June – August 2017 RESEARCH BULLETIN

Giuseppe Intini, DDS, PhD, Receives NIH/National Cancer Institute Award



Giuseppe Intini, DDS, PhD, assistant professor of Oral Medicine, Infection and Immunity, received an NIH/ National Cancer Institute grant to identify the role of cancer stem cells in osteosarcoma development and metastasis entitled, "A Multi-Fluorescent Intravital Microscopy Approach to Study Osteosarcoma."

Osteosarcoma (OS) is the most common non-hematological malignant primary tumor in bone, mainly diffused in children and often very aggressive. Today, despite numerous advances in treatment and even aggressive approaches such as limb amputation surgery, the survival rate for metastasized OS is still as low as twenty percent and osteosarcoma remains the second leading cause of cancer-related deaths in children and young adults. The lack of a robust in vivo OS model that allows for identification, quantification, and localization of each of the different cell types that contribute to the heterogeneity of OS and its microenvironment represents a major barrier to the development of novel cell-targeting therapeutics for OS.

To overcome this barrier, Intini will develop a multi-fluorescent cell stage-specific transgenic mouse model of OS based on the ability to drive the expression of three different fluorescent proteins during different stages of osteoblast differentiation with the possibility of inducing OS by conditional inactivation of p53 and Rb in the osteoblast lineage. Intini will explore the cellular architecture of the OS, describing the location of various fluorescent cell populations within the neoplastic tissue, and the role these cell populations may have in OS recurrence. Intini believes that the elucidation of the tumor architecture, the interpretations of the cell dynamics during neoplastic development, and the identification of the cell population responsible for OS recurrence will be useful to future studies aimed at designing novel approaches to OS cell-targeting therapy.

HSDM Awarded \$1.3m HRSA Cooperative Agreement



Dr. Christine Riedy Murphy, chair and associate professor of Oral Health Policy and Epidemiology, is the PI on HRSA-funded, "Equitable Care for Elders National Training and Technical Assistance Center."

According to The State of Aging and Health in America 2013, chronic disease affects two out of every three older Americans, and treatment for this population accounts for 66% of the country's health care budget. Unfortunately, these older adults may not have been able to access the health care services they need (e.g., only 21.4 percent of health centers offered dental services; only 6 percent offered mental health services; and only 10 percent offered enabling services (HRSA 2015 Health Center Program Grantee Data).

This project will provide training and technical assistance activities that will build on the expertise of HSDM, Harvard Medical School, Harvard T. H. Chan School of Public Health, Stony Brook University School of Nursing, Beth Israel Deaconess Medical Center, and the Simmons School of Social Work, to provide innovative and culturally competent models of care, inter-professional training and educational resources, and technical assistance to health care professionals providing care to this increasingly vulnerable population. The three main goals of the Center are to (1) to increase the number of patients from special and vulnerable populations effectively served by health centers, (2) to decrease the percentage of patients with type II diabetes with A1c greater than 9 percent, and (3) to increase the number of health centers providing services or engaged in partnerships that address social determinants of health.

HSDM Residents Receive Awards from the American Academy of Pediatric Dentistry (AAPD)



Dr. Chris Goodell, second year pediatric dental resident, DMD15, was the recipient of the Ralph E. McDonald Award (2017), NuSmile Graduate Student Award (2017), and Sunstar Postgraduate Research Fellowship (2016). Goodell received the Ralph E. McDonald Award for his research project, "Silver Diamine Fluoride has Little Effect on the Oral Microbiome," funded in part by the Sunstar Postgraduate Research

Fellowship. Goodell received the NuSmile Graduate Student Research Award, granted to the top eight finalists selected by the AAPD Council on Scientific Affairs based on abstract and manuscript submissions. His mentor is Dr. Rosalyn Sulyanto.



Dr. Michael Hong, second year pediatric dental resident, was the recipient of the NuSmile graduate student award in 2017, for his research project, "Association Between Sealant Placement and Caries Development in Primary Molars." Hong's mentors are Drs. Man Wai Ng and Rosalyn Sulyanto.



