

# HARVARD School of Dental Medicine RESEARCH BULLETIN

## 2016-2017 HSDM **Dean's Scholars**



Shek Man (Jacky) Chim, PhD, research fellow in Developmental Biology and member of the Rosen Lab, received an award for his project on the interplay of BMP and activin signaling regulating bon formation in the adult skeleton.



Joshua Chou, PhD, research fellow in Oral Medicine, Infection and Immunity and member of the Baron Lab, received an award for his project understanding the role of Yap/ Taz in osteocyte/osteoblast mechanosensing.



Sanjoy Khan, PhD, research fellow in Developmental Biology and member of the Yang Lab, received an award for his project understanding the molecular mechanisms of McCune-Albright mutation Gas in bone development and fibrous dysplasia.



Chia-Cheng Li, DDS, DMSc, instructor in Oral Medicine, Infection and Immunity and member of the Zhe Lab at BWH, received an award for her project understanding lineage tracing and clonal analysis of oral cancer initiating cells.

Dean's Scholar Continuation Grants were awarded to: Xuchen (Aimee) Duan, MS, PhD of the Olsen Lab; Shu-Chi (Allison) Yeh, PhD of the Intini Lab; and Yi Fan, DDS of the Lanske Lab.

## **HRSA Funds Center of Excellence for Oral Health Integration into Primary Care** Training

The Harvard School of Dental Medicine in collaboration with Harvard Medical School and University of Massachusetts Medical School was awarded a five-year, \$3.5 million dollar cooperative agreement grant from the Health Resources and Services Administration (HRSA).

"The surgeon general's landmark report Oral Health in America brought national attention to the importance of and disparities present in oral health. Furthermore, the Institute Of Medicine report, Improving Access to Oral Health Care for Vulnerable and Underserved Populations showed that unmet oral health care needs and barriers faced by these populations has a great impact on overall health (HRSA.gov)."

This HRSA-funded collaboration will result in the creation of a multi-disciplinary Center of Excellence for Oral Health Integration into Primary Care Training ("The Center of Excellence"), that will focus on addressing the oral health competency gap in primary care training. The Center of Excellence will convene experts in family medicine, general medicine, pediatrics and oral health in a new research partnership. The Center of Excellence will be led by multiple principal investigators including:

Christine A Riedy, PhD, MPH, interim chair and Delta Dental of Massachusetts associate professor of oral health policy and epidemiology, will serve as the lead and contact principal investigator for the Center of Excellence.

Russell Phillips, MD, professor of medicine and director of the Harvard Medical School Center for Primary Care will serve as the Harvard Medical School principal investigator.

Hugh Silk, MD, MPH, professor of family medicine and community health and medical director of the Primary Care Wellness Center at Community Healthlink, will serve as the University of Massachusetts Medical School principal investigator.



Andreia Ionescu, PhD, Received NIH-NIAMS R01 Award

### Andreia Ionescu, PhD, instructor in developmental biology, received funding from NIH-NIAMS for her R01 project, "Hypertrophy and Inflammation in Osteoarthritis: Epistasis or Synergy?"

Osteoarthritis (OA) is a degenerative joint disease characterized by irreversible loss of articular cartilage. There is no cure for OA. Current treatments provide, at best, relief from pain and inflammation associated with the more advanced phases of disease but they do not target the OA progression because the molecular mechanisms are not well understood. A major challenge in OA is halting cartilage damage before disease progression begins.

In this project, Ionescu will investigate the role of FoxA factors as potential regulators of articular cartilage hypertrophy and OA progression in both human OA and a murine model of this disease. To reach this objective, Ionescu will: 1. Determine whether loss of FoxA factors prevents cartilage hypertrophy and degradation following surgical destabilization of the knee joint. 2. Ascertain whether FoxA2-driven chondrocyte hypertrophy primes the articular cartilage for inflammatory cytokine signaling, or whether inflammation develops in the articular cartilage independent of hypertrophy. 3. Determine which pro-osteoarthritic signals induce expression of FoxA factors in human and murine articular chondrocytes. 4. Determine whether FoxA factors are induced in deteriorating articular cartilage from patients with OA.

Altogether, these results will provide a strong basis for development of drugs to treat patients with osteoarthritis. The long-term goal is a better understanding of the pathogenic mechanisms underlying OA onset and progression, in hopes of discovering potential targets for pharmacological intervention.

Ionescu received a PhD degree in Biochemistry and Biophysics from the University of Rochester Medical School. She received further research training at the Lassar Lab in the department of biological chemistry and molecular pharmacology at Harvard Medical School, where she discovered a new family of transcription factors (FoxA) that plays a crucial role in both cartilage development and osteoarthritis. Ionescu joined the Rosen Lab at HSDM in 2015, and is co-course director for Introduction to Research with Dr. Bjorn R. Olsen.



