BIOGRAPHICAL SKETCH

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NAME: INGBER, DONALD

eRA COMMONS USER NAME (credential, e.g., agency login):

POSITION TITLE: Member of Scientific Advisory Board

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	END DATE MM/YYYY	FIELD OF STUDY
Yale University , New Haven, CT	MA	05/1977	Molecular Biophysics and Biochemistry
Yale University , New Haven, CT	BA	05/1977	Molecular Biophyics and Biochemistry
Yale University, New Haven, CT	MPHIL	05/1981	Cell Biology
Yale University, New Haven , CT	PHD	05/1984	Cell Biology
Yale University, New Haven, CT	MD	05/1984	Medicine
Boston Children's Hospital , Boston, MA	Postdoctoral Fellow	1986	Vascular Biology
Harvard Medical School, Boston, MA	Postdoctoral Fellow	1986	Pathology

A. Personal Statement

My laboratory is interested in how microenvironmental cues, particularly mechanical forces and extracellular matrix, regulate epithelial organization, tissue morphogenesis, and organ-level pathophysiology. Our work covers a wide range of interests from fundamental studies of the molecular basis of cellular mechanotransduction to engineering of microdevices and nanotechnologies for basic research, as well as clinical diagnostics and therapeutics. A major effort is now focused on development and application of human “Organs on Chips” that are microfluidic culture models of major functional units of human organs, which can be used to create human disease models to study pathophysiological mechanisms in situ, as well as replace costly and time-consuming animal studies for drug development and toxicology applications. My team also has developed multiscale computational molecular simulation tools that we are applying to drug discovery.

1. Chen CS, Mrksich M, Huang S, Whitesides GM, Ingber DE. Geometric control of cell life and death. Science. 1997 May 30;276(5317):1425-8. PubMed PMID: 9162012.
2. Huh D, Matthews BD, Mammoto A, Montoya-Zavala M, Hsin HY, Ingber DE. Reconstituting organ-level lung functions on a chip. Science. 2010 Jun 25;328(5986):1662-8. PubMed Central PMCID: PMC8335790.
3. Ingber DE, Madri JA, Jamieson JD. Role of basal lamina in neoplastic disorganization of tissue architecture. Proc Natl Acad Sci U S A. 1981 Jun;78(6):3901-5. PubMed Central PMCID: PMC319681.
4. Wang N, Butler JP, Ingber DE. Mechanotransduction across the cell surface and through the cytoskeleton. Science. 1993 May 21;260(5111):1124-7. PubMed PMID: 7684161.

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

2021 -	Member of Scientific Advisory Board, Fulcrum Therapeutics
2020 -	Consultant, Estee Lauder Corporation
2019 -	Member of Board of Directors, Scientific Advisory Board & Consultant, Pareto Bio (formerly Consortia Tx)
2019 - 2019	Consultant, Eli Lilly and Company
2018 -	Consultant, F Hoffman-LaRoche
2018 -	Scientific Founder & Member of Board of Directors, BOA Biomedical Inc.
2018 - 2018	Consultant, L'Oreal
2017 -	Member of Scientific Advisory Board, SynDevRx
2017 - 2017	Consultant, SlipChip Corp.
2017 - 2017	Consultant , AstraZeneca, Inc.
2016 -	Scientific Founder, Chair of Scientific Advisory Board, FreeFlow Medical Devices
2015 -	Advisor, Puretech Health LLC
2015 - 2018	Scientific Founder, Chair of Scientific Advisory Board, Opsonix, Inc., Boston, MA
2014 -	Scientific Founder, Member of Board of Directors, Chair of the Scientific Advisory Board, Consultant, Emulate Inc., Boston, MA
2014 - 2017	Member of Board of Directors, Wyss Center for Bio and Neuro Engineering, Geneva
2014 - 2017	Member of Executive Advisory Board, Le Laboratoire, Cambridge, MA
2009 -	Founding Director, Wyss Institute for Biologically Inspired Engineering at Harvard
2008 -	Professor of Engineering, Harvard University
2008 - 2009	Interim Co-Director, Vascular Biology Program at Boston Children's Hospital
2004 -	Judah Folkman Professor of Vascular Biology, Harvard Medical School
2002 -	Senior Associate in Vascular Biology, Boston Children's Hospital
1999 -	Professor of Pathology, Harvard Medical School
1992 - 1999	Associate Professor of Pathology, Harvard Medical School
1988 - 1992	Assistant Professor of Pathology, Harvard Medical School
1988 - 1992	Instructor in Pathology, Harvard Medical School
1986 - 2002	Research Associate, Vascular Biology Program, Boston Children's Hospital

