



Harvard School of Dental Medicine OFFICE OF RESEARCH BULLETIN

November/December 2006



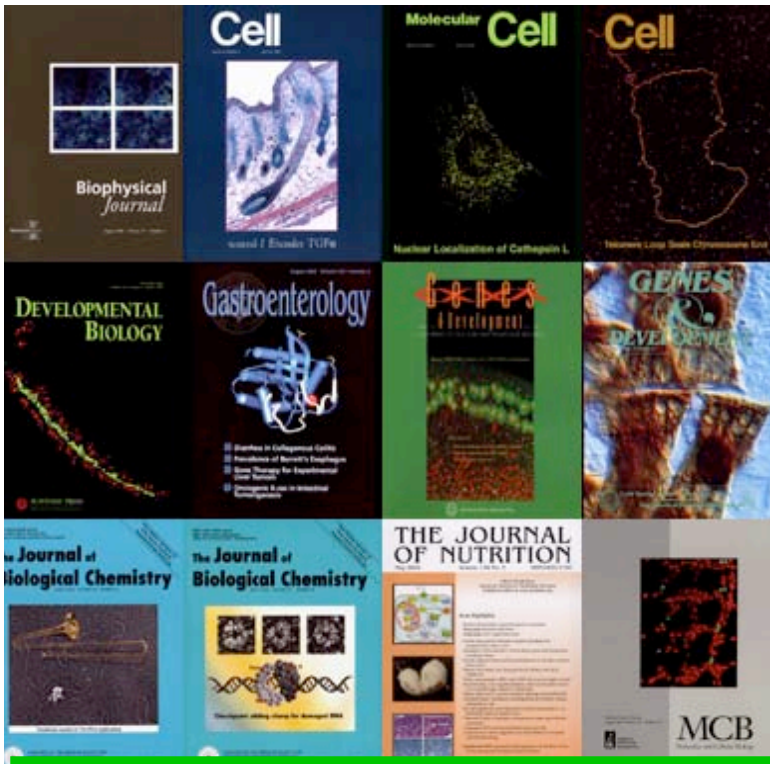
CONGRATULATIONS TO BEATE LANSKE, PHD, Associate Professor of Developmental Biology for her recent NIH R01 award for, Pathophysiologic regulation of Fgf-23 in phosphate homeostasis: Role of vitamin D.

Fibroblast growth factor-23 (FGF-23) is a recently identified molecule, and implicated in the pathogenesis of various human diseases, including in X-linked hypophosphatemia (XLH), oncogenic osteomalacia (OOM), autosomal dominant hypophosphatemic rickets (ADHR), familial tumor calcinosis (FTC) and chronic renal diseases. FGF-23 is one of the most important and determinant factors in maintaining phosphate homeostasis, and skeletal mineralization. The long-term objective of this grant proposal is to determine *in vivo* function, and regulation of FGF-23 in physiological and pathophysiological conditions. As a preliminary step of obtaining such objectives, we have recently generated mice, in which the *Fgf-23* gene has been successfully ablated by homologous recombination. These *Fgf-23* null mice exhibit hyperphosphatemia, increased vitamin-D activities, excessive mineralization in bone, and abnormal calcifications in the soft tissues. In this grant application, we propose to analyze the effects and interrelationship of three essential components, phosphate, Fgf-23 and vitamin-D, using *Fgf-23* null mice. To determine the *in vivo* roles and regulations of Fgf-23, we propose to define the role of sodium-phosphate co-transporters (NaPi) in abnormal phosphate homeostasis in *Fgf-23* null mice by generating *Fgf-23^{-/-}/NaPi 2a^{-/-}* double mutant mice, as outlined in (Specific Aim 1A). Further studies are also proposed to determine the effects of lowering serum phosphate by nicotinamide in *Fgf-23* null animals (Specific Aim 1B). We will also investigate whether circulating FGF-23, exclusively derived from a1(I) collagen (2.3 kb promoter) expressing osteoblasts, is sufficient to rescue the abnormal systemic phenotype of *Fgf-23* null animals. We, therefore, propose to generate a mouse model that is completely ablated for endogenous Fgf-23, but expresses FGF-23 in osteoblasts which is then released into circulation (Specific Aim 2). Furthermore, we proposed to study the role of vitamin D in Fgf-23 mediated functions, by generating and molecular characterization of *Fgf-23/1a hydroxylase* and *Fgf 23/vitamin D receptor* double mutant mice (*Fgf-23^{-/-}/1a(OH)ase^{-/-}; Fgf-23^{-/-}/VDR^{-/-}*) (Specific Aims 3A, 3B). In addition, we will examine the *in vivo* bioactivities of Fgf-23 in a normocalcemic/normophosphatemic microenvironment that are independent of vitamin D signaling (Specific Aim 3B). Finally, we propose to analyze the autocrine function of Fgf-23 *in vitro* using calvarial osteoblasts and explants and will investigate its role as an inhibitor of mineralization (Specific Aim 4). Successful completion of this proposed grant application would generate data that will form the basis to design strategies to manipulate abnormal phosphate homeostasis and defective skeletal mineralization in patients suffering from a wide range of diseases including rickets, XLH, ADHR, OOM, FTC, and chronic renal failure, using FGF-23 or its interacting molecules as a potential therapeutic tool.

