Donald E. Ingber

Donald E. Ingber,MD,PhD is the Founding Director of the Wyss Institute for Biologically Inspired Engineering at Harvard University, *Judah Folkman Professor of Vascular Biology* at Harvard Medical School and the Vascular Biology Program at Boston Children's Hospital, and Professor of Bioengineering at the Harvard John A. Paulson School of Engineering and Applied Sciences. He received his B.A., M.A., M.Phil., M.D. and Ph.D. from Yale University. Ingber is a pioneer in the field of biologically inspired engineering, and at the Wyss Institute, he currently leads scientific and engineering teams that cross a broad range of disciplines to develop breakthrough bioinspired technologies to advance healthcare and to improve sustainability. His work has led to major advances in mechanobiology, tumor angiogenesis, tissue engineering, systems biology, nanobiotechnology and translational medicine, with his most recent pioneering contribution being the development of human Organ-on-Chips as replacements for animal testing. He also has made great strides in translating his innovations into commercial products and many are now either in clinical trials or currently being sold. He has authored more than 500 publications and over 165 issued or pending U.S. patents, founded 5 companies, and has been a guest speaker at more than 550 events internationally. Ingber is a member of the National Academy of Medicine, National Academy of Engineering, National Academy of Inventors, American Institute for Medical and Biological Engineering, and the American Academy of Arts and Sciences. Ingber's Organ Chip technology was named one of the Top 10 Emerging Technologies by the World Economic Forum and Design of the Year by the London Design Museum. It was also acquired by the Museum of Modern Art (MoMA) in New York City for its permanent design collection.

Abstract:

This presentation will highlight advances that my team at the Wyss Institute has made in the engineering of human "Organ-on-a-Chip" (Organ Chip) microfluidic cultured devices lined by living human cells that recapitulate organ-level functions as a way to replace animal testing for drug development, mechanistic discovery, and personalized medicine. I will describe the engineering of multiple human organ chips, including lung, intestine, kidney, bone marrow, liver, lymph node, and coupled blood-brain barrier and brain neuronal network chips. By recreating organ-specific physical and chemical microenvironments, including fluid flow, mechanical motions, oxygen gradients, and the presence of complex living microbiome, we obtain a level of biomimicry of organ-level functions not possible in other in vitro models. These Organ Chip models also have been adapted to develop multiple human disease models (e.g., pulmonary edema, asthma, COPD, influenza, colitis, environmental enteric dysfunction, lung cancer, esophageal cancer, radiation toxicity, and rare bone marrow disorders), identify approved drugs that might potentially be repurposed as COVID19 therapies, and discover new therapeutics. A Bone Marrow Chip was recently developed that precisely mimics human bone marrow toxicities induced by clinically relevant (pharmacokinetic) exposures to drugs as well as by radiation exposure, and it also was used to create personalized models of a rare genetic disorder of the marrow that provided new mechanistic

insight into this disease. In addition, we engineered rat, dog, and human Liver Chips that recapitulate species-specific drug hepatotoxicities, which could help to replace use of these animals in preclinical drug development. Organ Chips also have been used recently to expedite repurposing of drugs for COVID-19. Finally, I will describe how we have integrated multiple Organ Chips into an automated 'Human Body-on-Chips' that enables real-time analysis of cellular responses to pharmaceuticals, chemicals, radiation, and toxins, as well as quantitative in vitro-to-in vivo extrapolation of human drug pharmacokinetics and pharmacodynamics.