Honors

2006 - 2016	Highly-cited Researcher (Cross Field Category), Web of Science
2021	Member, National Academy of Engineering
2021	Wilbur Cross Medal, Yale University
2019	Highly Cited Researcher Cross Field Category, Web of Science
2018	Lifetime Achievement Award, Albert Marquis
2017	Founders Award, Biophysical Society
2016	Member, American Academy of Arts and Sciences
2016	Shu Chien Award, Biomedical Engineering Society
2016	Pioneer Award, University of Pittsburgh
2016	Max Tischler Award, Tufts University
2015	Member, National Academy of Inventors
2015	Best Design of the Year and Product Design of the Year Award for Organs on Chips, London Design Museum
2015	100 Leading Global Thinkers , Foreign Policy
2014	Annual Award, Graham Clarke Oration
2013	New England's Breakthrough Invention and Inventor Honoree, Boston Patent Law Association

2013	NC3RS Award , National Centre for Replacement, Refinement and Reduction of Animals in Research
2013	World's Most Innovative People Award, New York World Summit on Innovation and Entrepreneurship
2012	Member, National Academy of Medicine
2012	Richard Bachrach Award, American Association of Orthopedics
2012	Webby Award for Science, International Academy of Digital Arts
2011	Scientific Breakthrough of the Year Award for Lung on a Chip, American Thoracic Society
2010	Rous Whipple Award, American Society of Investigative Pathology
2010	Lifetime Achievement Award, American Society for In Vitro Biology
2009	Pritzker Award, Biomedical Engineering Society
2008	Member, American Institute for Medical and Biological Engineering
2005	Talbot Medal in Theoretical Mechanics, University of Illinois, Urbana-Champaign

C. Contribution to Science

1. 1. My graduate research led to the discovery that changes in extracellular matrix (ECM) and tissue mechanics actively contribute to cancer formation, and that solid tumors can be induced to differentiate and revert to a non-growing state by being placed in contact with normal embryonic ECM. Prior to this work, ECM was viewed as a passive host barrier through which a malignant tumor must gain the ability to invade. Over the past 35 years, our group and others have confirmed these findings, and the importance of the tumor microenvironment for cancer development is well accepted in the field. This work has also led to development of new approaches to cancer differentiation therapy.
   a. Bischof AG, Yüksel D, Mammoto T, Mammoto A, Krause S, Ingber DE. Breast cancer normalization induced by embryonic mesenchyme is mediated by extracellular matrix biglycan. Integr Biol (Camb). 2013 Aug;5(8):1045-56. PubMed PMID: 23817524.
   b. Ingber DE, Madri JA, Jamieson JD. Role of basal lamina in neoplastic disorganization of tissue architecture. Proc Natl Acad Sci U S A. 1981 Jun;78(6):3901-5. PubMed Central PMCID: PMC319681.
   c. Ingber DE, Madri JA, Jamieson JD. Neoplastic disorganization of pancreatic epithelial cell-cell relations. Role of basement membrane. Am J Pathol. 1985 Nov;121(2):248-60. PubMed Central PMCID: PMC1888057.
   d. Ingber DE, Madri JA, Jamieson JD. Basement membrane as a spatial organizer of polarized epithelia. Exogenous basement membrane reorients pancreatic epithelial tumor cells in vitro. Am J Pathol. 1986 Jan;122(1):129-39. PubMed Central PMCID: PMC1888129.

