BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Ngan F. Huang, PhD

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

POSITION TITLE: Associate Professor of Cardiothoracic Surgery (Stanford University); and Biomedical Engineer (Veterans Affairs Palo Alto Health Care System)

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)*	Completion Date MM/YYYY	FIELD OF STUDY
Massachusetts Institute of Technology, Cambridge, MA	BS	06/2002	Chemical Engineering
University of California Berkeley & University of California San Francisco, Berkeley, CA	MS	12/2005	Bioengineering
University of California Berkeley & University of California San Francisco, Berkeley, CA	PhD	12/2006	Bioengineering
Stanford University, Stanford, CA	Postdoctoral	01/2007-07/2010	Cardiovascular Medicine

A. Personal Statement

My laboratory aims to understand the biochemical and mechanical interactions between extracellular matrix (ECM) proteins and stem cells that regulate cardiovascular differentiation, survival, and angiogenesis, with the goal of translating these basic insights to the design of biological therapies to treat cardiovascular disease. A major research focus of my laboratory is the treatment of peripheral arterial disease using stem cell and biomaterials strategies, in which we have employed both naturally derived biomaterials as well as biomimetic engineered hydrogels. I have extensive training in bioengineering, stem cell biology, and cardiovascular medicine. This multidisciplinary background uniquely positions me to develop new technologies to address medical challenges and biological questions from bench to bedside. I have developed strong leadership and organizational skills through my active awards from the NIH, Department of Veteran Affairs, and National Science Foundation to engage other collaborators in a productive and frequent manner with feasible timelines and milestones.

Ongoing and recently completed projects that I would like to highlight include:

R01 HL127113-01A1 (Huang: PI) 2/1/16-1/31/23 (NCE)
NIH / NHLBI
Aligned Nanofibrillar Scaffolds Enhance Angiogenesis and Viability in Ischemia

R01HL142718 (Huang/Heilshorn: MPI) 7/1/18-3/31/23 (NCE)
NIH / NHLBI
Engineered Matrix Microarrays to Enhance the Regenerative Potential of iPSC-Derived Endothelial Cells

1829534 (Huang: PI) 10/1/18-9/30/22 (NCE)
National Science Foundation/Center for the Advancement of Science in Space
Tissue Engineered Muscle in Microgravity as a Novel Platform to Study Sarcopenia

20IPA35360085 (Huang: PI) 1/1/21-12/31/22
Innovative Project Award, American Heart Association
iPSC-Derived Smooth Muscle Progenitors in Elastin Hydrogels for Treating Abdominal Aortic Aneurysm

Citations:

a. Hong G, Lee JC, Robinson JT, Raaz U, Xie L, Huang NF[#], Cooke JP, Dai H. Multi-Functional In Vivo Vascular Imaging Using Near-Infrared II Fluorescence. **Nat Med** 18:1841-6, 2012 ([#] co-corresponding author). PMCID: PMC3595196.

b. Hou L, Kim JJ, Wanjare M, Patlolla B, Coller J, Natu V, Hastie TJ, Huang NF. Combinatorial Extracellular Matrix Microenvironments for Probing Endothelial Differentiation of Human Pluripotent Stem Cells. **Sci Rep** 7, 6551, 2017. PMCID: PMC5529516

c. Zaitseva T, Alcazar C, Zamani M, Hou L, Sawamura S, Yakubov E, Hopkins M, Woo YJ, Paukshto M, Huang NF. Aligned Nanofibrillar Scaffolds for Controlled Delivery of Modified mRNA. **Tissue Eng Part A.** 25:121-130, 2019. PMCID: PMC6352505

d. Nakayama KH, Quarta M, Paine P, Alcazar C, Karakikes I, Garcia V, Abilez O, Calvo NS, Simmons CS, Rando TA, Huang NF. Treatment of Volumetric Muscle Loss Using Spatially Patterned Scaffolds Enhances Vascular Organization and Functional Integration. **Commun Biol** 2:170, 2019. PMCID: PMC6505043

B. Positions, Scientific Appointments, and Honors

Positions and Employment

2022 - Present	Associate Professor, Department of Cardiothoracic Surgery, Stanford University
2021 - Present	Courtesy Assistant Professor of Chemical Engineering, Stanford University
2013 - 2022	Assistant Professor, Department of Cardiothoracic Surgery, Stanford University
2012 - Present	Biomedical Engineer, Veterans Affairs Palo Alto Health Care System, Palo Alto, CA
2010 - 2012	Instructor, School of Medicine, Division of Cardiovascular Medicine, Stanford University
2007 - 2010	Postdoctoral Research Fellow, Stanford University, Division of Cardiovascular Medicine John Cooke, MD, PhD (mentor)
2002 - 2006	Doctoral candidate, University of California Berkeley & University of California San Francisco, Joint Graduate Program in Bioengineering, Berkeley, CA; Song Li, PhD (mentor)