Dr. Martin Berger, first year pediatric dental resident, DMD16, was the recipient of the Sunstar Postgraduate Research Fellowship for 2017, which provides \$7,500 in research funding. Berger will be presenting his work, "The Microbiologic and Mechanical Effects of Caries Arrest by Silver Diamine Fluoride" next year at the 71st Annual Session of AAPD. His mentor is also Dr. Rosalyn Sulyanto.

Beate Lanske, PhD, Receives NIH/ NIDDK R01 Award



Beate Lanske,
PhD, Professor of
Oral Medicine,
Infection and
Immunity,
received an
NIH/NIDDK
grant entitled,
"PTH Resistance
and Marrow
Adipogenesis."

Dr. Lanske is collaborating with Dr. Cliff Rosen, Director of the Center for Clinical and Translational Research at the Maine Medical Research Institute on this project.

For this study, The Lanske Lab is employing a novel genetic model of parathyroid hormone (PTH) resistance in order to delineate its actions on the skeleton. The Lanske Lab hypothesizes that PTH works to direct mesenchymal progenitor cells into the bone lineage and away from fat. Completion of this proposal should allow Lanske to more clearly delineate the mechanism whereby intermittent parathyroid hormone (PTH) increases bone mass, particularly in older individuals where marrow adiposity is prevalent.

"The recent work from The Lanske Laboratory provides significant insight into how PTH, the only approved anabolic treatment for osteoporosis, functions at the cellular level," Cliff Rosen, said. "This is important because the mechanism of altering cell fate may provide a roadmap for other novel treatments for osteoporosis."

For the first time, the bone building effect of PTH can be attributed to its ability to change cell fate. This significant finding could lead to a better understanding of how to treat osteoporosis and other diseases in humans.

HSDM Publications

DEVELOPMENTAL BIOLOGY

Chen J, Jacox L, Saldanha F, Sive H. Mouth development. Wiley Interdisciplinary Reviews: Developmental Biology 2017; May 17.

Fang J, Xiao L, Chen R, Zhao Z. Conditional removal of the canonical TGF- \hat{l}^2l signaling delays condylar cartilage degeneration induced by a partial discectomy in mice. PLoS One 2017;12(5):e0177826.

Jiang L, Wei X, He P, Feng D, Liu Y, Liu J, Chen J, Yu D, Tan N. Value of pulmonary artery pressure in predicting in-hospital and one-year mortality after valve replacement surgery in middle-aged and aged patients with rheumatic mitral disease: an observational study. British Medical Journal 2017;7(5):e014316.

Kokabu S, Nakatomi C, Matsubara T, Ono Y, Addison W, Lowery J, Urata M, Hudnall A, Hitomi S, Nakatomi M, Sato T, Osawa K, Yoda T, Rosen V, Jimi E. The transcriptional co-repressor TLE3 regulates myogenic differentiation by repressing the activity of the MyoD transcription factor. Journal of Biological Chemistry 2017; Jun 12.

Manosudprasit A, Haghi A, Allareddy V, Masoud M. Diagnosis and treatment planning of orthodontic patients with 3D dentofacial records. American Journal of Orthodontics and Dentofacial Orthopedics 2017;151(6):1083-1091.

Schulte F, Hardt M, Niehaus K. A robust protocol for the isolation of cellular proteins from Xanthomonas campestris in 2D-gel experiments. Electrophoresis 2017; Jun 12.

Wei X, Jiang L, Liu Y, Feng D, He P, Chen J, Yu D, Tan N. Prognostic value of hypoalbuminemia for adverse outcomes in patients with rheumatic heart disease undergoing valve replacement surgery. Science Reports 2017 May 16;7(1):1958.

Zwang Y, Jonas O, Chen C, Rinne M, Doench J, Piccioni F, Tan L, Huang H, Wang J, Ham Y, O'Connell J, Bhola P, Doshi M, Whitman M, Cima M, Letai A, Root D, Langer R, Gray N, Hahn W. Synergistic interactions with PI3K inhibition that induce apoptosis. *Elife* 2017; May 31:6.

ORAL HEALTH POLICY AND EPIDEMIOLOGY

Bakk L, Cadet T, Lien L, Smalley A. Home modifications among community-dwelling older adults: A closer look at race and ethnicity. Gerontological Social Work 2017; Jun 28.

