

Ethical, Legal, and Regulatory Issues Associated with Neural Chimeras and Organoids

Committee

Bernard Lo

Co-Chair

Bernard “Bernie” Lo, M.D., (NAM) is President and CEO Emeritus of the Greenwall Foundation. Previously, he was Professor of Medicine and Director of the Program in Medical Ethics at the University of California San Francisco.

Currently he is co-chair of the Standards Working Group of the California Institute of Regenerative Medicine, which recommends regulations for stem cell research funded by the state of California. At the National Institutes of Health (NIH), he serves on Data and Safety Monitoring Committees for HIV vaccine trials and the Long-term Oxygen Treatment Trial.

Dr. Lo serves on the Board of Directors of Association for the Accreditation of Human Research Protection Programs (AAHRPP) and on the Medical Advisory Panel of Blue Cross/Blue Shield. Formerly he was a member of the National Bioethics Advisory Commission under President Clinton, the NIH Recombinant DNA Advisory Committee, and the Ethics Subcommittee, and the Advisory Committee to the Director of the Centers for Disease Control and Prevention. He currently is a member of the Board of Life Sciences of the National Academy of Science (NAS).

Dr. Lo and his colleagues have published around 200 peer-reviewed articles on ethical issues concerning decision-making near the end-of-life, stem cell research, research with human participants and its oversight, the doctor-patient relationship, conflicts of interest, HIV infection, and public health. With colleagues on the UCSF stem cell research oversight committee, he has written articles on ethical issues in the procurement of embryos for research, oversight of stem cell lines derived in other institutions, informed consent for future research, and prohibiting the use of induced pluripotent stem cells for reproductive cloning.

Joshua R. Sanes

Co-Chair

Joshua R. Sanes, Ph.D., (NAS) is the Jeff C. Tarr Professor of Molecular and Cellular Biology and the Paul J. Finnegan Family Director of the Center for Brain Science at Harvard University. Dr. Sanes has spent his research career studying the connections among neurons, called synapses, which form the complex circuits responsible for our mental activities. He uses molecular, genetic, and imaging approaches to understand how synapses form, mature and function. The Center he directs supports an interdisciplinary approach that combines biology, chemistry, engineering, and psychology to look at the circuit level questions in neuroscience.

After graduating from Yale University in 1970 with degrees in Biochemistry and Psychology, Dr. Sanes earned a Ph.D. in Neurobiology from Harvard in 1976. Following postdoctoral work at the University of California at San Francisco, he joined the faculty of Washington University in St. Louis, where he spent over 20 years and held an Endowed Chair. In 2004, he returned to Harvard, assuming his current position. Dr. Sanes has authored over 300 publications and is a highly-sought after presenter at national and international symposia

Dr. Sanes is a member of the U.S. National Academy of Sciences, a Fellow of the American Association for the Advancement of Science and the American Academy of Arts and Sciences, and recipient of the Alden Spencer Award of Columbia University. He has served on the National Advisory Council of the National Institute of Neurological Diseases and Stroke, the Council of the Society for Neuroscience, and advisory panels for the Muscular Dystrophy Association, the Amyotrophic Lateral Sclerosis (ALS) Association, the Klingenstein Neuroscience Fund, the Searle Scholars Fund, the Stowers Institute, and the Howard Hughes Medical Institute.

Paola Arlotta

Member

Paola Arlotta, Ph.D., is the Chair and Golub Family Professor of Harvard's Department of Stem Cell and Regenerative Biology and a Harvard College Professor. She is also Associate Member of the Stanley Center for Psychiatric Research at the Broad Institute of MIT and Harvard.

Collectively, the Arlotta lab research program explores the interface between development and engineering of the neocortex, to gain fundamental understanding of both the principles that govern normal cortical development and of previously-inaccessible mechanisms of human neurodevelopmental disease. The lab aims to understand and model complex human cortical pathology, focusing on the development of new high-throughput in vitro models of human cortical development and neurodevelopmental disease using stem cell-derived 3D brain organoids.

