BIOGRAPHICAL SKETCH

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NAME: Hae Lin Jang

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

POSITION TITLE: ASSISTANT PROFESSOR/BRIGHAM AND WOMEN'S HOSPITAL

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
Seoul National University, Seoul, Korea	B.S.	02/2008	Materials Science and Engineering
Seoul National University, Seoul, Korea	M.S.	02/2010	Materials Science and Engineering
Seoul National University, Seoul, Korea	Ph.D.	02/2014	Materials Science and Engineering, Hybrid Materials
Research Institute of Advanced Materials, Seoul National University, Seoul, Korea	Post-doc.	04/2015	Biomedical Engineering
[1]Brigham and Women's Hospital, Harvard Medical School and [2]Harvard-MIT Division of Health Sciences and Technology, [3]Wyss Institute for Biologically Inspired Engineering, Harvard University	Post-doc.	09/2016	Biomedical Engineering

A. Personal Statement

Dr. Hae Lin Jang is an Assistant Professor at Brigham and Women's Hospital and Harvard Medical School. She is also leading the Laboratory for Advancing Biomaterials and Biotechnologies. Her research is at the interface of materials science, nanotechnology, and biomedical engineering to develop innovative biomaterials and biotechnologies for the treatment of incurable diseases, especially related to bone. She was the first to develop a facile, large-scale synthetic method of whitlockite ($Ca_{18}Mg_2(HPO_4)_2(PO_4)_{12}$) nanoparticles, which is the second most abundant bone mineral in the human body. She has also developed hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$)-coated polyetheretherketone (PEEK) hybrid material to overcome the inertness of PEEK to treat degenerative spine diseases (transferred to a startup company and protected by two patents.) In addition, she has developed advanced *in vitro* modeling systems to recapitulate sophisticated cellular structures of human tissues using 3D bioprinting and microfluidic vascularized organ-on-a-chip, which were applied for studying pathological mechanisms in bone and testing innovative engineered therapeutics in a 3D tissue context. This effort had led Dr. Jang and her team to discover a novel immune evasion mechanism mediated by intercellular nanotubes through where mitochondria (energy sources) trafficking occurred (published in *Nature Nanotechnology*, 2022.) She has also developed a next-generation antibiotic-device combination for treating bone infection (published in *Nature Biomedical Engineering*, 2022.) Overall, she has rich experience in engineering bone-related materials and characterizing their physicochemical and biological properties at the nanometer scale using biomedical approaches to develop next-generation therapies for bone diseases and injuries.

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

NIH R01AR073135, multi-PI, 2018-2023
3D printed muscle-bone organ implant for treating large injuries

NIH R01CA236702, multi-PI, 2019-2024

Whitlockite nanoparticle-based immunotherapy for bone metastasis

DoD PC180355, PI, 2019-2022
Prostate cancer-derived bone metastasis on a chip platform to model immune response

DoD CA201065, PI, 2021-2025
Developing novel immunotherapy to suppress cancer metastasis and recurrence in bone

Citations:

a. Sumana Ghosh, Mau Sinha, Ritwik Samanta, Suresh Sadhasivam, Anamika Bhattacharyya, Ashis Nandy, Swamini Saini, Nupur Tandon, Himanshi Singh, Swati Gupta, Anjali Chauhan, Keerthi Kumar Aavula, Sneha Susan Varghese, Pujie Shi, Sudip Ghosh, Mukesh Kumar Garg, Tanmoy Saha, Aparna Padhye, Shamik Ghosh*, **Hae Lin Jang***, Shiladitya Sengupta* "A potent antibiotic-loaded bone cement implant against staphylococcal bone infections" *Nature Biomedical Engineering* (2022)
b. Tanmoy Saha, Chinmayee Dash, Ruparoshni Jayabalan, Sachin Khiste, Arpita Kulkarni, Kiran Kurmi, Jayanta Mondal, Pradip Majumder, Aditya Bardia, **Hae Lin Jang***, Shiladitya Sengupta* "Intercellular nanotubes mediate mitochondrial trafficking between cancer and immune cells" *Nature Nanotechnology* 17(1):98-106 (2022).
c. **Hae Lin Jang***, Shiladitya Sengupta* "Transcellular transfer of nanomedicine" *Nature Nanotechnology* 14:731-732 (2019).
d. Emine Alarcin, Tae Yong Lee, Sobha Karuthedom, Marzieh Mohammadi, Meadhbh A Brennan, Dong Hoon Lee, Alessandra Marrella, Jin Zhang, Denata Syla, Yu Shrike Zhang, Ali Khademhosseini*, **Hae Lin Jang*** "Injectable shear thinning hydrogels for delivering osteogenic and angiogenic cells and growth factors" *Biomaterials Science* 6(6):1604-1615 (2018).

