WE ARE PLEASED to present this special supplement to the Penn Dental Medicine Journal with highlights from four research conferences held by Penn Dental Medicine in 2013. In June, Penn Dental Medicine hosted two conferences that brought together leading researchers and clinicians from across the country and around the world—the 5th International Congress on Adhesive Dentistry and the Penn Periodontal Conference 2013. And in May, our faculty and students gathered to share their recent research through the School’s annual Faculty Research Retreat and Student Research Day—programs that demonstrated the great depth of research activities by our faculty and students. The level of information shared through all four gatherings was tremendous, which will be shared with you through a selection of abstracts from each on the pages that follow.

Creating such forums facilitate the exchange of ideas among investigators and help build new collaborations, which is a vital part of the School’s mission and important to our ongoing research growth and leadership. Multidisciplinary research that reaches across schools, across fields of study, and across the globe is the hallmark of Penn as a world-class research institution and of Penn Dental Medicine’s research enterprise. Whether building collaborations between our own basic and clinical science departments, among colleagues from the other Penn schools, or with other universities throughout the country and around the world, this integration of knowledge advances the science and practice of oral biology and dental medicine.

The impact of the School’s research and scholarship is far reaching. This is evidenced not only by the number of publications from the School’s faculty, but also by the number and frequency of faculty publications cited in the scholarship of other researchers. The charts on page 60 offer a snapshot of that impact over a five-year period, showing the average h index of faculty in each of the School’s academic departments as well as the top 20 h index levels and number of publications achieved by individual faculty members during that time. The impact of research from both the clinical and basic science departments spotlights the breadth of the School’s research activities and Penn Dental Medicine’s continuing strength as an international leader in the generation of new knowledge and treatment modalities in oral health.

Dana Graves, DDS, DMSc
Vice Dean for Research and Scholarship
MORE THAN 550 attendees representing 20 countries attended the 5th International Congress on Adhesive Dentistry (IAD), hosted by Penn Dental Medicine June 14–15, 2013. This marked the first time that the Congress was held in the United States, and Dr. Markus Blatz, Chair and Professor of Preventive and Restorative Sciences at Penn Dental Medicine, served as President of the historic gathering and head of the organizing committee.

“As an internationally renowned academic institution, it is our responsibility to be at the forefront of modern dentistry and participate in the research and education of novel and proven treatment protocols, such as dental adhesion,” says Dr. Blatz. “We were, therefore, very proud when the Japanese Adhesive Society asked us a few years ago to host the IAD in Philadelphia.”

The intensive two-day program, held in the Annenberg Center for the Performing Arts, brought together clinicians, researchers, and the dental industry to discuss the state-of-the-art in adhesive technologies and resin bonding. The opening day of the scientific program addressed the history, current state, and future of dental adhesion, while the second day focused on adhesive restorative materials and treatment options, including updates on composite resin materials for direct restorations and on adhesion to indirect materials, such as dental ceramics. The program also included a scientific corporate forum where industry leaders discussed their latest innovations and developments.

“While research and science were the main focal points of the IAD, the program featured several more clinically oriented presentations to emphasize the importance of clinical relevance in scientific efforts,” adds Dr. Blatz.

In addition, a pre-Congress hands-on course, held June 13 and presented in limited-attendance format, featured two internationally acclaimed clinicians who demonstrated their techniques for ultimate esthetic and functional success with anterior and posterior adhesive restorations.

“Adhesive dentistry has become the center of research and development in restorative dentistry, fundamentally altering and literally transforming our field with significantly less invasive, more esthetic, and longer-lasting dental restorations,” says Dr. Blatz. “In addition, adhesive technologies and resin bonding have vastly expanded clinical treatment options and become key elements of almost every specialty area in modern dentistry.”

A total of 107 peer-reviewed scientific and clinical poster presentations on all aspects of adhesive dentistry were also part of the Congress, with scientific awards presented for the winning posters selected by members of the IAD Scientific Advisory Board (see abstracts of the three winning poster presentations, page 49–50).

“Complementing information shared on the main podium, these presentations were invaluable for clinicians and researchers to get the latest scientific information and to gauge current clinical and research trends,” notes Dr. Blatz.

The complete proceedings of the Congress and the abstracts accepted for presentation at the IAD are scheduled for publication in a special supplement with the November 2013 issue of The Compendium of Continuing Education in Dentistry.

The gathering also offered a forum for the founding meeting of The International Academy for Adhesive Dentistry, a new international organization and information platform to foster the benefits of adhesive and minimally invasive dentistry among researchers, dentist, dental students, the dental industry, and patients.

