Stanford

Nidhi Bhutani

Associate Professor of Orthopaedic Surgery

Bio

ACADEMIC APPOINTMENTS

- Associate Professor, Orthopaedic Surgery
- Member, Bio-X
- Member, Wu Tsai Human Performance Alliance
- Member, Maternal & Child Health Research Institute (MCHRI)

LINKS

- My Lab website: https://med.stanford.edu/bhutanilab

Research & Scholarship

CURRENT RESEARCH AND SCHOLARLY INTERESTS

The long-term goal of our research is to understand the fundamental mechanisms that govern and reprogram cellular fate during development, regeneration and disease. We are specifically interested in-

1.Reprogramming approaches for musculoskeletal regeneration

Discovery of induced pluripotency by Yamanaka and colleagues has revolutionized the field of regenerative medicine. Induced pluripotent stem cells (iPSC), generated by introduction of a few defined factors in a somatic cell, provide an ideal patient-specific source for disease modeling, drug discovery and cellular therapies. Clinically, these findings have uncovered the possibility of unprecedented sources for patient-autologous cells with far reaching implications in a variety of diseases. From the basic biology perspective, these findings have revealed that cell fates are inherently plastic and are dynamically regulated. Our research is geared towards applying reprogramming approaches towards musculoskeletal regeneration especially cartilage regeneration that remains an unmet medical need.

2.Mechanisms underlying stem cell self-renewal, differentiation and cancer

We are interested in understanding the role of the extracellular matrix in regulating stem cell self-renewal and differentiation, and how this regulation goes awry in cancer. Understanding the acquisition and maintenance of the ‘differentiated’ state can provide important clues regarding the ‘dedifferentiation’ associated with cancer.

3.Epigenetic regulation in development and disease

DNA methylation is an epigenetic mark associated with long-term gene silencing during early development and lineage specification. The other side of the coin i.e. DNA demethylation has received scant attention over the years mainly due to the inability to identify enzymes that could mediate the removal of the methylation marks. Recent studies by our group and others have uncovered novel DNA repair based DNA demethylation pathways. Another exciting discovery is that of the 'sixth base' in DNA i.e. hydroxylation of methylated cytosines (5mC) by enzymes leading to '5hmC' that is present in many tissues. The role and effect of 5hmC on 5mC turnover and hence DNA demethylation, on gene expression per se and stem cell fate and differentiation is a topic of vigorous interest. We are exploring the role of these novel DNA demethylation regulators in cartilage development, regeneration and disease. Our recent studies have uncovered a dysregulation of the DNA demethylation pathways in the widely prevalent age-associated disorder, Osteoarthritis. We are currently investigating the mechanistic details of these epigenetic pathways in Osteoarthritis.

Teaching

COURSES

2021-22

- Orthopaedic Tissue Engineering: ORTHO 270 (Win)

2020-21

- Orthopaedic Tissue Engineering: ORTHO 270 (Win)

2019-20

- Orthopaedic Tissue Engineering: ORTHO 270 (Win)

2018-19

- Orthopaedic Tissue Engineering: ORTHO 270 (Win)

STANFORD ADVISEES

Med Scholar Project Advisor

Claire Rhee

Doctoral Dissertation Reader (AC)

Eva Gonzalez Diaz, Malachia Hoover, Dhiraj Indana, Ericka von Kaeppler

Postdoctoral Faculty Sponsor

Yudhishtar Bedi, Akshay Pandey, Neety Sahu, Mamta Singla

Postdoctoral Research Mentor

Akshay Pandey, Neety Sahu, Mamta Singla

GRADUATE AND FELLOWSHIP PROGRAM AFFILIATIONS

- Cancer Biology (Phd Program)

Publications

PUBLICATIONS

- **A dysfunctional TRPV4-GSK3beta pathway prevents osteoarthritic chondrocytes from sensing changes in extracellular matrix viscoelasticity.** *Nature biomedical engineering*
  Agarwal, P., Lee, H., Smeriglio, P., Grandi, F., Goodman, S., Chaudhuri, O., Bhutani, N.
  2021