B. Positions, Scientific Appointments, and Honors

Positions and Employment

03/2014-04/2015	Postdoctoral Researcher, Research Institute of Advanced Materials, Seoul National University, Seoul, Korea
07/2015-09/2016	Postdoctoral Researcher, [1]Brigham and Women's Hospital, Harvard Medical School and [2]Harvard-Massachusetts Institute of Technology Division of Health Sciences and Technology, Massachusetts Institute of Technology, [3]Wyss Institute for Biologically Inspired Engineering, Harvard University
12/2015-10/2017	Nanotechnology subgroup leader in Biomaterials Innovation Research Center (BIRC)
10/2016-04/2019	Instructor of Medicine, Harvard Medical School
10/2016-present	Associate Bioengineer, Division of Engineering in Medicine, Department of Medicine, Brigham and Women's Hospital
04/2018-03/2019	Scientific Advisory Board member of the 3D printing company Aether
09/2018-04/2019	Consultant of the Biopharmaceutical company Vyome Biosciences
05/2019-present	Assistant Professor of Medicine, Harvard Medical School
03/2020-present	Director of the Scientific Advisory Board in biomedical company Curer Inc.
05/2022-present	Investigator, Division of Rheumatology, Inflammation and Immunity, Department of Medicine, Brigham and Women's Hospital
2022-present	Assistant Professor of Orthopedic Surgery, Harvard Medical School (in the process of appointment)

Selected Awards and Honors

National Science and Technology Scholarship, Korea (2004-2007), Grand Prize for Thesis Research, Material Science and Engineering, Seoul National University (2007); Full Tuition Scholarship, Seoul National University (2008); Brain Korea 21 Fellowship (2008-2010, 2012-2013); Lecture & Research Scholarship, Seoul National University, Korea (2010); Honorable Mention for Young Chemist from Metrohm US (2016); DoD Prostate Cancer Research Program Idea Development Award (2019); Brigham Research Institute (BRI) NextGen Award (2019); DoD Peer Reviewed Cancer Research Program Career Development Award, Scholar (2020); NIH National Cancer Institute (NCI) Small Business Technology Transfer (STTR) Award (2022).

Mentoring

Research Advisor for >30 Undergraduate, Graduate, and Post-Doctoral protégés.