Arlotta received her M.S. in biochemistry from the University of Trieste, Italy and her Ph.D. in molecular biology from the University of Portsmouth, UK. She subsequently completed her postdoctoral training in neuroscience at Harvard Medical School. Arlotta is the recipient of many awards, including the 2017 George Ledlie Prize from Harvard, The Fannie Cox Prize for excellence in science teaching, the 2018 Friedrich Wilhelm Bessel Research Award from the Humboldt Foundation, and a 2019 Harvard College Professorship.

R. A. Charo

Member

R. Alta Charo, J.D., (NAM) is on the faculty of the Law School and the Department of Medical History and Bioethics at the Medical School at the University of Wisconsin at Madison. She also serves on the faculty of the UW Masters in Biotechnology Studies program and lectures in the MPH program of the Department of Population Health Sciences.

Professor Charo (B.A. biology, Harvard 1979; J.D. Columbia, 1982) is an elected member (2004) of the World Technology Network and (2005) the Wisconsin Academy of Sciences, Arts and Letters. And in 2006 she was elected to membership in the National Academy of Medicine.

Professor Charo has served on several expert advisory boards of organizations with an interest in stem cell research, including CuresNow, the Juvenile Diabetes Research Foundation, the International Society for Stem Cell Research and WiCell, as well as on the advisory board to the Wisconsin Stem Cell Research Program. From 2005-2009 she was a member of the ethics standards working group of the California Institute for Regenerative Medicine. Also in 2005, she helped to draft the National Academies' Guidelines for Embryonic Stem Cell Research, and in 2006 she was appointed to co-chair the National Academies' Human Embryonic Stem Cell Research Advisory Committee.

Professor Charo's advisory committee service for the federal government includes the 1994 NIH Human Embryo Research Panel, and (1996-2001) President Clinton's National Bioethics Advisory Commission where she participated in drafting its reports on "Cloning Human Beings"(1997); Research Involving Persons with Mental Disorders that May Affect Decision-making Capacity"(1998); "Research Involving Human Biological Materials: Ethical Issues and Policy Guidance"(1999); "Ethical Issues in Human Stem Cell Research"(1999); "Ethical and Policy Issues in International Research: Clinical Trials in Developing Countries" (2001); and "Ethical and Policy Issues in Research Involving Human Participants" (2001).

At the National Academies, from 2001-2008 she was a member of the Board on Life Sciences. She served as its liaison to the Committee on Research Standards and Practices to Prevent Destructive Applications of Biotechnology as well as its committee to develop national voluntary guidelines for stem cell research. She also served as a member of the National Academy of Medicine's Committee on Smallpox Vaccination Program Implementation and since 2006 she has served on its Board on Population Health and Public Health Practice. In 2005-2006, she was a member of the committee to review the FDA and the U.S. national system for the assurance of drug safety.

John H. Evans

Member

John H. Evans, Ph.D., is Tata Chancellor's Chair in Social Sciences, Associate Dean of Social Sciences, and Co-director of the Institute for Practical Ethics at UCSD. He earned his B.A from Macalester College and his Ph.D. from Princeton. He has been a visiting member at the Institute for Advanced Study, a post-doctoral fellow at Yale University and has held visiting professorial fellowships or honorary professorships at the Universities of Edinburgh, Muenster, Ben Gurion, and Queensland.

Originally trained as a sociologist of religion, throughout his career he has been focused on the abstract human concerns often addressed by Western religions such as the nature of the human, inter-generational responsibility, and societal value pluralism. More specifically his research focuses on politics, religion, science, and ethics, with a particular interest in examining humanistic questions using quantitative and qualitative social science methodologies. He has published seven books and over 50 articles and volume chapters. From 2015-2017 he was a member of the National Academies of Sciences, Engineering and Medicine's Committee on Human Gene Editing: Scientific, Medical and Ethical Considerations.

Fred H. Gage

Member

Fred H. Gage, Ph.D., (NAS, NAM) is President and Professor at the Laboratory of Genetics and the Vi and John Adler Chair for Research on Age-related Neurodegenerative Disease at the Salk Institute for Biological Studies in La Jolla, California. He earned a B.S. from the University of Florida, and both an M.S. and Ph.D. from Johns Hopkins University.