LANSKE LAB (left to right): Beate Lanske PhD, Mohammed S. Razzaque MD, PhD, Despina Sitara PhD, Yukiko Maeda PhD, Stephelynn DeLuca, Somi Kim, Carolyn Ferrick



PUBLICATIONS



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AWARDS & ACHIEVEMENTS

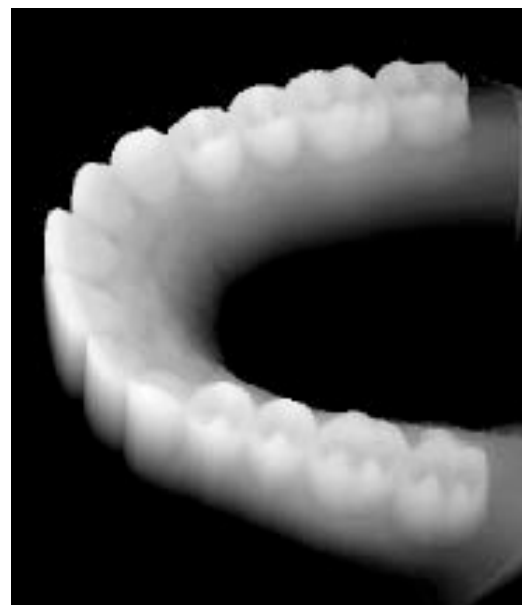
CONGRATULATIONS to the following students and faculty in the Department of Restorative Dentistry and Biomaterials Sciences for their recent awards.

DR. SAMI SHERIF (DMSc '07) (bottom left photo) and **DR. SANG PARK** (bottom right photo) received travel grants and awards from the Massachusetts Section Meeting of the American College of Prosthodontists (ACP) this past October. Dr. Sherif presented, [A five-year analysis of peri-implant soft tissue health surrounding screw versus cement-retained prostheses.](#) Dr. Park presented, [Immediate loading as an interdisciplinary prosthodontic, surgical educational training model.](#)



Dr. Park and Dr. Sherif will both present at the annual session of the ACP in Miami. They will be joined in Miami by **DR. OSCAR SUAREZ-SANCHEZ** (MMSc 07) who will present his table clinic on, [The Harvard multidimensional diagnostic/ACP classification model for oral health, disease, trauma, and dysfunction](#) and **DR. MICHAEL O'TOOLE** (MMSc '06) who will present, [An analysis of sandblasted and acid-etched and machined implant surfaces.](#)

Olympus Corporation launched a new dental spectrophotometer "Crystaleye" at the October ADA meeting in Las Vegas, Nevada. **DR. SHIGEMI NAGAI** and **DR. JOHN DASILVA** were invited by Olympus to attend this launching. The academic brochure for the Crystaleye is based on a clinical study at HSDM conducted by Dr. Shigemi Nagai and her colleagues.



IMPORTANT DATES & CLINICAL RESEARCH SPOTLIGHT

DONALD B. GIDDON, DMD, PhD

Clinical Professor of Developmental Biology



We are pleased to highlight a few of the clinical research projects in Orthodontic and Related Programs in the Department of Developmental Biology. Dr. Giddon received his DMD from Harvard University and his PhD in Psychology from Brandeis University following an AB degree from Brown University and a MA from Boston University, also in psychology.

DECEMBER 7, 2005

DMSc 2008 must turn in the Approval of their thesis proposal topic to the Office of Research.

DECEMBER 2005

DMD 2010 students should meet with their Predoc Research Advisor and begin thinking about a proposal to submit to the Office of Enrichment Program. DMD 2009, 2008 and 2007 students should provide the Office of Research with an update on their research project if they have not already done so.

FEBRUARY 8, 2007

The Harvard Forsyth annual research symposium will be held at The Forsyth Institute on February 8th from 12pm-7pm.

FEBRUARY 9, 2007

HSDM Grand Rounds featuring Matthew Warman, MD, new Director of Orthopedic Research at Children's Hospital, Boston. Grand Rounds will be held in the HSDM REB Auditorium from 12pm-1pm.

The author of more than 100 published articles, abstracts, reviews and books, and over 120 lectures on self-image, the psychophysiology of stress and disease, pain and facial deformity, and the physical bases of the perception of facial and body appearance, Dr. Giddon continues to be involved in teaching and research, private practice and consulting.

Under the direction of Dr. Giddon, the clinical research of the Behavioral Medicine Group of the Department of Developmental Biology focuses on two major areas: 1) the application of psychophysical methods for determining anthropometric bases of subjective judgments of facial and body appearance, ethnic/racial classification of faces, personality attributes. 2) psychophysiological correlates of lateralized chronic pain, including TMD, in studies being conducted at BWH and BIDMC.

Other clinical research under the direction Dr. Giddon's colleague, **DR. NINA ANDERSON**, Clinical Instructor in Developmental Biology, includes the relation of second to fourth digit ratio as an indicator of gender dimorphism and dentofacial morphology; psychobiological correlates of lateralization of dental implant failures.



LESLIE WILL, DMD, MMSc

Associate Professor of Developmental Biology & Program Director of Orthodontics

In addition to Drs. Giddon and Anderson's work, is the clinical research being conducted by Dr. Will and the orthodontic faculty and students in the Department of Developmental Biology which includes several projects that look at various aspects of cleft etiology and treatment: factors in the dentoskeletal pattern of children with clefts that may predict the need for future maxillary advancement surgery; the relationship between dental developmental delay and short stature in children with clefts; and comparison between treatment outcomes of patients who were treated with preoperative maxillary infant orthopedics with those who were not. Other studies explore the relationship between the basal areas of the jaws and the dental arches which is critical to achieving a stable occlusion during orthodontic treatment, and, the relationship of these changes to age and different malocclusions. Finally, a project is being developed in collaboration with Dr. Michael Levin to determine the developmental bases of craniofacial symmetry in identical twins, using the Forsyth twin study sample.



QUESTIONS? COMMENTS? SUGGESTIONS?

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