BIOGRAPHICAL SKETCH

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NAME: Hung, Clark

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

POSITION TITLE: Professor, Biomedical Engineering & Orthopaedic Surgery

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
Brown University, Providence, RI	BS	05/1990	Bioengineering
University of Pennsylvania, Philadelphia, PA	MENG	05/1992	Bioengineering
University of Pennsylvania, Philadelphia, PA	PHD	12/1995	Bioengineering
University of Pennsylvania, Philadelphia, PA	Postdoctoral Fellow	06/1996	NASA research
Columbia University, New York, NY	Postdoctoral Fellow	06/1997	Cartilage bioengineering

A. Personal Statement

Dr. Hung has been pursuing in-depth multidisciplinary collaborations with faculties and students from the Departments of Biological Sciences, Mechanical Engineering, Chemical Engineering and Orthopaedic Surgery using with state-of-the-art biological and engineering tools to perform research aimed at the study of physical effects (e.g., cell deformation, fluid flow effects, hydrostatic pressure) on cells and tissues, and the incorporation of these forces in strategies to develop functional tissue substitutes of clinical relevance. An understanding of the effects of physical forces on cells is important in the development of effective tissue replacements which mimic or restore normal tissue structure-function in orthopaedic and other load-bearing tissues of the body. Such studies are aim at alleviating the most prevalent and chronic problems afflicting the musculoskeletal system such as arthritis, and problems related to sports and occupational injuries.

1. Stefani RM, Lee AJ, Tan AR, Halder SS, Hu Y, Guo XE, Stoker AM, Ateshian GA, Marra KG, Cook JL, and Hung CT, *Sustained low-dose dexamethasone delivery via a PLGA microsphere-embedded agarose implant for enhanced osteochondral repair.* Acta Biomater, 2020. **102**: p. 326-340. 31805408
2. Stefani RM, Barbosa S, Tan AR, Setti S, Stoker A, Ateshian GA, Cadossi R, Vunjak-Novakovic G, Aaron RK, Cook JL, Bulinski JC, Hung CT. Pulsed Electromagnetic Fields Promote Repair of Focal Articular Cartilage Defects with Engineered Osteochondral Constructs. *Bioeng Biotechnology,* 2020. **117**(5):1584-1596. 31985051
3. Lima EG, Tan AR, Tai T, Bian L, Stoker AM, Ateshian GA, Cook JL, Hung CT. Differences in interleukin-1 response between engineered and native cartilage. Tissue Eng Part A. 2008 Oct;14(10):1721-30. PubMed PMID: 18611148.
4. Tan AR, Alegre-Aguarón E, O'Connell GD, VandenBerg CD, Aaron RK, Vunjak-Novakovic G, Chloe Bulinski J, Ateshian GA, Hung CT. Passage-dependent relationship between mesenchymal stem cell mobilization and chondrogenic potential. Osteoarthritis Cartilage. 2015 Feb;23(2):319-27. PubMed PMID: 25452155; PubMed Central PMCID: PMC4369922.

B. Positions and Honors

Positions and Employment

1990 - 1995	Predoctoral Fellow, Department of Bioengineering and Orthopaedic Surgery, University of Pennsylvania, Philadelphia, PA
1995 - 1995	Instructor, Department of Bioengineering, University of Pennsylvania, Philadelphia, PA
1996 - 1996	Postdoctoral Fellow, Department of Biomedical Engineering, University of Pennsylvania, Philadelphia, PA
1996 - 1997	Postdoctoral Fellow, Center for Biomedical Engineering, New York, NY
1997 - 2001	Assistant Professor, Department of Biomedical Engineering, Columbia University, New York, NY
1998 -	Director, Cellular Engineering Laboratory, Department of Biomedical Engineering, Columbia University, New York, NY
1998 -	Director, Summer High School Course in BME (Physical Effects on Cells), School of Continuing Education, Columbia University, New York, NY
2002 - 2009	Associate Professor of Biomedical Engineering, Department of Biomedical Engineering, Columbia University, New York, NY
2009 -	Professor, Department of Biomedical Engineering, Columbia University, New York, NY
2014 - 2020	Chair, Undergraduate Committee, Department of Biomedical Engineering, Columbia University, New York, NY