# Yingzi Yang, PhD, Received NIH-NIAMS R01 Award

### Yingzi Yang, PhD, professor of developmental biology, received funding from NIH-NIAMS for her R01 project, "Gas-Hedgehog Signaling in Intramembranous Bone Formation and Expansion."

How osteoblast cells are induced at the outset of bone development is a central question for understanding the organizational principles underpinning a functional skeletal system. Extraskeletal or heterotopic ossification occurs as a common complication of trauma, or in rare genetic disorders and can be disabling and lethal.

Research in the Yang Lab has provided significant insights into the molecular and cellular regulation of bone development and recently they have identified a novel Gas-Hedgehog (Hh) signaling axis that critically regulates ectopic osteoblast differentiation in progressive osseous heteroplasia. This project will build upon Yang's unique perspective and test her central hypothesis: Gas-Hh signaling axis is required to regulate osteoblast differentiation during intramembranous bone formation and recruit wild type cells into the ectopic bone during progressive progressive osseous heteroplasia.

Yang anticipates that her findings will have broad significance with respect to cell-fate specification and reprogramming processes during development, repair, and regeneration of many other organ systems where Gas-Hh and Gas-Wnt signaling plays a critical role and enhance the understanding of these signaling pathways in human diseases including cancer.

### A publication of the Office of Research

188 Longwood Avenue — Boston, MA 02115 www.hsdm.harvard.edu

Bjorn R. Olsen, MD, PhD, Dean for Research Dawn M. DeCosta, Editor and Layout Heather M. Denny, Editing Leanne "Jake" Jacobellis, Editing Lia Sgourakes, Editing

For information regarding the Research Bulletin, please contact Dawn DeCosta at dawn\_decosta@hsdm.harvard.edu, or 617.432.1121.



Nathaniel Treister, DMD, DMSc, Received NIH-NIDCR R34 Award

Dr. Nathaniel Treister, assistant professor of Oral Medicine, Infection and Immunity, and Chief, Division of Oral Medicine and Dentistry at BWH, received an R34 Award for, "Extraorally Delivered Low Level Light Therapy for Prevention of Oropharyngeal Mucositis in Pediatric Patients Undergoing Hematopoietic Stem Cell Transplantation."

The aim of this proposal is to prevent mucositis, a very painful and common problem that occurs following chemotherapy and hematopoietic cell transplantation. The most promising intervention appropriate for use in children is external low level light therapy. Treister and colleagues plan to evaluate whether this therapy can prevent mucositis and thus, improve the health of children with cancer undergoing hematopoietic cell transplantation. Treister is working with co-PI, Christy Duncan, MD, pediatric transplant physician in the Department of Pediatric Oncology, Dana-Farber Cancer Institute and Boston Children's Hospital.

# HMS Center for Global Health Delivery-Dubai Grants Cooperative Award to HSDM and Mediclinic, UAE



Drs. Christine Riedy and Hawazin Elani (HSDM) and Dr. Munzer Ramahi (Mediclinic, UAE) will serve as co-PIs on, **"Oral Health and** 

Diabetes in Emirati Adults: A Mixed Methods Study," funded by the HMS Center for Global Health Delivery-Dubai.

The HMS Center for Global Health Delivery-Dubai promotes research optimizing the 'last mile' of health care delivery. The Mediclinic/HSDM collaboration will employ a mixed methods design to examine Type 2 diabetes among Emirati adults residing in Dubai, UAE. A quantitative approach will be used to assess the prevalence of periodontitis in diabetic Emirati adults, examine the association between prevalence of periodontitis and uncontrolled diabetes and assess patient's treatment compliance/adherence. A qualitative approach will be used to examine the lived experiences of controlled and uncontrolled diabetics. This knowledge will be used to inform and tailor future targeted behavioral interventions in this population.

# John Ahern, MD, DMD, MPH, Joins HSDM as a Fulbright Scholar from Dublin, Ireland



The Fulbright Program has timeless prestige and offers immeasurable opportunities to learn, build relationships and foster academic collaboration. To that end, we proudly welcome Dr. John Ahern as a Fulbright Scholar to HSDM. As a

dual-qualified clinician in both medicine and dentistry, Ahern is passionate about the integration of oral health with general health. Ahern (above left) is being presented his Fulbright Award in Dublin Castle in 2015.

During his Fulbright, Ahern will be based in the Office of Global and Community Health at the HSDM, and is looking forward to engaging in scholarly activity with both faculty and students. Ahern stated, "I believe oral health professionals have a responsibility to advocate for an integrated model of care with other health professionals. Expanding oral health competencies to primary care clinicians will faciliate greater access to oral health care by enabling screening, early detection and the delivery of preventive interventions. The integration of oral health with primary care will also encourage patients to engage with oral health services and strengthen interprofessional collaboration between health professionals."