Honors

2017	Rising Star Award, Cellular and Molecular Bioengineering Annual Conference
2017	Young Innovator Award, journal of *Cellular and Molecular Bioengineering*
2017	Young Investigator Award, Tissue Engineering and Regenerative Medicine-Americas
2017	American Heart Association Council on Peripheral Vascular Disease, Jay D. Coffman Young Investigator Award, 2nd Place Winner
2016	Fellow of the American Heart Association (FAHA), Council of Peripheral Vascular Disease
2015	McCormick and Gabilan Fellow, Stanford University
2014	Stanford CHEM-H (Chemistry, Engineering & Medicine for Human Health) Fellow
2012	American Heart Association, Council on Peripheral Vascular Disease, Robert W Hobson II MD Early Career Investigator Award
2011	Society for Vascular Medicine Jay D. Coffman Young Investigator Award, 1st Place

Grant Reviewer

01/2022	Stem Cell Network, Impact Awards, Review Panelist
11/2021	American Heart Association, Bioengineering Fellowship Panel reviewer
10/2021	NIH Director's New Innovator Award Program (DP2)
2021/04	National Institutes of Health; Heart Lung and Blood Program Project Review Committee
2021/03	American Heart Association, Bioengineering Fellowship Panel reviewer
2020/06	Review Panelist, Peer Reviewed Medical Research Program on the Discovery - Musculoskeletal Health - 2 (DIS-MSH-1 & DIS-MSH-2)
2020/05	Review Panelist, National Science Foundation, Biomechanics and Mechanobiology
2020/03, 2020/12	Adhoc panelist, NHLBI Catalyze Special Emphasis Panel [ZHL1-CSR-RM1]
2020/02	Adhoc panelist, NIH MTE – Musculoskeletal Tissue Engineering
2019/06	Review Panelist, Congressionally Directed Medical Research Program; Peer Review Medical Research Program (PRMRP)
2019/01	Review Panelist, National Science Foundation, Biomechanics and Mechanobiology
2018-2019	Review Panelist, Congressionally Directed Medical Research Program; Peer Review Orthopedic Research Program (PRORP)
2017	Review Panelist, NIH CVRS IRG - Myocardial Ischemia and Metabolism [MIM]

2014-2016 Review Panelist, American Heart Association National Innovative Research Grant

National/International Committee Service:

04/2021-Present Chair, Cardiovascular Biomaterials special interest group, Society for Biomaterials
04/2021-Present Chair, Tissue Engineering Special Interest Group, Society for Biomaterials
01/2021-Present International Affairs Subcommittee Member, Subcommittee of Membership Committee, Biomedical Engineering Society
01/2021-Present Diversity Committee Member, Biomedical Engineering Society
12/2020-Present Mid-Career Subcommittee, of the Council Operations Committee, American Heart Association
07/2020-Present Women's Leadership Committee, American Heart Association, Council on Arteriosclerosis Thrombosis and Vascular Biology
07/2020-Present Membership and Communications Committee Member, American Heart Association, Council on Peripheral Vascular Disease
02/2020-Present Membership Committee Member, Biomedical Engineering Society
04/2019-03/2021 Vice Chair, Cardiovascular Biomaterials special interest group, Society for Biomaterials
04/2019-03/2021 Vice Chair, Tissue Engineering Special Interest Group, Society for Biomaterials
01/2019-Present Affiliations Committee Member, Biomedical Engineering Society
01/2019-Present Membership Committee Member, Tissue Engineering and Regenerative Medicine-Americas
12/2019-Present Chair, Cardiac & Vascular Regeneration and Remodeling Thematic Working Interest Group, Tissue Engineering and Regenerative Medicine-Americas
05/2018-Present Chair of Membership Committee, International Society for Applied Cardiovascular Biology (ISACB)
01/2018-Present Grants Liaison, Society for Biomaterials,
06/2017-2018 Diversity Committee, Subcommittee on Education and Community Outreach, American Heart Association, Council on Arteriosclerosis Thrombosis and Vascular Biology
12/2017-2019 Vice Chair, Cardiac & Vascular Regeneration and Remodeling Thematic Working Interest Group, Tissue Engineering and Regenerative Medicine-Americas
05/2017-4/2019 Tissue Engineering Special Interest Group, Society for Biomaterials, web representative
01/2017-Present New Organ Alliance Roadmap Committee Member—Cardiovascular
12/2016-12/2017 Secretary, Cardiac & Vascular Regeneration and Remodeling Thematic Working Interest Group, Tissue Engineering and Regenerative Medicine-Americas
10/2016-2017 International Committee Member, Biomedical Engineering Society
01/2014-12/2016 American Heart Association, Council on Peripheral Vascular Disease, Early Career and Fellows in Training Committee member