Selected Lectureships

Lecture in Introduction to Electro-Optical-Mechanical, Seoul National University (2011), Lecture in Introduction to Biomaterials, Seoul National University (2012), Lecture in Biomedical Materials, Seoul National University (2012), Lecture in Introduction to Biology for Materials Science and Engineering, Seoul National University (2013), Invited Session Lecturer for Global Biotechnology Congress, Boston, US (2017). Oral Presentation in Biomedical Engineering Society, Phoenix, US (2017), Invited Seminar in School of Chemical and Biological Engineering, Seoul National University (2017), Invited Seminar in Biophotonics and Nano Engineering Lab, Seoul National University (2017), Invited Seminar in Korea Institute of Science and Technology (2017), Invited Seminar in Transplantation Research Center, BWH, Boston, US (2018), Invited Seminar in Orthopaedic Translational Research Seminars at the Department of Orthopaedic Surgery, BWH, Boston, US (2018), Invited Keynote Speaker for the Novel Fluidic Technologies with an Emphasis on Tissue Engineering workshop, Izmir, Turkey (2018), Invited Seminar at the Division of Engineering in Medicine Symposium, BWH, Boston, US (2018), Invited Speaker for IEEE-Nano/Molecular Medicine and Engineering (2018), Invited Seminar at the Department of Chemical Engineering, Northeastern University (2019), Invited Keynote Speaker for the SNU-EU Workshop at the Department of Materials Science and Engineering, Seoul National University, Korea (2019), Invited Seminar at the Graduate School of Convergence Science and Technology, Seoul National University, Korea (2019). Invited Seminar at the Department of Materials Science and Metallurgy, University of Cambridge, UK (2019); Session speaker at the NIH NCI Cancer Systems Biology Consortium (CSBC)/Physical Sciences Oncology Network (PS-ON), and the Big Data Scientist Training Enhancement Program (BD-STEP) Junior Investigator Meeting (2020); Invited Talk, Korean Society for Biomaterials (K SBM), Virtual Meeting, Korea (2020); Invited Seminar at the Division of Rheumatology, Inflammation, and Immunity, BWH/HMS, Boston, US (2021); Invited Seminar at the Department of BioMedical-Chemical Engineering, Catholic University of Korea (2021). Invited Talk at the Bladder Research Meeting, Bladder Cancer Program, Dana-Farber Cancer Institute (2022); Keynote Speaker at National Biotechnology Conference, Anaheim, CA, US (2022); Invited Talk at Musculoskeletal Biology and Bioengineering Gordon Conference, Andover, NH, US (2022); Invited Talk at Longwood Orthopedic Grand Round, Virtual Meeting, MA, US (2022); Invited Talk at DoD Convergent Science Virtual Cancer Center (CSVCC) Workshop, Los Angeles, CA, US (2022); Keynote Speaker at Biomedical Engineering Society (BMES), San Antonio, TX, US (2022); Invited Speaker at Biomedical Engineering Society (BMES), San Antonio, TX, US (2022); Invited Talk at NIH Alliance for Nanotechnology in Cancer Annual PI Meeting, Virtual Meeting, US (2022); Invited Talk at the Third Annual Combined Mass General Brigham (MGB) Orthopedic Research Retreat, MA, US (2022).

Professional Role

Micro- and Nanotechnologies for Medicine: Emerging Frontiers and Applications workshop, Cambridge, MA, USA, Nanotechnology Session Chair. (2016 and 2017); Scientific Committee for the Novel Fluidic Technologies with an Emphasis on Tissue Engineering workshop, Izmir, Turkey (2018); Session Chair for Discover Brigham and Women's Hospital, USA (2019); Virginia Commonwealth University Pilot Grant Reviewer, USA (2020); National Science Center Poland Grant reviewer (2020); National Science Foundation (NSF) Mathematical and Physical Sciences (MPS)/Materials Research (DMR)/Biomaterials (BMAT)/ Grant reviewer, USA (2021); French National Research Agency (ANR), Grant reviewer (2021); The Chief Scientist Office (CSO) of the Scottish Government, Translational Clinical Study (TCS), Grant reviewer (2021); European Science Foundation Grant Reviewer (2022); Organizing Committee member for the Mass General Brigham (MGB) Combined Orthopedic Research Seminar Series, Boston, MA, US (2022-present); National Science Center Poland Grant reviewer (2022); Basic Abstract Reviewer for the Third Annual Combined MGB Orthopedic Research Retreat (2022); Session Chair in Cancer Technologies Track at Biomedical Engineering Society (BMES), San Antonio, TX, US (2022); Organizing Committee member for the Annual Combined MGB Orthopaedic Research Retreat, Boston, MA, US (2022-present); Organizer and Chair for the Workshop on Engineered Immunotherapeutics to Treat Currently Incurable Diseases, Boston, MA, USA (scheduled).