2. In my graduate work, I also proposed the theory that living cells are constructed as tensegrity (tensional integrity) structures that stabilize their shape by establishing a state of isometric tension (prestress) in their cytoskeleton. A corollary of this theory is that cellular mechanotransduction - the process by which living cells sense mechanical forces and transduce them into changes into intracellular biochemistry - is mediated by transmembrane receptors, such as integrins, that provide a

   specific molecular path for force transmission from ECM and to the cytoskeleton and nucleus. In later studies, my group and others provided experimental confirmation for these theories. Prior to this work, cells were generally viewed as membranous structures filled with a viscous cytoskeleton, and little was known about the molecular basis of cellular mechanotransduction. This work helped to birth the field of Mechanobiology.

   a. Chen CS, Mrksich M, Huang S, Whitesides GM, Ingber DE. Geometric control of cell life and death. Science. 1997 May 30;276(5317):1425-8. PubMed PMID: 9162012.

b. Ingber DE. Cellular tensegrity: defining new rules of biological design that govern the cytoskeleton. J Cell Sci. 1993 Mar;104 (Pt 3):613-27. PubMed PMID: 8314865.
c. Maniotis AJ, Chen CS, Ingber DE. Demonstration of mechanical connections between integrins, cytoskeletal filaments, and nucleoplasm that stabilize nuclear structure. Proc Natl Acad Sci U S A. 1997 Feb 4;94(3):849-54. PubMed Central PMCID: PMC19602.
d. Wang N, Butler JP, Ingber DE. Mechanotransduction across the cell surface and through the cytoskeleton. Science. 1993 May 21;260(5111):1124-7. PubMed PMID: 7684161.

3. In my postdoctoral research, I demonstrated the key role that ECM and integrins play in control of tumor angiogenesis, and that new capillary blood vessel formation is required for the transition from pre-malignancy to cancer formation. Prior to this work virtually all of the work in the angiogenesis field was focused on the role of soluble angiogenesis factors, and angiogenesis was only thought to be important for expansion of existing cancers. This work also led to the discovery of one of the first angiogenesis inhibitors (TNP-470) to enter human clinical trials, which produced complete cancer remissions in a subset of patients.

a. Folkman J, Watson K, Ingber D, Hanahan D. Induction of angiogenesis during the transition from hyperplasia to neoplasia. Nature. 1989 May 4;339(6219):58-61. PubMed PMID: 2469964.
b. Ingber D, Folkman J. Inhibition of angiogenesis through modulation of collagen metabolism. Lab Invest. 1988 Jul;59(1):44-51. PubMed PMID: 2455830.
c. Ingber D, Fujita T, Kishimoto S, Sudo K, Kanamaru T, Brem H, Folkman J. Synthetic analogues of fumagillin that inhibit angiogenesis and suppress tumour growth. Nature. 1990 Dec 6;348(6301):555-7. PubMed PMID: 1701033.
d. Ingber DE, Madri JA, Folkman J. A possible mechanism for inhibition of angiogenesis by angiostatic steroids: induction of capillary basement membrane dissolution. Endocrinology. 1986 Oct;119(4):1768-75. PubMed PMID: 2428602.

4. My work on mechanobiology also led me to adapt methods used for computer microchip manufacturing to develop a new method for microengineering ECM adhesive substrates and microfluidic devices that provide precise control of cell adhesion, position, shape on the micrometer scale. Using this soft lithography-based ‘microcontact printing’ method, we were able to unequivocally demonstrate that cells can be switched between different fates (e.g., growth, differentiation, apoptosis, directional motility) solely by physical changes in cell shape and cytoskeletal organization, again confirming predictions of the cellular tensegrity model. Prior to this work, virtually all models of cell regulation assumed that biological control was based on binding interactions between soluble factors and cellular receptors. We also later confirmed that cell growth, tissue development (angiogenesis), and whole organ formation (tooth) are regulated by mechanical forces in vivo, and we defined the molecular mechanisms by which these mechanical forces produce alterations in gene transcription.