C. Contributions to Science

1. Stem Cell Therapeutics for Treatment of Ischemic Cardiovascular Diseases: To identify promising stem cell candidate for tissue engineering and regenerative medicine applications, we have made substantial progress in evaluating the efficacy of adult and pluripotent stem cells for cardiovascular remodeling and for restoring function and revascularization to ischemic cardiovascular tissues, such as the limbs or myocardium. These cells include those derived from embryonic stem cells, induced pluripotent stem cells (iPSCs), and bone marrow-derived mesenchymal stem cells. We have focused on iPSCs, owing to their autologous nature, for the treatment of peripheral arterial disease. Our early studies of injecting iPSC-derived endothelial cells in saline alone demonstrate therapeutic benefit in enhancing blood perfusion and angiogenesis. We further developed shear-thinning protein hydrogels and three-dimensional porous scaffolds that protect the iPSC-ECs during transplantation, leading to improved cell survival, leading to improved angiogenesis. The biomaterials could be further functionalized with pro-angiogenic factors for added potency for therapeutic revascularization. These studies highlight the importance of instructive biomaterial interactions to enhance cell survival.

a. Abdul Jalil R, Huang NF*, Jame S, Lee J, Nguyen HN, Byers B, De A, Okogbaa J, Rollins MD, Reijo-Pera R, Gambhir SS, Cooke JP. Endothelial cells derived from human iPSCs increase capillary density and improve perfusion in a mouse model of peripheral arterial disease. **Arterioscler Thromb Vasc Biol**, 31:e72-79, 2011 (*co-first author). PMCID: PMC3210551.
b. Mulyasasmita W, Cai L, Dewi RE, Jha A, Ullmann SD, Luong RH, Huang NF, Heilshorn SC. Avidity-controlled hydrogels for injectable co-delivery of induced pluripotent stem cell-derived endothelial cells and growth factors. **J Control Release** 191:71-81, 2014. PMCID: PMCID: PMC4518026.

c. Foster AA, Dewi RE, Cai L, Hou L, Strassberg Z, Alcazar CA, Heilshorn SC, Huang NF. Protein-engineered hydrogels enhance the survival of induced pluripotent stem cell-derived endothelial cells for treatment of peripheral arterial disease. **Biomater Sci**. 6:614-622, 2018 PMCID: PMC5829050.
d. Wanjare M, Kawamura M, Hu C, Alcazar C, Wang H, Woo YJ, Huang NF. Vascularization of engineered spatially patterned myocardial tissue derived from human pluripotent stem cells in vivo. **Front Bioeng Biotechnol** 7:208, 2019. PMCID: PMC6733921

2. Aligned Nanofibrillar Scaffolds for Cell and Gene Delivery: Within our biomaterials research, we have also focused our research efforts on the role of parallel-aligned (anisotropic) nanofibrillar scaffolds as cell delivery vehicles for promoting endothelial cell survival, cytoskeletal reorganization, directed motility, and angiogenesis cues. Furthermore, aligned nanofibrillar scaffolds are also multi-functional because they can be used to deliver therapeutic agents such as growth factors and chemically modified mRNA. We showed that aligned nanofibrillar scaffolds that deliver vascular endothelial growth factor-C protein, in conjunction with lymph node transfer, could successfully enhance lymphatic angiogenesis in a porcine lymphedema model. With this positive finding, we now have an ongoing Phase I clinical trial to evaluate the therapeutic efficacy of aligned nanofibrillar scaffolds to treat patients with lymphedema. Additionally, aligned nanofibrillar scaffolds could enable transient release chemically modified mRNA encoding angiogenic growth factors such as hepatocyte growth factor for enhancing angiogenesis. We were the first to demonstrate mRNA delivery from aligned nanofibrillar scaffolds, which afford spatiotemporal control of gene delivery, in small and large animal models of limb ischemia. These publications highlight the application of spatial patterning for translational applications for cell and gene delivery.