C. Contributions to Science

Dr. Jang has been focusing on advancing the fields of biomaterials, biomedical engineering, and immunotherapy for tissue regeneration and disease treatment, especially related to bone.

1. Nanotechnology-based synthesis of biocrystals: Natural hard tissues are composed of well-organized nanoscale components. For example, bone tissue is composed of calcium phosphate nanocrystals, hydroxyapatite (HAP) and whitlockite (WH), which are assembled in a 3D collagen matrix. While HAP has been actively investigated as it is the most thermodynamically stable calcium phosphate compound under physiological conditions, WH has largely been ignored by the research community, despite there being

significant amounts of WH in our bone and teeth. This lack of attention is largely due to the difficulty in the synthesis of WH. Rather, bulk β-TCP ($Ca_3(PO_4)_2$), the synthetic analog of WH, has been used even though it does not exist *in vivo*. Dr. Jang successfully reported a novel synthetic method of pure WH nanoparticles and demonstrated its superior biocompatibility compared to HAP and β-TCP *in vitro* and *in vivo*. In addition, to confirm cellular nutrient uptake depending on nanochannel supply, she created nanochannel built-in bioceramic scaffolds, grew cells on top of the scaffold platform, and evaluated cellular proliferation levels and activities.

a. **Hae Lin Jang**, Kyoungsuk Jin, Jaehun Lee, Younghye Kim, Seung Hoon Nahm, Kug Sun Hong and Ki Tae Nam "Revisiting whitlockite, the second most abundant biomineral in bone: nanocrystal synthesis in physiologically relevant condition and biocompatibility evaluation" *ACS Nano* 8(1):634-641 (2014).
b. **Hae Lin Jang**, Keunho Lee, Chan Soon Kang, Hye Kyoung Lee, Hyo-Yong Ahn, Kyoungsuk Jin, Sunghak Park, Seul Cham Kim, Tae-Youl Yang, Hui-Yun Jeong, Jimin Park, Jin Hong Kim, Seon Ae Shin, Heung Nam Han, Kyu-Hwan Oh, Ho-young Lee, Kug Sun Hong, Jun Lim, Malcolm L. Snead, Jimmy Xu and Ki Tae Nam "Nano-capillary self-powered supply of growth factors and nutrients in a ceramic biomaterial" *ACS Nano* 9(4):4447-57 (2015). PMCID: PMC4485927
c. **Hae Lin Jang**, Guang Bin Zheng, Jungha Park, Hwan D. Kim, Hae-Ri Baek, Hye Kyoung Lee, Keunho Lee, Heung Nam Han, Choon-Ki Lee, Nathaniel S. Hwang, Jae Hyup Lee and Ki Tae Nam "*In vitro* and *in vivo* evaluation of whitlockite biocompatibility: comparative study with hydroxyapatite and β-tricalcium phosphate" *Advanced Healthcare Materials* 5(1):128-136 (2016).
d. Hwan D. Kim*, **Hae Lin Jang***, Hyo-Yong Ahn, Hye Kyoung Lee, Jungha Park, Eun-seo Lee, Eunjee A. Lee, Yong-Hoon Jeong, Do-Gyoon Kim, Ki Tae Nam, Nathaniel S. Hwang "Biomimetic whitlockite inorganic nanoparticles-mediated in situ remodeling and rapid bone regeneration" *Biomaterials* 112:31-43 (2017)