Ahern received his medical (2015) and dental degrees (2010) at Trinity College Dublin, Ireland. He has worked as a medical and dental clinician in primary, secondary and tertiary care settings in Ireland. He pursued a part-time masters in public health from the London School of Hygiene and Tropical Medicine (2013), and worked with the World Health Organization in Geneva.

Outside of work, Ahern is a sports and fitness enthusiast, and particularly loves being outdoors. He plays a lot of tennis and has worked abroad for numerous summers as a tennis coach, so he would love to find some people to play with while in Boston. As a "Fulbrighter" to the United States, Ahern has been instructed to socialize and immerse himself in local culture which, as an Irishman in Boston, he expects will be a very easy and enjoyable task to fulfill.

# **HSDM Publications**

#### DEVELOPMENTAL BIOLOGY

Alikhani M, Lopez J, Alabdullah H, Vongthongleur T, Sangsuwon C, Alikhani M, Alansari S, Oliveira S, Nervina J, Teixeira C. High-frequency acceleration: Therapeutic tool to preserve bone following tooth extractions. *Dental Research* 2016;95(3):311-318.

Chang C, Garg P, Giddon D. Boarding school influence on self-reported concern for perceived body and face morphology in Taiwan. *Asian Journal of Psychiatry* 2016; 22:96-101.

Fang J, Xu L, Li Y, Zhao Z. Roles of TGF-beta 1 signaling in the development of osteoarthritis. *Histology and Histopathology* 2016;11779.

Hamilton J, Nagao M, Levine B, Chen D, Olsen B, Im H. Targeting VEGF and its receptors for the treatment of osteoarthritis and associated pain. *Bone and Mineral Research* 2016;31(5):911-24.

Jin Y, Yang Y. LGR4: A new receptor for a stronger bone. *Science China Life Sciences* 2016; May 13.

Wu W, Li W, Chen H, Jiang L, Zhu R, Feng D. FUNDC1 is a novel mitochondrial-associated-membrane protein required for hypoxia-induced mitochondrial fission and mitophagy. *Autophagy* 2016; Jun 17.

#### ORAL AND MAXILLOFACIAL SURGERY

Abramowicz S, Kim S, Prahalad S, Chouinard A, Kaban L. Juvenile arthritis: Current concepts in terminology, etiopathogenesis, diagnosis, and management. *International Oral and Maxillofacial Surgery* 2016; May 6.

Passeri L, Choi J, Kaban L, Lahey E. Morbidity and mortality rates after maxillomandibular advancement for treatment of obstructive sleep apnea. *Oral and Maxillofacial Surgery* 2016; Apr 21.

Resnick C, Inverso G, Wrzosek M, Padwa B, Kaban L, Peacock Z. Is there a difference in cost between standard and virtual surgical planning for orthognathic surgery? *Oral and Maxillofacial Surgery* 2016; Apr 22.

Resnick C, Rottgers S, Langenfeld C, Mulliken J, Padwa B. Novel rigid external distraction device improves stability and controls the vector during midfacial advancement. *Craniofacial Surgery* 2016; May 20.

Selvi F, Messina J, Faquin W, Keith D. Relapsing polychondritis concomitant with synovial chondromatosis of the temporomandibular joint. *Oral and Maxillofacial Surgery* 2016 May 18.

#### MULTI-DEPARTMENTAL

Liu M, Reed D, Cecchini G, Lu X, Ganjawalla K, Gonzales C, Monahan R, Luan X, Diekwisch T. Varanoid tooth eruption and implantation modes in a late cretaceous mosasaur. *Frontiers in Physiology* 2016;7:145.

Padwa B, Dentino K, Robson C, Woo S, Kurek K, Resnick C. Pediatric chronic nonbacterial osteomyelitis of the jaw: Clinical, radiographic, and histopathologic features. *Oral and Maxillofacial Surgery* 2016; May 26.

Rider D, Furusho H, Xu S, Trachtenberg AJ, Kuo WP, Hirai K, Susa M, Bahammam L, Stashenko P, Fujimura A, Sasaki H. Elevated CD14 (cluster of differentiation 14) and toll-like receptor 4 signaling deteriorate periapical inflammation in TLR2 deficient mice. *Anatomical Records (Hoboken)* 2016; Jun 17.

Rosen E, Donoff R, Riedy C. U.S. dental school deans' views on the value of patient-reported outcome measures in dentistry. *Dental Education* 2016; 80:721-725.

#### ORAL HEALTH POLICY AND EPIDEMIOLOGY

Ramoni R, Asher S, White J, Vaderhobli R, Ogunbodede E, Walji M, Riedy C, Kalenderian E. Honoring dental patients' privacy rule right of access in the context of electronic health records. *Dental Education* 2016;80(6):691-696.