Burke S, Maramaldi P, Cadet T, Kukull W. Decreasing hazards of Alzheimer's disease with the use of antidepressants: mitigating the risk of depression and apolipoprotein E. International Journal of Geriatric Psychiatry 2017; May 31.

Greenberg B, Glick M, Tavares M. Addressing obesity in the dental setting: What can be learned from oral health care professionals' efforts to screen for medical conditions. Journal of Public Health Dentistry 2017; May 26.

Martin S, Simon L. Oral health and medicine integration: Overcoming historical artifact to relieve suffering. American Journal of Public Health 2017;107(S1):S30-S31.

Nelson S, Slusar M, Albert J, Riedy C. Do baby teeth really matter? Changing parental perception and increasing dental care utilization for young children. Contemporary Clinical Trials 2017; May 4.

Seymour B, Shick E, Chaffee B, Benzian H. Going global: Toward competency-based best practices for global health in dental education. *Dental Education* 2017;81(6):707-715.

Simon L, Sue K, Williams R, Beckmann D, Tobey M, Cohen M. Dental student-delivered care at astudent-faculty collaborative clinic in a correctional facility. American Journal of Public Health 2017;107(S1):S85-S87.

So M, Ellenikiotis Y, Husby H, Paz C, Seymour B, Sokal-Gutierrez K. Early childhood dental caries, mouth pain, and malnutrition in the Ecuadorian amazon region. *International Journal of Environmental Research in Public Health* 2017;14(5).

ORAL MEDICINE, INFECTION AND IMMUNITY

Al-Hebshi N, Nasher A, Maryoud M, Homeida H, Chen T, Idris A, Johnson N. Inflammatory bacteriome featuring Fusobacterium nucleatum and Pseudomonas aeruginosa identified in association with oral squamous cell carcinoma. *Science Reports* 2017;7(1):1834.

Carvalho A, DeMambro V, Guntur A, Le P, Nagano K, Baron R, de Paula F, Motyl K. High fat diet attenuates hyperglycemia, body composition changes, and bone loss in male streptozotocin-induced type 1 diabetic mice. Journal of Cell Physiology 2017; Jun 20.

Hu Y, Yu P, Yu X, Hu X, Kawai T, Han X. Kota S, Kota S. IL-21/anti-Tim1/CD40 ligand promotes B10 activity in vitro and alleviates bone loss in experimental periodontitis in vivo. *Biochimica et Biophysica* Acta 2017; Jun 2.

Kota S, Kota S. Noncoding RNA and epigenetic gene regulation in renal diseases. Drug Discovery Today 2017; May 6.

Kurgan Ş, Kansal S, Nguyen D, Stephens D, Koroneos Y, Hasturk H, Van Dyke T, Kantarci A. Strain-specific impact of fusobacterium nucleatum on neutrophil function. Periodontology 2017;88(4):380-389.

Kuten-Shorrer M, Treister N, Stock S, Kelley J, Ji Y, Woo SB, Lerman M, Palmason S, Sonis S, Villa A. Safety and tolerability of topical clonazepam solution for management of oral dysesthesia. Oral Surgery Oral Medicine Oral Pathology Oral Radiology 2017; May 11.

Lorenzen M, Boisen I, Mortensen L, Lanske B, Juul A, Blomberg Jensen M. Reproductive endocrinology of vitamin D. Molecular Cell Endocrinology 2017; Mar 22.

Nashef A, Abu-Toamih Atamni H, Buchnik Y, Hasturk H, Kantarci A, Stephens D, Wiess E, Houri-Haddad Y, Iraqi F. Collaborative cross mouse population for studying the alveolar bone changes and impaired glucose tolerance comorbidity after high fat diet consumption. Periodontology 2017; May 19:1-14.

Naqvi A, Mu L, Hasturk H, Van Dyke T, Mukamal K, Goodson J. The impact of docosahexaenoic acid therapy on subgingival plaque microbiota. Periodontology 2017; 18:1-13.

Sultan A, Woo SB. An asymptomatic diffuse palatal mass. Oral Surgery Oral Medicine Oral Pathology Oral Radiology 2017; Mar 14.

Van Dyke T. Pro-resolving mediators in the regulation of periodontal disease. Molecular Aspects of Medicine 2017; May 5.