2. Engineering biomaterials that can deliver living cells and drugs: Dr. Jang has fabricated various designs of scaffolds and implants with different therapeutic purposes. For example, since injectable biomaterials are capable of filling any irregularly shaped defects in tissue, Dr. Jang developed various types of injectable biomaterials that can deliver cells and growth factors for improved tissue healing. Injectable biomaterials could also be simultaneously injected into 3D constructs through syringes and needles and can be modified into bioinks to be printed into 3D tissue constructs.
    a. Hao Cheng, Aditya Chawla, Yafeng Yang, Yuxiao Li, Jin Zhang, **Hae Lin Jang***, Ali Khademhosseini* "Development of nanomaterials for bone targeted drug delivery" *Drug Discovery Today*. 22(9):1336-50 (2017).
    b. Emine Alarcin, Tae Yong Lee, Sobha Karuthedom, Marzieh Mohammadi, Meadhbh A Brennan, Dong Hoon Lee, Alessandra Marrella, Jin Zhang, Denata Syla, Yu Shrike Zhang, Ali Khademhosseini*, **Hae Lin Jang*** "Injectable shear thinning hydrogels for delivering osteogenic and angiogenic cells and growth factors" *Biomaterials Science* 6(6):1604-1615 (2018).
    c. **Hae Lin Jang***, Shiladitya Sengupta* "Transcellular transfer of nanomedicine" *Nature Nanotechnology* 14:731-732 (2019).
    d. Bumseok Namgung, Kalpana Ravi, Pooja Prathyushaa Vikraman, Shiladitya Sengupta*, **Hae Lin Jang*** "Engineered cell-laden alginate microparticles for 3D culture" *Biochemical Society Transactions* 49(2):761-73 (2021).

3. Development of biomedical devices for tissue engineering: Dr. Jang developed various biomedical devices to control the structure of biomaterials at the micro and nanoscales. For example, she developed customized 3D bioprinter and microfluidic devices to build 3D tissue structures with distinct functional compartments. Such a compartmentalized tissue structure can support the growth and activity of multiple types of cells that require different physicochemical conditions of microenvironments.
    a. Wei Wei, Yuxiao Li, Huazhe Yang, Reza Nassab, Fatemeh Shahriyari, Ali Akpek, Xiaofei Guan, Yanhui Liu, Shahrouz Taranejoo, Ali Tamayol, Yu Shrike Zhang, Ali Khademhosseini*, **Hae Lin Jang*** "3D printed anchoring sutures for permanent shaping of tissues" *Macromolecular Bioscience*, 17(12):1700304 (2017).
    b. Wanjun Liu, Yu Shrike Zhang, Marcel A Heinrich, Fabio De Ferrari, **Hae Lin Jang**, Syeda Mahwish Bakht, Mario Moisés Alvarez, Jingzhou Yang, Yi-Chen Li, Grissel Trujillo-de Santiago, Amir K Miri, Kai Zhu, Parastoo Khoshakhlagh, Gyan Prakash, Hao Cheng, Xiaofei Guan, Zhe Zhong, Jie Ju,

Geyunjian Harry Zhu, Xiangyu Jin, Su Ryon Shin, Mehmet Remzi Dokmeci and Ali Khademhosseini* "Rapid continuous multimaterial extrusion bioprinting" *Advanced Materials* 29(3):1604630 (2016).

c. Mehma K. Kolly, Shiladitya Sengupta, Hongqing Dai, **Hae Lin Jang** "Engineering breast cancer mammospheres using vibration" *FASEB Journal* 34 (2020).

d. May S. Freag, Bumseok Namgung, Maria E. Reyna Fernandez, Ermanno Gherardi, Shiladitya Sengupta*, **Hae Lin Jang*** "Human nonalcoholic steatohepatitis on a chip" *Hepatology Communication* 5(2):217-33 (2021).

4. *In vitro* modeling platform for recapitulating tissue microenvironment: Dr. Jang has reconstituted tissue microenvironment *in vitro*, especially by incorporating cells in 3D biomaterials, in which physicochemical properties were tuned to support the growth and activity of encapsulated cells. These *in vitro* modeling platforms were used to understand mechanisms underlying tissue development or disease progression at the cellular and molecular levels, or test the efficacy and safety of innovative therapies. In particular, she used a microfluidic chip to encapsulate cells in a tissue-mimetic 3D matrix where she could form perfusable blood vessels using endothelial cells to recapitulate a vascularized niche and develop dynamic flow.