- **Encapsulated Mesenchymal Stromal Cell Microbeads Promote Endogenous Regeneration of Osteoarthritic Cartilage Ex Vivo.** *Advanced healthcare materials*

Sahu, N. n., Agarwal, P. n., Grandi, F. n., Bruschi, M. n., Goodman, S. n., Amanatullah, D. n., Bhutani, N. n.
2021: e2002118

- **Single-cell mass cytometry reveals cross-talk between inflammation-dampening and inflammation-amplifying cells in osteoarthritic cartilage** *Science Advances*
  Grandi, F. ., Baskar, R., Smeriglio, P., Murkherjee, S., Indelli, P., F. Amanatullah, D., Goodman, S., Chu, C., Bendall , S., Bhutani, N.
  2020; 6 (11)
- **Inhibition of TET1 prevents the development of osteoarthritis and reveals the 5hmC landscape that orchestrates pathogenesis.** *Science translational medicine*
  Smeriglio, P. n., Grandi, F. C., Davala, S. n., Masarapu, V. n., Indelli, P. F., Goodman, S. B., Bhutani, N. n.
  2020; 12 (539)
- **Early induction of a prechondrogenic population allows efficient generation of stable chondrocytes from human induced pluripotent stem cells** *FASEB JOURNAL*
  Lee, J., Taylor, S. E., Smeriglio, P., Lai, J., Maloney, W. J., Yang, F., Bhutani, N.
  2015; 29 (8): 3399-3410
- **A Quick and Efficient Method for the Generation of Immunomodulatory MSC from Human iPSC.** *Tissue engineering. Part A*
  Bruschi, M., Sahu, N., Singla, M., Grandi, F., Agarwal, P., Chu, C., Bhutani, N.
  2021
- **Viscoelasticity and Adhesion Signaling in Biomaterials Control Human Pluripotent Stem Cell Morphogenesis in 3D Culture.** *Advanced materials (Deerfield Beach, Fla.)*
  Indana, D., Agarwal, P., Bhutani, N., Chaudhuri, O.
  2021: e2101966
- **Preparation of Human Chondrocytes for Profiling Using Cytometry by Time-of-flight (cyTOF).** *Bio-protocol*
  Grandi, F. C., Bhutani, N.
  2021; 11 (14): e4086
- **Single Cell Omics for Musculoskeletal Research.** *Current osteoporosis reports*
  Rai, M. F., Wu, C., Capellini, T. D., Guilak, F., Dicks, A. R., Muthuirulan, P., Grandi, F., Bhutani, N., Westendorf, J. J.
  2021
- **Mapping 5-Hydroxymethylcytosine (5hmC) Modifications in Skeletal Tissues Using High-Throughput Sequencing.** *Methods in molecular biology (Clifton, N.J.)*
  Grandi, F. C., Bhutani, N.
  2021; 2221: 101–8
- **TET1 Directs Chondrogenic Differentiation by Regulating SOX9 Dependent Activation of Col2a1 and Acan In Vitro.** *JBMR plus*
  Smeriglio, P., Grandi, F. C., Taylor, S. E., Zalc, A., Bhutani, N.
  2020; 4 (8): e10383
- **Epigenetic Therapies for Osteoarthritis.** *Trends in pharmacological sciences*
  Grandi, F. C., Bhutani, N.
  2020
- **Transient non-integrative expression of nuclear reprogramming factors promotes multifaceted amelioration of aging in human cells.** *Nature communications*
  Sarkar, T. J., Quarta, M. n., Mukherjee, S. n., Colville, A. n., Paine, P. n., Doan, L. n., Tran, C. M., Chu, C. R., Horvath, S. n., Qi, L. S., Bhutani, N. n., Rando, T. A., Sebastiano, et al
  2020; 11 (1): 1545
- **Platelet-Rich Plasma (PRP) From Older Males With Knee Osteoarthritis Depresses Chondrocyte Metabolism and Upregulates Inflammation** *JOURNAL OF ORTHOPAEDIC RESEARCH*
  O'Donnell, C., Migliore, E., Grandi, F., Koltsov, J., Lingampalli, N., Cisar, C., Indelli, P. F., Sebastiano, V., Robinson, W. H., Bhutani, N., Chu, C. R.
  2019; 37 (8): 1760–70
- **Platelet-Rich Plasma (PRP) from Older Males with Knee Osteoarthritis Depresses Chondrocyte Metabolism and Upregulates Inflammation.** *Journal of orthopaedic research : official publication of the Orthopaedic Research Society*