a. Hadamitzky C, Zaitseva TS, Bazalova-Carter M, Paukshto MV, Hou L, Strassberg Z, Ferguson J, Matsuura Y, Dash R, Yang PC, Kretchetov S, Vogt PM, Rockson SG, Cooke JP, Huang NF. Aligned nanofibrillar collagen scaffolds - Guiding lymphangiogenesis for treatment of acquired lymphedema. **Biomaterials** 102:259-67, 2016. PMCID: PMC5157930.
b. Zaitseva T, Alcazar C, Zamani M, Hou L, Sawamura S, Yakubov E, Hopkins M, Woo YJ, Paukshto M, Huang NF. Aligned Nanofibrillar Scaffolds for Controlled Delivery of Modified mRNA. **Tissue Eng Part A.** 25:121-130, 2019. PMCID: PMC6352505
c. Nakayama KH, Hong G, Lee JC, Patel J, Edwards B, Zaitseva TS, Paukshto MV, Dai H, Cooke JP, Woo YJ, Huang NF. Aligned-Braided Nanofibrillar Scaffold with Endothelial Cells Enhances Arteriogenesis. **ACS Nano**, *9:* 6900–6908, 2015. PMCID: PMC4757475.
d. Zaitseva TS, Yang G, Dionyssiou D, Zamani M, Sawamura S, Yakubov E, Ferguson J, Hallet RL, Fleischmann D, Paukshto MV, Huang NF. Delivery of hepatocyte growth factor mRNA from nanofibrillar scaffolds in a pig model of peripheral arterial disease. **Regen Med** 15:1761-1773, 2020. PMCID: PMC7380169.

3. Novel Engineering Microdevices to Study Mechanobiology: To study the role of mechanical factors on endothelial cells, we have engineered novel microdevices that overcome existing technological limitations. We developed microscale high-throughput arrayed platforms for studying combinatorial extracellular matrix proteins on stem cell fate and endothelial phenotype under ischemia-mimetic environments in a facile manner. This systematic approach revealed important insights into how endothelial cells respond to diverse extracellular matrix signaling cues, to mimic the complex extracellular matrix microenvironment of the endothelial basement membrane. Importantly, multi-component extracellular matrices were more potent in promoting endothelial differentiation and cell survival in hypoxic conditions, and multi-factorial analysis delineated the contribution of individual matrix proteins within a multi-component mixture. Additionally, to study the role of hemodynamic shear stress gradients on endothelial behavior, we developed a novel fluid flow device that recapitulates shear stress gradients and disturbed flow, while being compatible with live-cell time lapse imaging. Using this novel shear stress device, we patterned endothelial cells using aligned nanofibrillar scaffolds and applied shear stress orthogonal to the direction of spatially patterned endothelial cells. To our surprise, shear stress could not perturb cell alignment along the direction of the aligned nanofibrils, suggesting that spatial patterning cues are much stronger than hemodynamic shear stress. This work reveals new insight into how endothelial cells respond to concomitant mechanical cues of shear stress and extracellular matrix proteins.

a. Ostrowski MA, Huang NF, Walker TW, Verwijlen T, Poplawski C, Khoo AS, Cooke JP, Fuller GG, Dunn AR. Microvascular Endothelial Cells Migrate Upstream and Align Against the Shear Stress Field Created by Impinging Flow. **Biophys J** 106:366-374, 2014. PCMID: PMC 3907231.
b. Hou L, Coller J, Natu V, Hastie TJ, Huang NF. Combinatorial Extracellular Matrix Microenvironments Promote Survival and Phenotype of Human Induced Pluripotent Stem Cell-Derived Endothelial Cells in Hypoxia. **Acta Biomater.** 44: 199-199, 2016. PMCID: PMC5045796.

c. Nakayama KH, Surya VN, Gole M, Walker TW, Yang W, Lai ES, Ostrowski MA, Fuller GG, Dunn AR, Huang NF. Nanoscale Patterning of Extracellular Matrix Alters Endothelial Function under Shear Stress. **Nano Lett,** 16:410-9, 2016. PMCID: PMC4758680.
d. Hou L, Kim JJ, Wanjare M, Patlolla B, Coller J, Natu V, Hastie TJ, Huang NF. Combinatorial Extracellular Matrix Microenvironments for Probing Endothelial Differentiation of Human Pluripotent Stem Cells. **Sci Rep** 7, 6551, 2017. PMCID: PMC5529516