Seymour B, Yang H, Getman R, Barrow J, Kalenderian E. Patient-centered communication: Exploring the dentist's role in the era of e-patients and health 2.0. *Dental Education* 2016;80(6):697-704.

#### **RESTORATIVE DENTISTRY AND BIOMATERIALS SCIENCES**

Gallucci G, Avrampou M, Taylor J, Elpers J, Thalji G, Cooper L. Maxillary implant-supported fixed prosthesis: A survey of reviews and key variables for treatment planning. *International Journal of Oral and Maxillofacial Implants* 2016;31 Suppl:s192-197.

#### ORAL MEDICINE, INFECTION AND IMMUNITY

Chen P, Mancini M, Sonis S, Fernandez-Martinez J, Liu J, Cohen E, Toback F. A novel peptide for simultaneously enhanced treatment of head and neck cancer and mitigation of oral mucositis. *PLoS One* 2016 Apr 6;11(4):e0152995.

Colombo N, Ribas L, Pereira J, Kreling P, Kressirer C, Tanner A, Duque C. Antimicrobial peptides in saliva of children with severe early childhood caries. *Archives of Oral Biology* 2016;69:40-46.

Ide N, Olauson H, Sato T, Densmore M, Wang H, Hanai J, Larsson T, Lanske B. In vivo evidence for a limited role of proximal tubular Klotho in renal phosphate handling. *Kidney International* 2016; Jun 9.

Krishnan K, Chen T, Paster B. A practical guide to the oral microbiome and its relation to health and disease. *Oral Diseases* 2016; May 24.

Login G. A 5-year perspective on a removable overdenture appliance for a patient with osteonecrosis of the jaw, a mandibular resection, and rampant caries. *Prosthetic Dentistry* 2016; Mar 18.

Machtei E, Kim D, Karimbux N, Zigdon-Giladi H. The use of endothelial progenitor cells combined with barrier membrane for the reconstruction of peri-implant osseous defects: an animal experimental study. *Clinical Periodontology* 2016;43(3):289-297.

Nevins M, Aimetti M, Parma-Benfenati S, De Angelis N, Yu Y, Kim D. Treatment of moderate to severe buccal gingival recession defects with placental allografts. *International Periodontics Restorative Dentistry* 2016;36(2):171-177.

Ng MW, Fida Z. Dental hygienist-led chronic disease management system to control early childhood caries. *Evidenced Based Dental Practice* 2016;16 Suppl:20-33.

Nishimura K, Shindo S, Movila A, Kayal R, Abdullah A, Savitri I, Ikeda A, Yamaguchi T, Howait M, Al-Dharrab A, Mira A, Han X, Kawai T. TRAPpositive osteoclast precursors mediate ROS/NO-dependent bactericidal activity via TLR4. Free *Radicals in Biology and Medicine* 2016; Jun 22.

Simsek Kiper PO, Saito H, Gori F, Unger S, Hesse E, Yamana K, Kiviranta R, Solban N, Liu J, Brommage R, Boduroglue K, Bonafe L, Campos-Xavier B, Dikoglu E, Eastell R, Gossiel F, Harshman K, Nishimura G, Girisha K, Stevenson B, Takita H, Rivolta C, Superti-Furga S, Baron R. Cortical bone fragility-Insights from sFRP4 deficiency in Pyle's disease. *New England Journal of Medicine* 2016;374(26):2553-2562.

Sonis S. Ultrasound mediated drug delivery. Oral Diseases 2016; May 12.

Sonis S, Amaral Mendes R. Could the PI3K canonical pathway be a common link between chronic inflammatory conditions and oral carcinogenesis? *Oral Pathology and Medicine* 2016; Mar 15.

Vartoukian S, Moazzez R, Paster B, Dewhirst F, Wade W. First cultivation of health-associated Tannerella sp. HOT-286 (BU063). *Dental Research* 2016; May 18.

Zhang W, Yu X, Kwak M, Xu L, Zhang L, Yu Q, Jin J. Maturation of dendritic cells by pullulan promotes anti-cancer effect. *Oncotarget* 2016.

Zecha J, Raber-Durlacher J, Nair R, Epstein J, Sonis S, Elad S, Hamblin M, Barasch A, Migliorati C, Milstein D, Genot M, Lansaat L, van der Brink R, Arnabat-Dominguez J, van der Molen L, Jacobi I, van Diessen J, de Lange J, Smeele L, Schubert M, Bensadoun R. Low level laser therapy/ photobiomodulation in the management of side effects of chemoradiation therapy in head and neck cancer: part 1: mechanisms of action, dosimetric, and safety considerations and part 2: proposed applications and treatment protocols. *Supportive Care In Cancer* 2016;24(6):2781-2805.