O'Donnell, C., Migliore, E., Grandi, F. C., Koltsov, J., Lingampalli, N., Cisar, C., Indelli, P. F., Sebastiano, V., Robinson, W. H., Bhutani, N., Chu, C. R.
2019

- **4 Effect of trabecular metal on the elution of gentamicin from Palacos cement** *JOURNAL OF ORTHOPAEDIC RESEARCH*
  Mooney, J. A., Manasherob, R., Smeriglio, P., Bhutani, N., Amanatullah, D. F.
  2019; 37 (5): 1018–24

- **Effect of Trabecular Metal on the Elution of Gentamicin from Palacos Cement.** *Journal of orthopaedic research : official publication of the Orthopaedic Research Society*
  Mooney, J. A., Manasherob, R., Smeriglio, P., Bhutani, N., Amanatullah, D. F.
  2019

- **Optimizing Clinical Use of Biologics in Orthopaedic Surgery: Consensus Recommendations From the 2018 AAOS/NIH U-13 Conference** *JOURNAL OF THE AMERICAN ACADEMY OF ORTHOPAEDIC SURGEONS*
  Chu, C. R., Rodeo, S., Bhutani, N., Goodrich, L. R., Huard, J., Irrgang, J., LaPrade, R. F., Lattermann, C., Lu, Y., Mandelbaum, B., Mao, J., McIntyre, L., Mishra, et al
  2019; 27 (2): E50–E63

- **Step-Wise Chondrogenesis of Human Induced Pluripotent Stem Cells and Purification Via a Reporter Allele Generated by CRISPR-Cas9 Genome Editing.** *Stem cells (Dayton, Ohio)*
  Adkar, S. S., Wu, C., Willard, V. P., Dicks, A., Ettyreddy, A., Steward, N., Bhutani, N., Gersbach, C. A., Guilak, F.
  2018

- **Highly Efficient Chondrogenic Differentiation of Human iPSCs and Purification via a Reporter Allele Generated by CRISPR-Cas9 Genome Editing**
  Adkar, S. S., Wu, C., Willard, V. P., Dicks, A., Ettyreddy, A., Steward, N., Bhutani, N., Gersbach, C. A., Guilak, F.
  CELL PRESS.2018: 36

- **Men and Women Differ in the Biochemical Composition of Platelet-Rich Plasma** *AMERICAN JOURNAL OF SPORTS MEDICINE*
  Xiong, G., Lingampalli, N., Koltsov, J. B., Leung, L. L., Bhutani, N., Robinson, W. H., Chu, C. R.
  2018; 46 (2): 409–19

- **Human iPSC-derived chondrocytes mimic juvenile chondrocyte function for the dual advantage of increased proliferation and resistance to IL-1 beta** *STEM CELL RESEARCH & THERAPY*
  Lee, J., Smeriglio, P., Chu, C. R., Bhutani, N.
  2017; 8: 244

- **Soluble Collagen VI treatment enhances mesenchymal stem cells expansion for engineering cartilage.** *Bioengineering & translational medicine*
  Smeriglio, P., Lee, J., Bhutani, N.
  2017; 2 (3): 278–84

- **The first international workshop on the epigenetics of osteoarthritis** *CONNECTIVE TISSUE RESEARCH*
  Meulenbelt, I. M., Bhutani, N., den Hollander, W., Gay, S., Oppermann, U., Reynard, L. N., Skelton, A. J., Young, D. A., Beier, F., Loughlin, J.
  2017; 58 (1): 37-48

