMR 1163 unit in the Imagine Institute. She conducts research on mitochondrial DNA disorders and their consequences on human early embryos. She investigates the potential impacts of mtDNA mutations over human embryofetal development, and develops methods of prevention and treatment of mtDNA disorders.

**B.K. Thelma, Ph.D.** is a Professor and J C Bose fellow at the Department of Genetics at the University of Delhi. Thelma established the DNA-based diagnosis facilities for fragile X syndrome and her laboratory is one of the few which offers this national level diagnostic service. Her research interests include causal gene identification in intellectual disability, schizophrenia and Parkinson's disease, and she is currently undertaking work on analysis of whole exome sequencing for rare variants in these disorders and functional analysis of variants thus identified. She has been involved in a number of long-term follow-up studies and has contributed to a number of expert committees in areas of science and ethics. She received the

Stree Shakti Science Samman award in 2012 and is a fellow of the Indian National Science Academy, Indian Academy of Sciences and the National Academy of Sciences (India). Thelma completed her B.Sc. and M.Sc. in Zoology from Bangalore University and received her Ph.D. in Zoology from the University of Delhi.

**Doug Turnbull, M.D. Ph.D. FMedSci** is Professor of Neurology and Director of the Wellcome Centre for Mitochondrial Research at Newcastle University. The Wellcome Centre for Mitochondrial Research focuses on understanding the clinical course of patients with mitochondrial disease and how this relates to the underlying disease mechanisms, identifying the molecular and genetic mechanisms causing mitochondrial disease, and developing techniques to prevent the transmission of mtDNA disease and improve treatment for patients with mitochondrial disease. He also Director of the MRC Centre for Ageing and Vitality which is focused on understanding how ageing mechanisms are influenced by lifestyle interventions and studies aimed at promoting healthy ageing. He is also Lead for the NHS Highly Specialised Services for Rare Mitochondrial Services for Adults and Children. This service provides optimum care for patients with mitochondrial disease throughout the UK with Centres in Newcastle, London and Oxford. This service was built on the back of clinical and basic research and the Newcastle Centre reviews in excess of 1000 patients per year. The service has developed care pathways and patient guidelines that are used worldwide of the benefit of patients. He was elected a Fellow of the Academy of Medical Sciences in 2004 and elected a Fellow of the Royal Society in 2019. Sir Doug Turnbull received a knighthood in the Queen's Birthday Honours 2016 "for services to Health Care Research and Treatment particularly Mitochondrial Disease". He received his Bachelor of Medicine, Bachelor of Surgery, M.D. and Ph.D. from Newcastle University.

**Haoyi Wang, Ph.D.** leads a research group in the State Key Laboratory of Stem Cell and Reproductive Biology at the Chinese Academy of Sciences' Institute of Zoology. The Wang laboratory focuses on developing novel technologies to achieve efficient and specific genome engineering, and applying them to study the function of genes and establish novel therapeutic methods. His laboratory has developed Zygote Electroporation of Nuclease (ZEN) method to generate genetically modified mouse models with high throughput and efficiency, Casilio method to regulate gene transcription, as well as method to generate CAR-T cells with multiplex gene editing. He previously worked on the development of a variety of genome engineering technologies, including a transposon-based "Calling Card" method for determining the genome-wide binding locations of transcription factors, TALEN-mediated genome editing in human pluripotent stem cells and mice, CRISPR-mediated multiplexed genome editing in mice, and CRISPR-mediated gene activation in human cells.

**Anna Wedell, M.D., Ph.D** is Head of the Centre for Inherited Metabolic Diseases at Karolinska University Hospital and Professor of medical genetics at Karolinska Institute, Sweden. She leads a translational centre combining clinical and laboratory medicine, and basic experimental science. The centre performs nationwide clinical diagnostics of inborn errors of metabolism, including the national neonatal screening program ("PKU test"). Another strong focus is mitochondrial medicine. By combining whole genome sequencing and mechanistic studies in

model systems, novel monogenic diseases are discovered and pathogenetic mechanisms are explored. Wedell received her M.D. in 1988 and her Ph.D. in medical genetics in 1994 at Karolinska Institute. In 2006, she became board certified in clinical genetics after training at the Karolinska University Hospital. She is a member of the Royal Swedish Academy of Sciences.

## Staff Officer

**Katherine Bowman, Ph.D.** is a Senior Program Officer with the Board on Life Sciences of the U.S. National Academies of Sciences, Engineering, and Medicine. She manages studies across a range of life sciences topics and participates in National Academies' activities addressing the potential implications of developments in science and technology. She was most recently involved in the study *Biodefense in the Age of Synthetic Biology*, released in 2018 and served as study director for the 2017 reports *Human Genome Editing: Science, Ethics, and Governance* and *Microbiomes of the Built Environment: A Research Agenda for Indoor Microbiology, Human Health, and Buildings*. In addition, she is involved in international activities, many conducted collaboratively with the InterAcademy Partnership, national academies of sciences, and international scientific unions, that explore advances in science and their potential impacts on implementation of the Biological and Chemical Weapons Conventions. Recent activities include the proceedings *Governance of Dual Use Research in the Life Sciences: Advancing Global Consensus on Research Oversight* (2018). She received her Ph.D. in Biomedical Engineering from Johns Hopkins University.