Dr. Gage concentrates on the unexpected plasticity and adaptability to the environment that mammals have throughout life. His lab showed that human beings are capable of growing new nerve cells throughout life, in a process called neurogenesis. Gage's team explores how these cells can be prompted to become mature, functioning nerve cells in the adult brain and spinal cord. Dr. Gage uses these reprogrammed cells to make human brain organoids to model the more complex three dimensional nature of the brain. To achieve vascularization, and better survival of the organoids, he has transplanted the cells to the brains of immunocompromised mice. He has also showed that environmental enrichment and physical exercise can enhance the growth of new brain cells. His team continues to study the underlying cellular and molecular mechanisms of neurogenesis to find possible avenues to repair damaged or aging brains.

Gage's lab also models diseases in the laboratory using human stem cells. By reprogramming human skin cells and other cells from patients with neurologic and psychiatric diseases into induced pluripotent stem cells (iPSCs) and induced neurons (iN), his work seeks to decipher the progression and mechanisms that lead to brain cell dysfunction. Dr. Gage uses these reprogrammed cells to make human brain organoids to model the more complex three dimensional structure of the brain. To achieve vascularization, and better survival of the organoids, he has transplanted the cells to the brains of immunocompromised mice. Gage has also revealed that mobile sequences of DNA called "jumping genes" are active in neural stem cells contributing to genomic mosaicism. Specifically, he is interested in how this mosaicism (different sets of genes within a single organism) may lead to differences in brain function between individuals.

Henry T. Greely

Member

Henry T. “Hank” Greely, J.D., is Deane F. and Kate Edelman Johnson Professor of Law and Professor, by courtesy, of Genetics at Stanford University.

Professor Greely specializes in ethical, legal, and social issues arising from advances in the biosciences, particularly from genetics, neuroscience, and human stem cell research. He directs the Stanford Center for Law and the Biosciences, chairs the California Advisory Committee on Human Stem Cell Research, and serves on the Neuroscience Forum of the National Academy of Medicine. From 2007 to 2010 he was a co-director of the Law and Neuroscience Project. In 2006, he was elected a fellow of the American Association for Advancement of Science.

Professor Greely graduated from Stanford in 1974 and from Yale Law School in 1977. He served as a law clerk for Judge John Minor Wisdom on the United States Court of Appeals and for Justice Potter Stewart of the United States Supreme Court. After working during the Carter Administration in the Departments of Defense and Energy, he entered private practice in Los Angeles in 1981 as a litigator with the law firm of Tuttle & Taylor, Inc. He began teaching at Stanford in 1985.

Patricia A. King

Member

Patricia A. King, J.D., (NAM) is Professor Emerita of Law at Georgetown University Law Center. Professor King’s expertise is in the study of law, medicine, ethics and public policy. She is also an adjunct professor in the Department of Health Policy and Management, School of Hygiene and Public Health at Johns Hopkins University. She is the co-author of Cases and Materials on Law, Science and Medicine. She teaches Family Law courses and offers a seminar in Bioethics and the Law. She is a member of the American Law Institute and the Institute of Medicine and a Fellow of the Hastings Center. Her work in the field of bioethics has included service on the HEW-Advisory Recombinant DNA Advisory Committee, the President’s Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research, the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, and the Ethics, Legal and Social Issues Working Group of the Human Genome Project. She is a fellow of the Harvard Corporation and a member of the Board of Trustees of Wheaton College. Her professional experience before joining the Law Center faculty in 1973 was primarily in the civil rights field; she was the Deputy Director of the Office of Civil Rights and Special Assistant to the Chairman of the EEOC. She also served as a Deputy Assistant Attorney General in the Civil Division of the Department of Justice.

She earned her B.A. from Wheaton College and her J.D. from Harvard Law School.

William T. Newsome

Member

William T. “Bill” Newsome, Ph.D., (NAS) is the Harman Family Provostial Professor of Neurobiology at the Stanford University School of Medicine, and the Vincent V.C. Woo Director of the Wu Tsai Neurosciences Institute. He received a B.S. degree in physics from Stetson University and a Ph.D. in biology from the California Institute of Technology.