Yuan Q, Xiong Q, Gupta M, López-Pintor R, Chen X, Seriwatanachai D, Densmore M, Man Y, Gong P. Dental implant treatment for renal failure patients on dialysis: A clinical guideline. *International Journal* of Oral Science 2017; Jun 23.

ORAL AND MAXILLOFACIAL SURGERY

Geisler B, Ji Y, Peacock Z. Value in oral and maxillofacial surgery: A systematic review of economic analyses. Journal of Oral and Maxillofacial Surgery 2017; May 18.

Wicheta S, Van der Groen T, Faquin W, August M. Minor salivary gland biopsy-An important contributor to the diagnosis of Sjögren Syndrome. *Journal of Oral and Maxillofacial Surgery* 2017; May 3.0

MULTI DEPARTMENTALAlqaderi H, Redline S, Tavares M, Goodson J. Effect of late bedtime on salivary glucose and abdominal obesity in children. Sleep and Biological Rhythms 2017; May 29.

Palla B, Burian E, Fliefel R, Otto S. Systematic review of oral manifestations related to hyperparathyroidism. Clinical Oral Investigation 2017; Jun 14.

Park S, Donoff RB, Saldana F. Interprofessional collaborative learning experience. *Medical Principles & Practice* 2017; Jun 23.

Shaefer J, Lee S, Anderson N. A vibration device to control injection discomfort. *Compendium of Continuing Education in Dentistry* 2017;38(6):e5-e8.

RESTORATIVE DENTISTRY AND BIOMATERIALS SCIENCES

Bavarian R, Sultan A, Mignogna M. Comments regarding "Four cases of mucous membrane pemphigoid with clinical features of oral lichen planus" and on the utility of immunofluorescence. *International Journal of Dermatology* 2017; May 29.

Gil M, Ishikawa-Nagai S, Elani H, Da Silva J, Kim D, Tarnow D, Schulze-Späte U, Bittner N. A prospective clinical trial to assess the optical efficacy of pink neck implants and pink abutments on soft tissue esthetics. *Journal of Esthetic and Restorative Dentistry* 2017; Jun 5.

Kämmerer P, Thiem D, Alshihri A, Wittstock G, Bader R, Al-Nawas B, Klein M. Cellular fluid shear stress on implant surfaces-establishment of a novel experimental set up. *International Journal of Implant Dentistry* 2017;3(1):22.

Lin J, Jang A, Kurylo M, Hurng J, Yang F, Yang L, Pal A, Chen L, Ho S. Periodontal ligament entheses and their adaptive role in the context of dentoalveolar joint function. *Dental Materials* 2017; May 2.

Park C, Sheinbaum J, Tamada Y, Chandiramani R, Lian L, Lee C, Da Silva J, Ishikawa-Nagai S. Dental students' perceptions of digital assessment software for preclinical tooth preparation exercises. *Journal of Dental Education* 2017;81(5):597-603.



This past June, Bjorn R. Olsen, MD, PhD, professor of Developmental Biology and dean for research, received an honorary doctorate degree from the University of Oulu in Finland for his outstanding contributions to the extracellular matrix field. Olsen is photographed with Johanna Myllyharju, PhD, Professor of Molecular Biology and Scientific Director of Biocenter Oulu at the University of Oulu.

Postdoctoral Fellows



David E. Maridas, PhD, a native of Nouméa, New Caledonia, France, joins us from Maine Medical Center where he worked in the laboratory of Cliff Rosen on endocrinology and skeletal phenotyping. Maridas received his MPhil in clinical research, as well as his MSc in reproductive health and human genetics in 2011 from the University of Sydney, and PhD in biomedical sciences from the

University of Maine in 2017. At HSDM, Maridas is a postdoctoral fellow in Developmental Biology in The Rosen Lab and plans to contribute to the Vlk project developed by Drs. Vicki Rosen and Malcolm Whtiman.



Yusuke Mikasa, DDS, a native of Osaka, Japan, joined the Nagai Lab as a postdoctoral research fellow in the Department of Restorative Dentistry and Biomaterials Sciences. Mikasa received his dental degree from Iwate Medical University in Iwate, Japan. In the Nagai Lab, Mikasa's research will focus on oral cancer awareness and prevention and the clinical development of a color caries test.