- **CD24 enrichment protects while its loss increases susceptibility of juvenile chondrocytes towards inflammation** *ARTHRITIS RESEARCH & THERAPY*
  Lee, J., Smeriglio, P., Dragoo, J., Maloney, W. J., Bhutani, N.
  2016; 18

- **Identification of Human Juvenile Chondrocyte-Specific Factors that Stimulate Stem Cell Growth** *TISSUE ENGINEERING PART A*
  Taylor, S. E., Lee, J., Smeriglio, P., Razzaque, A., Smith, R. L., Dragoo, J. L., Maloney, W. J., Bhutani, N.
  2016; 22 (7-8): 645-653

- **Stable 5-Hydroxymethylcytosine (5hmC) Acquisition Marks Gene Activation During Chondrogenic Differentiation** *JOURNAL OF BONE AND MINERAL RESEARCH*
  Taylor, S. E., Li, Y. H., Smeriglio, P., Rath, M., Wong, W. H., Bhutani, N.
  2016; 31 (3): 524-534

- **Genome-Wide Mapping of DNA Hydroxymethylation in Osteoarthritic Chondrocytes** *ARTHRITIS & RHEUMATOLOGY*
  Taylor, S. E., Li, Y. H., Wong, W. H., Bhutani, N.
  2015; 67 (8): 2129-2140

- **Collagen VI Enhances Cartilage Tissue Generation by Stimulating Chondrocyte Proliferation.** *Tissue engineering. Part A*
  Smeriglio, P., Dhulipala, L., Lai, J. H., Goodman, S. B., Dragoo, J. L., Smith, R. L., Maloney, W. J., Yang, F., Bhutani, N.
  2015; 21 (3-4): 840-849

- **Comparative potential of juvenile and adult human articular chondrocytes for cartilage tissue formation in three-dimensional biomimetic hydrogels.** *Tissue engineering. Part A*
  Smeriglio, P., Lai, J. H., Dhulipala, L., Behn, A. W., Goodman, S. B., Smith, R. L., Maloney, W. J., Yang, F., Bhutani, N.
  2015; 21 (1-2): 147-155

- **3D Hydrogel Scaffolds for Articular Chondrocyte Culture and Cartilage Generation.** *Journal of visualized experiments : JoVE*
  Smeriglio, P., Lai, J. H., Yang, F., Bhutani, N.
  2015

- **A global increase in 5-hydroxymethylcytosine levels marks osteoarthritic chondrocytes.** *Arthritis & rheumatology (Hoboken, N.J.)*
  Taylor, S. E., Smeriglio, P., Dhulipala, L., Rath, M., Bhutani, N.
  2014; 66 (1): 90-100

- **A critical role for AID in the initiation of reprogramming to induced pluripotent stem cells** *FASEB JOURNAL*
  Bhutani, N., Decker, M. N., Brady, J. J., Bussat, R. T., Burns, D. M., Corbel, S. Y., Blau, H. M.
  2013; 27 (3): 1107-1113

- **Cathepsins L and Z Are Critical in Degrading Polyglutamine-containing Proteins within Lysosomes** *JOURNAL OF BIOLOGICAL CHEMISTRY*
  Bhutani, N., Piccirillo, R., Hourez, R., Venkatraman, P., Goldberg, A. L.
  2012; 287 (21): 17471-17482

- **DNA Demethylation Dynamics** *CELL*
  Bhutani, N., Burns, D. M., Blau, H. M.
  2011; 146 (6): 866-872

- **Reprogramming towards pluripotency requires AID-dependent DNA demethylation** *NATURE*
  Bhutani, N., Brady, J. J., Damian, M., Sacco, A., Corbel, S. Y., Blau, H. M.
  2010; 463 (7284): 1042-U57

- **Nuclear reprogramming in heterokaryons is rapid, extensive, and bidirectional** *FASEB JOURNAL*
  Palermo, A., Doyonnas, R., Bhutani, N., Pomerantz, J., Alkan, O., Blau, H. M.
  2009; 23 (5): 1431-1440