Other Experience and Professional Memberships

-	Member, American Society of Mechanical Engineers (ASME)
-	Ad hoc Reviewer, Clin Orthop Rel Res, Biophys J, J Biomechanics, J Orthop Res, J Biomech Eng, Arthritis Res, Arthritis Rheum, Biochem Biophysica Acta, J Microscopy, Bone, J Bone Miner Res, Osteoarthritis Cartilage, Calcified Tissue, Ann Biomed Eng, Tissue Eng, Acta Biomaterialia, Med Eng Physics, Stem Cells, Langmuir, Bioeng Biotech, Proteomics, Biotech Prog, J Tissue Eng Regen Med, Nature Protocols, Cartilage, e Cells Mater J, PNAS, Biomaterials, Biomedical Engineering Online
-	Member, Orthopaedic Research Society (ORS)
-	Member, Biomedical Engineering Society (BMES)
-	Member, American Institute of Medical & Biological Engineering (AIMBE)
2000 - 2000	Guest Co-Editor (Cell & Tissue Engineering Issue), Journal of Biomechanical Engineering
2006 - 2012	Associate Editor, Journal of Biomechanical Engineering
2008 -	Editorial Board Member, The Open Orthopaedics Journal
2008 - 2014	Deputy Editor, Journal of Orthopaedic Research (Editors: Buckwalter & Wright)
2009 -	Orthopaedic Research and Reviews (Dove Press), Editor-in-Chief
2011 - 2014	Editorial Board Member, Tissue Engineering: Parts A, B, C
2014 -	Associate Editor, Journal of Orthopaedic Research (Editor: Sandell)
2016 - 2019	Editorial Board Member, Tissue Engineering: Parts A, B, C

Honors

1990	NIH Bone & Cartilage Traineeship (T32), Department of Orthopaedic Surgery, University of Pennsylvania
1996	Solomon R. Pollack Award for Excellence in Graduate Bioengineering Reseach, Department of Bioengineering, University of Pennsylvania
1996	Whitaker Special Opportunity Award Postdoctoral Fellow, Columbia University
1996	Postdoctoral Fellowship (NASA-Wistar Institute-Bioengineering), University of Pennsylvania
2002	Edward & Carole Kim Award for Faculty Involvement, FFSEAS, Columbia University
2003	Negma-Lerads Prize, 3rd International Symposium on Mechanobiology of Cartilage and Chondrocyte, Brussels, Belgium, May 16-17
2004	The John Paul Stapp Best Paper Award, 47th Stapp Car Crash Conference
2009	Fellow, American Institute for Medical and Biological Engineering (AIMBE)

2010	Fellow, American Society of Mechanical Engineers (ASME)
2012	Standing Member, CSR Skeletal Biology Structure and Regeneration (SBSR) Study Section
2016	Marshall R. Urist Award for Excellence in Tissue Regeneration Research, Orthopedic Research Society
2018	Fellow, Biomedical Engineering Society (BMES), October 17
2019	Fellow, International Combined Orthopaedic Research (ICORS), Montreal, Canada, June 22

C. Contributions to Science

1. Functional Tissue Engineering: Our laboratory has pioneered the application of applied deformational loading (10% deformation, 1 Hz, 3 hours daily) to promote development of tissues with functional properties of cartilage. Our recent work has focused on further characterization of our engineered tissues (e.g., quantification of radial and depth-dependent properties, friction measurements, and structural organization of the extracellular matrix) as well as optimization of tissue culture methods to further improve and expedite cultivation time of functional tissues. Achieving some major advances in engineered cartilage tissue properties (Young's Modulus: 1000 kPa and GAG content: 6-8%, similar to native cartilage in 8 weeks or less). We have used proteomic analyses to optimize cell sources for engineering cartilage. Additionally, we are looking into strategies to increase collagen content of our tissues, such as with controlled enzymatic digestion and co-culture with TMAO. Recently, we have focused on functional tissue engineering of the synovium and mechanobiology of synovial cells as they play a role in OA as well as the limited repair capacity of cartilage.
   a. Mauck RL, Soltz MA, Wang CC, Wong DD, Chao PH, Valhmu WB, Hung CT, Ateshian GA. Functional tissue engineering of articular cartilage through dynamic loading of chondrocyte-seeded agarose gels. J Biomech Eng. 2000 Jun;122(3):252-60. PubMed PMID: 10923293.
   b. Estell EG, Murphy LA, Silverstein AM, Tan AR, Shah RP, Ateshian GA, and Hung CT, *Fibroblast-like synoviocyte mechanosensitivity to fluid shear is modulated by interleukin-1alpha.* J Biomech, 2017. **60**: p. 91-99. PubMed PMID: PMC5788292
   c. Silverstein AM, Stefani RM, Sobczak E, Tong EL, Attur MG, Shah RP, Bulinski JC, Ateshian GA, and Hung CT, *Toward understanding the role of cartilage particulates in synovial inflammation.* Osteoarthritis Cartilage, 2017. **25**(8): p. 1353-1361. PubMed PMID: PMC5554538
   d. Stefani RM, Halder SS, Estell EG, Lee AJ, Silverstein AM, Sobczak E, Chahine NO, Ateshian GA, Shah RP, and Hung CT, *A Functional Tissue Engineered Synovium Model to Study Osteoarthritis Progression and Treatment.* Tissue Eng Part A, 2019. **25**(7-8):538-553. PMC6482911