Dr. Newsome is a leading investigator in systems and cognitive neuroscience. He has made fundamental contributions to our understanding of the neural mechanisms underlying visual perception and simple forms of decision making. Among his honors are the Rank Prize in Optoelectronics, the Spencer Award, the Distinguished Scientific Contribution Award of the American Psychological Association, the Dan David Prize of Tel Aviv University, the Karl Spencer Lashley Award of the American Philosophical Society, and the Champalimaud Vision Award. His distinguished lectureships include the 13th Annual Marr Lecture at the University of Cambridge the 9th Annual Brenda Milner Lecture at McGill University, and most recently, the Distinguished Visiting Scholar lectures at the Kavli Institute of Brain and Mind, UCSD. He was elected to membership in the National Academy of Sciences in 2000, and to the American Philosophical Society in 2011. Newsome co-chaired the NIH BRAIN working group, charged with forming a national plan for the coming decade of neuroscience research in the United States.

Sally Temple

Member

Sally Temple, Ph.D., is the Scientific Director of the Neural Stem Cell Institute and oversees scientific programs with the goal of understanding the role of neural stem cells in Central Nervous System (CNS) development, maintenance, and repair. Dr. Temple is past member of the board of directors and president of the International Society for Stem Cell Research. A native of York, England, Dr. Temple leads a team of 30 researchers focused on using neural stem cells to develop therapies for eye, brain, and spinal cord disorders. In 2008, she was awarded the MacArthur Fellowship Award for her contribution and future potential in the neural stem cell field.

Dr. Temple received her undergraduate degree from Cambridge University, specializing in developmental biology and neuroscience. She performed her Ph.D. work in optic nerve development at University College London, UK. She received a Royal Society fellowship to support her postdoctoral work at Columbia University, NY, where she focused on spinal cord development.

In 1989, Dr. Temple discovered that the embryonic mammalian brain contained a rare stem cell that could be activated to proliferate in vitro and produce both neurons and glia. Since then, her lab has continued to make pioneering contributions to the field of stem cell research, by characterizing neural stem cells and the intrinsic and environmental factors that regulate their behavior. Her lab's research on the characterization of neural stem and progenitors brings us closer to developing effective clinical treatments for central nervous system damage in which tissue is lost, for example, due to neurodegenerative diseases or trauma.

Using patient-derived induced pluripotent stem cells (iPSCs), Dr. Temple's research group is building models to study neurodegenerative diseases, with the goal of identifying therapies. Dr. Temple helps lead the iPSC effort of the Tau Consortium, an international, collaborative group focused on understanding and developing therapies for dementias. This work includes generating human iPSC-derived 3D organoids and assembloids to model neuropathology across different affected brain regions. Her group also models retinal degeneration using iPSC technology and collaborates with Dr. Jeff Stern and a team developing a cell therapy for age-related macular degeneration using an adult stem cell they discovered in the human retina.

S. Lawrence Zipursky

Member

S. Lawrence “Larry” Zipursky, Ph.D., (NAS) is the Jerome J. Belzer Chair of Medical Research and Distinguished Professor of Biological Chemistry at University of California, Los Angeles and an Investigator of the Howard Hughes Medical Institute.

Dr. Zipursky studies brain development, focusing on how neural circuits are formed during development. His laboratory has provided insights into various aspects of circuit assembly, including the molecular basis of neuronal identity through their work on the Dscam1 locus in Drosophila. Zipursky was elected Fellow of the American Academy of Arts and Sciences in 1998 and a member of the National Academy of Sciences in 2009. He received the Louisa Gross Horwitz Prize for Biology and Biochemistry from Columbia University in 2015.

Dr. Zipursky received his PhD in Molecular Biology at Albert Einstein College of Medicine, where he completed his thesis with Dr. Jerard Hurwitz, studying DNA replication in E. coli. In 1981, he moved to the California Institute of Technology to study neural development in Drosophila with Dr. Seymour Benzer as a Helen Hay Whitney Postdoctoral Fellow. He joined the department of biological chemistry at UCLA as a faculty member in 1985 and the Howard Hughes Medical Institute as an investigator in 1991. He has served on the National Advisory Council of the National Institute of Neurological Disease and Stroke, and various scientific advisory panels including the McKnight, the Helen Hay Whitney, and the Alfred P. Sloan Foundations.

Anne-Marie C. Mazza

Staff Officer