   a. Emine Alarcin, Xiaofei Guan, Sara Saheb Kashaf, Khairat Elbaradie, Huazhe Yang, **Hae Lin Jang***, Ali Khademhosseini* "Recreating composition, structure, functionalities of tissues at nanoscale for regenerative medicine" *Regenerative Medicine* (2016).

   b. Yafeng Yang, Aditya Chawla, Jin Zhang, Adam Esa, **Hae Lin Jang***, Ali Khademhosseini* "Applications of nanotechnology for regenerative medicine: Healing tissues at the nanoscale" In *Principles of regenerative medicine* (pp. 485-504). Academic Press. (2019).

   c. May S. Freag, Bumseok Namgung, Maria E. Reyna Fernandez, Ermanno Gherardi, Shiladitya Sengupta*, **Hae Lin Jang*** "Human nonalcoholic steatohepatitis on a chip" *Hepatology Communication* 5(2):217-33 (2021).

   d. Tanmoy Saha, Chinmayee Dash, Ruparoshni Jayabalan, Sachin Khiste, Arpita Kulkarni, Kiran Kurmi, Jayanta Mondal, Pradip Majumder, Aditya Bardia, **Hae Lin Jang***, Shiladitya Sengupta* "Intercellular nanotubes mediate mitochondrial trafficking between cancer and immune cells" *Nature Nanotechnology* 17(1):98-106 (2022).

5. Creation of next-generation drug-medical device combinations and *in vivo* evaluation for clinical translation: Dr. Jang has fabricated various designs of drug-device combinations for effective tissue regeneration and disease treatment. She also made composite 3D implants that incorporate multiple types of tissues for treating large injuries. She designed various scales of pores in the implant to assess tissue growth, host immune response and overall biocompatibility *in vivo.*

   a. Jae Hyup Lee*, **Hae Lin Jang***, Kyung Mee Lee, Hae-Ri Baek, Kyoungsuk Jin, Kug Sun Hong, Jun Hong Noh and Hyun-Kyung Lee "*In vitro* and *in vivo* evaluation of the bioactivity of hydroxyapatite-coated polyetheretherketone biocomposites created by cold spray technology" *Acta Biomaterialia* 9(4):6177-6187 (2013).

   b. Jae Hyup Lee*, **Hae Lin Jang***, Kyung Mee Lee, Hae-Ri Baek, Kyoungsuk Jin, Jun Hong Noh "Cold-spray coating of hydroxyapatite on a three-dimensional polyetheretherketone implant and its biocompatibility evaluated by *in vitro* and *in vivo* minipig model" *Journal of Biomedical Materials Research Part B: Applied Biomaterials* 105(3):647-657 (2015).

   c. **Hae Lin Jang**, Guang Bin Zheng, Jungha Park, Hwan D. Kim, Hae-Ri Baek, Hye Kyoung Lee, Keunho Lee, Heung Nam Han, Choon-Ki Lee, Nathaniel S. Hwang, Jae Hyup Lee and Ki Tae Nam "*In vitro* and *in vivo* evaluation of whitlockite biocompatibility: Comparative study with hydroxyapatite and β-tricalcium phosphate" *Advanced Healthcare Materials* 5(1):128-136 (2016).

   d. Sumana Ghosh, Mau Sinha, Ritwik Samanta, Suresh Sadhasivam, Anamika Bhattacharyya, Ashis Nandy, Swamini Saini, Nupur Tandon, Himanshi Singh, Swati Gupta, Anjali Chauhan, Keerthi Kumar Aavula, Sneha Susan Varghese, Pujie Shi, Sudip Ghosh, Mukesh Kumar Garg, Tanmoy Saha, Aparna Padhye, Shamik Ghosh*, **Hae Lin Jang***, Shiladitya Sengupta* "A potent antibiotic-loaded bone cement implant against staphylococcal bone infections" *Nature Biomedical Engineering* (accepted 2022)

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