a. Chen CS, Mrksich M, Huang S, Whitesides GM, Ingber DE. Geometric control of cell life and death. Science. 1997 May 30;276(5317):1425-8. PubMed PMID: 9162012.
b. Mammoto A, Connor KM, Mammoto T, Yung CW, Huh D, Aderman CM, Mostoslavsky G, Smith LE, Ingber DE. A mechanosensitive transcriptional mechanism that controls angiogenesis. Nature. 2009 Feb 26;457(7233):1103-8. PubMed Central PMCID: PMC2708674.
c. Mammoto T, Mammoto A, Torisawa YS, Tat T, Gibbs A, Derda R, Mannix R, de Bruijn M, Yung CW, Huh D, Ingber DE. Mechanochemical control of mesenchymal condensation and embryonic tooth organ formation. Dev Cell. 2011 Oct 18;21(4):758-69. PubMed Central PMCID: PMC3199351.
d. Singhvi R, Kumar A, Lopez GP, Stephanopoulos GN, Wang DI, Whitesides GM, Ingber DE. Engineering cell shape and function. Science. 1994 Apr 29;264(5159):696-8. PubMed PMID: 8171320.

5. Throughout my career, I have combined approaches from molecular cell biology, physics, engineering, computer science, systems biology, and nanotechnology to develop multiple new approaches for translational medicine. A major effort is now focused on development of human “Organs on Chips” that use methods of miniaturization originally developed to make microchips for the computer industry to build functional circuits with living cells as components. We currently are building tiny, complex, three-dimensional models of human organs that can be used to study pathophysiological mechanisms in situ, as well as replace costly and time consuming animal studies for drug development and toxicology applications. We also have applied reverse gene network engineering approaches to identify genes that are causally involved in driving breast cancer formation, and then developed nanotherapeutic delivery systems for siRNAs that target these genes which prevent cancer formation in a mouse transgenic breast cancer model. In addition, we have developed a novel dialysis-like therapeutic device for sepsis therapy that uses a genetically engineered human opsonin to remove pathogens and toxins from blood circulating through a microfluidic device when external magnetic fields are applied. These efforts have helped to bring the level of interdisciplinary research in translational medicine to a higher level. [Intestine Chip publications are listed above]

    a. Benam KH, Novak R, Nawroth J, Hirano-Kobayashi M, Ferrante TC, Choe Y, Prantil-Baun R, Weaver JC, Bahinski A, Parker KK, Ingber DE. Matched-Comparative Modeling of Normal and Diseased Human Airway Responses Using a Microengineered Breathing Lung Chip. Cell Syst. 2016 Nov 23;3(5):456-466.e4. PubMed PMID: 27894999.
    b. Chou DB, Frismantas V, Milton Y, David R, Pop-Damkov P, Ferguson D, MacDonald A, Vargel Bölükbaşı Ö, Joyce CE, Moreira Teixeira LS, Rech A, Jiang A, Calamari E, Jalili-Firoozinezhad S, Furlong BA, O'Sullivan LR, Ng CF, Choe Y, Marquez S, Myers KC, Weinberg OK, Hasserjian RP, Novak R, Levy O, Prantil-Baun R, Novina CD, Shimamura A, Ewart L, Ingber DE. On-chip recapitulation of clinical bone marrow toxicities and patient-specific pathophysiology. Nat Biomed Eng. 2020 Apr;4(4):394-406. PubMed Central PMCID: PMC7160021.
    c. Reilly C, Ingber DE. Art Advancing Science: Filmmaking Leads to Molecular Insights at the Nanoscale. ACS Nano. 2017 Dec 26;11(12):12156-12166. PubMed PMID: 29043776.
    d. Sontheimer-Phelps A, Chou DB, Tovaglieri A, Ferrante TC, Duckworth T, Fadel C, Frismantas V, Sutherland AD, Jalili-Firoozinezhad S, Kasendra M, Stas E, Weaver JC, Richmond CA, Levy O, Prantil-Baun R, Breault DT, Ingber DE. Human Colon-on-a-Chip Enables Continuous In Vitro Analysis of Colon Mucus Layer Accumulation and Physiology. Cell Mol Gastroenterol Hepatol. 2020;9(3):507-526. PubMed Central PMCID: PMC7036549.