2. Mechanobiology of Cartilage and Chondrocytes: A portion of the lab is dedicated to basic science studies of physical regulation of articular chondrocytes. A better understanding of how cells perceive and respond to applied physical stimuli may provide greater insights to the role that physical forces play in the etiology of degenerative joint disease and osteoarthritis, as well as in normal maintenance of articular cartilage. These studies have formed the underpinning of our functional tissue engineering efforts using applied physiologic deformational loading and osmotic loading to promote engineered cartilage tissue development in culture. We are also exploring the role of other physical forces, including applied electric fields to guide cell migration in healing or forming tissues as well as to optimize cell sources.

   a. Hung CT, Henshaw DR, Wang CC, Mauck RL, Raia F, Palmer G, Chao PH, Mow VC, Ratcliffe A, Valhmu WB. Mitogen-activated protein kinase signaling in bovine articular chondrocytes in response to fluid flow does not require calcium mobilization. J Biomech. 2000 Jan;33(1):73-80. PubMed PMID: 10609520.
   b. Chao PH, West AC, Hung CT. Chondrocyte intracellular calcium, cytoskeletal organization, and gene expression responses to dynamic osmotic loading. Am J Physiol Cell Physiol. 2006 Oct;291(4):C718-25. PubMed PMID: 16928775.
   c. Sampat SR, Dermksian MV, Oungoulian SR, Winchester RJ, Bulinski JC, Ateshian GA, Hung CT. Applied osmotic loading for promoting development of engineered cartilage. J Biomech. 2013 Oct 18;46(15):2674-81. PubMed PMID: 24035014; PubMed Central PMCID: PMC3902123.

d. O'Connell GD, Tan AR, Cui V, Bulinski JC, Cook JL, Attur M, Abramson SB, Ateshian GA, Hung CT. Human chondrocyte migration behaviour to guide the development of engineered cartilage. J Tissue Eng Regen Med. 2015 Jan 28;PubMed PMID: 25627968; PubMed Central PMCID: PMC4531108.

3. Preservation Strategies for Osteochondral Grafts: Our laboratory has developed strategies for preservation of cartilage explants (excised cartilage tissue from a diarthrodial joint) using tissue culture techniques and incorporation of applied physiologic loading. We have demonstrated for the first time that our optimized culture media formulation (serum-free) can actually increase material properties of native cartilage tissue in culture. With collaborators from the University of Missouri, we have extended this media in a modified form to successfully preserve osteochondral allografts at room temperature for over 70 days. By increasing the shelf life of tissue grafts, our efforts would significantly increase the clinical impact of living cartilage grafts.

   a. Bian L, Lima EG, Angione SL, Ng KW, Williams DY, Xu D, Stoker AM, Cook JL, Ateshian GA, Hung CT. Mechanical and biochemical characterization of cartilage explants in serum-free culture. J Biomech. 2008;41(6):1153-9. PubMed PMID: 18374344; PubMed Central PMCID: PMC3387278.
   b. Bian L, Stoker AM, Marberry KM, Ateshian GA, Cook JL, Hung CT. Effects of dexamethasone on the functional properties of cartilage explants during long-term culture. Am J Sports Med. 2010 Jan;38(1):78-85. PubMed PMID: 19959744; PubMed Central PMCID: PMC2929560.
   c. Stoker A, Garrity JT, Hung CT, Stannard JP, Cook J. Improved preservation of fresh osteochondral allografts for clinical use. J Knee Surg. 2012 May;25(2):117-25. PubMed PMID: 22928429.
   d. Cook JL, Stoker AM, Stannard JP, Kuroki K, Cook CR, Pfeiffer FM, Bozynski C, Hung CT. A novel system improves preservation of osteochondral allografts. Clin Orthop Relat Res. 2014 Nov;472(11):3404-14. PubMed PMID: 25030100; PubMed Central PMCID: PMC4182376.