4. Engineering Cardiac and Skeletal Muscle: By marrying our research interests in stem cells with biomaterials, we have built prototypes of engineered cardiovascular and muscular tissue. These constructs employ nanoscale or microscale cues derived from the extracellular matrix to induce spatial patterning, resulting in engineered tissues with physiologically relevant morphology. Towards increasing scalability, our recent efforts sought to create vascularized tissues with spatially patterned cellular organization to better mimic the physiology of native muscle, and then we showed their therapeutic benefit in preclinical muscle injury models. These vascularized engineered tissues reveal important roles of both anisotropic cues and endothelial interactions in modulating the function of skeletal muscle progenitors or induced pluripotent stem cell-derived cardiomyocytes.
a. Levenberg S, Huang NF, Lavik E, Rogers AB, Itskovitz-Eldor J, Langer R. Differentiation of Human Embryonic Stem Cells on Three-Dimensional Polymer Scaffolds. **Proc Natl Acad Sci U S A** 100:12741-46, 2003.
b. Wanjare M, Hou L, Nakayama KH, Kim JJ, Mezak NP, Abilez OJ, Tzatzalos E, Wu JC, Huang NF. Anisotropic microfibrous scaffolds enhance the organization and function of cardiomyocytes derived from induced pluripotent stem cells. **Biomat Sci.** 5: 1567–1578, 2017. PMCID: PMC5348721
c. Wanjare M, Kawamura M, Hu C, Alcazar C, Wang H, Woo YJ, Huang NF. Vascularization of engineered spatially patterned myocardial tissue derived from human pluripotent stem cells in vivo. **Front Bioeng Biotechnol** 7:208, 2019. PMCID: PMC6733921
d. Nakayama KH, Quarta M, Paine P, Alcazar C, Karakikes I, Garcia V, Abilez O, Calvo NS, Simmons CS, Rando TA, Huang NF. Treatment of Volumetric Muscle Loss Using Spatially Patterned Scaffolds Enhances Vascular Organization and Functional Integration. **Commun Biol** 2:170, 2019. PMCID: PMC6505043

5. Tracking Revascularization Using Near Infrared Imaging in the Second Window (NIR-II): To improve existing non-invasive imaging capacities, we have tested near infrared fluorophores in the second window (1400-1800nm emission), where there is minimal tissue autofluorescence. When these agents were delivered systemically, they served as multi-functional vascular contrast agents that could simultaneously quantify blood flow and blood perfusion, while being to visualize microvascular network architecture at high architectural resolution. This technique was pioneered in our **Nat Med** publication, and then refined in subsequent publications with improved agents. These fluorophores allow us to study the temporal process of revascularization in unprecedented resolution.
a. Hong G, Lee JC, Robinson JT, Raaz U, Xie L, Huang NF#, Cooke JP, Dai H. Multi-Functional In Vivo Vascular Imaging Using Near-Infrared II Fluorescence. **Nat Med**, 18:1841-6, 2012 (#co-corresponding author). PMCID: PMC3595196.
b. Nakayama KH, Hong G, Lee JC, Patel J, Edwards B, Zaitseva TS, Paukshto MV, Dai H, Cooke JP, Woo YJ, Huang NF. Aligned-Braided Nanofibrillar Scaffold with Endothelial Cells Enhances Arteriogenesis. **ACS Nano** *9:* 6900–6908, 2015. PMCID: PMC4757475.
c. Zhong Y, Ma Z, Zhu S, Yue J, Zhang M, Antaris AL, Yuan J, Cui R, Wan H, Zhou Y, Wang W, Huang NF, Luo J, Hu Z, Dai H. Boosting the down-shifting luminescence of rare-earth nanocrystals for biological imaging beyond 1500 nm. **Nat Commun**. 8:737, 2017. doi: 10.1038/s41467-017-00917-6. PMCID: PMC5622117
d. Ma Z, Zhang M, Yue J, Alcazar C, Zhong Y, Doyle TC, Dai H, Huang NF. Near-Infrared IIb Fluorescence Imaging of Vascular Regeneration with Dynamic Tissue Perfusion Measurement and High Spatial Resolution. **Adv Funct Mater** 28: 1803417, 2018. PMCID: PMC6640151

List of Published Work: https://www.ncbi.nlm.nih.gov/pubmed/?term=huang+nf