Noriko Ide, MD, PhD, Promoted to Instructor



Dr. Noriko Ide has been promoted to instructor in Oral Medicine, Infection and Immunity. Ide received her MD degree and PhD degree in cardiovascular and renal medicine from Saga University School of Medicine in Saga, Japan. In 2012, Ide came to HSDM as a research fellow in The Lanske Lab in the Department of Oral Medicine, Infection and Immunity, where she become

an independent investigator. Ide's research focus is on mineral excess targets, intermittent filaments, and causes of defects in mechanotransduction.

Reshma Menon, DDS, DMSc, Oral and Maxillofacial Pathology Resident, Recieves the Gorlin Award



Reshma Menon, DDS, DMSc'17, won the top resident's research award - the Gorlin Award - at the annual meeting of the American Academy of Oral and Maxillofacial Pathology for her project, "WNT Signaling in Oral Cancer Initiating Cells." Menon's research mentor is, Chia-Cheng Li, DDS, DMSc, instructor in Oral Medicine, Infection and Immunity at HSDM. The Gorlin Award is granted in recognition of an outstanding resident that is enrolled in a graduate residency-training program in the specialty of oral pathology. Menon also received The James H. Shaw Award, a recognition of research that greatly advances knowledge in a particular discipline at graduation.

Sang Lee, DMD and Brett Stein, DMD, Receive GNYAP Grant





Dr. Sang Lee, assistant professor of Restorative Dentistry and Biomaterials Sciences and director of advanced graduate education at HSDM, along with Brett Stein, DMD, prosthodontic's resident, received a grant from the Greater New York Academy of Prosthodontics for their project, "A Quantitative Analysis of the Selective-Impression Technique Using CAD/ CAM Technology." For this study, Lee and Stein will take multiple impressions of the edentulous alveolar ridge with, and without, different magnitudes of spacer in otherwise identical custom trays and convert these impressions into digital STL files using CAD/ CAM technology. These digital representations will, therefore, allow us to compare multiple impressions using 3D image analysis software.

Alessandro Villa, DDS, PhD, Receives NIH/NLM Award



Dr. Alessandro Villa, Associate Surgeon in the Division of Oral Medicine and Dentistry at BWH/DFCI and, Program Director for the Oral Medicine residency at HSDM, was recently awarded a grant from NIH/National Library of Medicine.

The main objective of this project is to improve understanding of human papillomavirus (HPV) infection and HPV vaccine among dentists and dental hygienists across New England. As the co-chair for

the Massachusetts Oral HPV prevention task force, Dr. Villa will work with the Massachusetts Department of Public Health to promote HPV vaccination and HPV-related cancer awareness among oral health care providers. The mission of the Maureen E. Russo nonprofit organization, also known as Team Maureen, is to improve the lives of women and families affected by cervical cancer by generating support and funding for the most promising cervical cancer research, while raising awareness regarding the benefits of Cervical Cancer/HPV prevention and early diagnosis and treatment through educational outreach.

Dr. Villa studied dental medicine at the University of Milano, and obtained a PhD from the University of Sassari, Italy. He obtained his Master of Public Health from AT Still University, MO. He completed a surgical residency in oral medicine at BWH/HSDM and a post-doctoral fellowship in cancer epidemiology and genetics at the National Cancer Institute at NIH in Bethesda, MD. Dr. Villa is board certified in oral medicine. His clinical interests include the treatment of oral mucosal diseases, salivary gland disorders and oral complications from cancer therapy. Dr. Villa's research interests are focused primarily on potentially malignant disorders of the oral cavity and oral toxicities from cancer treatment.



The *Journal of Clinical Investigation* cover image above was published on September 4, 2012, and reveals reduced trabecular bone density in mice with conditional deletion of VEGF. This image was created by Mr. John Martin with HSDM's Micro CT Core Facility, and used in the publication, Liu Y, Berendsen A, Jia S, Lotinun S, Baron R, Ferrara N, Olsen BR. Intracellular VEGF regulates the balance between osteoblast and adipocyte differentiation. *Journal of Clinical Investigation* 2012;122(9):3101-3113.

This Bulletin is dedicated to Mr. John R. Martin Research Technician in the Office of Research





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