4. Stem Cell Applications for Musculoskeletal Tissue Engineering: Our laboratory has investigated the use of mesenchymal stem cells (MSCs), such as derived from fat, synovium and bone marrow, as a clinically-relevant cell source for cell-based therapies of cartilage and bone repair. Chemical and physical priming strategies have been used to optimize differentiation and tissue elaboration capacity.

   a. Tan AR and Hung CT, Concise Review: Mesenchymal Stem Cells for Functional Cartilage Tissue Engineering: Taking Cues from Chondrocyte-Based Constructs. Stem Cells Transl Med, 2017. **6**(4): p. 1295-1303. PubMed PMID: 28177194. PubMed Central PMCID: PMC5442836.
   b. Alegre-Aguaron, E., S.R. Sampat, J.C. Xiong, R.M. Colligan, J.C. Bulinski, J.L. Cook, G.A. Ateshian, L.M. Brown, and C.T. Hung, Growth factor priming differentially modulates components of the extracellular matrix proteome in chondrocytes and synovium-derived stem cells. Plos One, 2014. **9**(2): p. e88053. PubMed PMID: 24516581. PubMed Central PMCID: PMC3917883
   c. Oswald ES, Brown LM, Bulinski JC, and Hung CT, Label-free protein profiling of adipose-derived human stem cells under hyperosmotic treatment. J Proteome Research, 2011. **10**(7): p. 3050-3059. PMID: 21604804. PubMed Central PMCID: PMC3153440.
   d. Grayson WL, Bhumiratana S, Chao PHG, Hung CT, and Vunjak-Novakovic G, Spatial regulation of human mesenchymal stem cell differentiation in engineered osteochondral constructs: effects of pre-differentiation, soluble factors and medium perfusion. Osteoarthritis Cartilage, 2010. **18**(5): p. 714-23. PMID: 20175974. PubMed Central PMCID: PMC2862865.

Complete List of Published Work in My Bibliography:
https://www.ncbi.nlm.nih.gov/pubmed/?term=hung+ct+and+columbia+or+hung+c+and+columbia+and+engineering

D. Additional Information: Research Support and/or Scholastic Performance

5P41EB002520, NIH
Vunjak-Novakovic, Gordana (PI)
09/01/14-05/31/2020
Tissue Engineering Resource Center (Bioreactor Core)

The focus of this core will be on the development and utilization of novel bioreactors to control the cellular microenvironment, impart multiple physical stimuli, and enable real time imaging of cells and tissues (osteochondral and myocardium) at various hierarchical scales.
Role: Co-I

1R01AR068133-04 NIH/NIAMS
Hung, Clark (PI)
5/16/16-4/30/22
Incorporation of Dexamethasone Delivery within Engineered Cartilage
This application examines release of the steroid dexamethasone from degradable polymer microspheres that are encapsulated together with cells in a biocompatible hydrogel scaffold for cartilage tissue engineering. Year 3-4: diversity supplement and year 3: gender effects administrative supplement.
Role: PI

DOD PR171360
Ateshian, Gerard (PI)
Adaptively Conforming Osteochondral Allografts for Joint Replacements
09/01/18-08/31/21
Investigate engineering techniques to modify the curvature of osteochondral allografts for joint repair.
Role: Co-I

1R01AR073289-01A1 NIH/NIAMS
Ateshian, GA, Vukelic, S (Co-PIs)
Laser Treatment Modality for Strengthening Osteoarthritic Cartilage
9/1/18-8/31/23
The purpose of this new R01 grant application is to develop a novel laser-based treatment for early-stage cartilage lesions to prevent the progression of cartilage degeneration.
Role: Co-I

SEAS SIRS
Hung, Clark and Stockwell, Brent (Co-PIs)
9/1/19-8/30/20
Ferrostatins as a Therapeutic Strategy to Prevent Blood-Induced Synovial Joint Damage
The study is aimed at studying the role of ferroptosis in blood-induced chondrocyte death as a potential avenue for development of therapeutic strategies to mitigate synovial joint injury associated with bleeding with hemophilia or trauma.
Role: Co-PI

R21AR075245A1 NIH/NIAMS
Hung, Clark (PI)
3/1/19-8/31/21
Cell Cycle-Mediated Optimization of Cartilage Tissue Development”
The purpose of this high risk-high reward grant application is to modulate cell cycle phase as a strategy for functional tissue engineering of articular cartilage.

DARPA
Sia, Samuel (PI)
3/20-3/23
Bioelectronics for Tissue Regeneration (BETR)
The study is aimed at a cutting edge technology for smart healing of skin wounds incorporating nanosensors, focused ultrasound triggering of drug delivery, biomaterials and modeling.
Role: Co-I

Orthopaedic Scientific Research Foundation (OSRF 19_005)
Shah, Roshan (Co-PI)
1/1/2020 – 12/31/20
Determination of Biomarkers for OA using a Novel Synovial Joint Model System
This application examines response of cartilage and synovium co-culture with clinical synovial fluid samples.
Role: Co-PI