“Following a strong tradition of previous IAD meetings held in Japan, China, and Korea, the 5th IAD was an incredible success, and the wealth of knowledge and ideas shared during the meeting was tremendous,” says Dr. Blatz. “The fast-paced clinical improvements, scientific discoveries, and industry developments in adhesive dentistry, as impressively displayed during the Congress, are simply fascinating. We are just beginning to understand the impact they will have on the future of our profession.”

The program sponsors included Kuraray; Shofu; 3M ESPE; Dentsply-Caulk; GC Corporation; Sun Medical Co.; BISCO Dental Products, Inc.; Ivoclar Vivadent, Inc.; Tokuyama Dental Corporation; DMG Dental Material Gesellschaft mbH; Ultradent; Danville Materials; and GlasSpan; with publishing partners Aegis Publications LLC and Quintessence Publishing Co. Inc.
IAD SELECTED ABSTRACTS

Following are the abstracts of the three winning poster presentations from the 5th International Congress on Adhesive Dentistry (IAD), selected by members of the IAD Scientific Advisory Board.

Non-destructive Non-staining 3D Analysis of Marginal and Internal Microgaps

Sadr A., Shimada Y., Bista B., Bakhsh T.A., Sumi Y., Tagami J.

1Tokyo Medical and Dental University, Japan;
2National Center for Geriatrics and Gerontology, Japan

The objective of this work was to (3D) visualize marginal and internal gaps with different bonding agents using optical coherence tomography (OCT). Tapered cylindrical cavities (3 mm in diameter and 2 mm in depth) were prepared on flattened occlusal surfaces of molars and treated with either the two-step self-etch adhesive Clearfil SE Bond (CSE, Kuraray) or one of the all-in-one adhesives Clearfil S3 Bond Plus (S3P, Kuraray), G-aenial Bond (GCB, GC), or Xeno V (XNV, Dentsply).

After bonding agent application, the preparations were bulk-filled with a low-viscosity composite (Estelite Flow Quick, Tokuyama). After 24 h, the specimens were scanned using swept-source dental OCT (Prototype-II, Panasonic Health Care). 3D image segmentation was performed in Avizo software (VSG). Depth-dependent interfacial binary thresholds were defined to overcome OCT signal attenuation while detecting the defects.

Quantitative 3D comparisons were performed by calculating the proportion of sealed interface. Enamel interfacial microgaps were observed in the form of detached areas extending from external margins towards internal walls that only occasionally continued into dentin walls.

The majority of dentin microgaps were detected as interconnected areas of debonding at the pulp floor extending towards the bottom third of the walls. These areas were rarely a continuation of the external marginal gaps. Smaller isolated patches of interfacial defects were observed less frequently throughout the dentin interface.

Based on the sealed area, the results suggest the following ranking of bonding agents: CSE=S3P>GCB>XNV. Cross-sectional microscopy showed adhesive-composite detachment at the bottom with all-in-one adhesives. 3D analysis of microgaps without dye penetration suggests that debonding of external margins and gaps at the pulpal floor under high-C factor occurred independently.

Some all-in-one adhesives showed short-term results comparable to the gold-standard two-step self-etch system. OCT allows for non-destructive evaluation of marginal and internal microgaps with a potential application in clinical trials.

Commentary and clinical relevance: Optical coherence tomography (OCT) has exhibited a unique capability for time-resolved analysis of defect formation in dental restorative composites during and after placement and polymerization. The non-destructive testing methodology is based on the optical contrast between the media filling the defects and the surrounding biomaterial or tissue which results in a detectable reflectivity signal peak. The technical evolution of this methodology has now enabled 3D visualization of voids and microgaps without the need for a staining agent or dye penetration that are required in conventional microleakage studies.

With OTC, marginal integrity can even be assessed clinically for existing restorations. Therefore, the results are not only important for research in adhesive dentistry to answer questions about polymerization shrinkage stress and adhesion, but the goal is to allow dentists to have access to this revolutionary technology chair-side for an objective and quick evaluation of marginal integrity and internal adaptation of existing resin-based restorations in clinics.
IAD SELECTED ABSTRACTS

QCM-D Analysis of Chemical Adsorption of Functional-monomer with HAp Sensor
Takagaki T., Nikaido T., Matsui N., Sato T., Tagami J. Tokyo Medical and Dental University, Japan

Previous reports suggest that the functional monomer 10-methacryloxydecyl dihydrogen phosphate (MDP) has the ability to chemically bind to hydroxyapatite (HAp). This study investigated the chemical adsorption of four different functional monomers on HAp. Quartz crystal microbalance with dissipation (QCM-D, Q-Sense) was used to measure the amount of functional monomer adsorbed on the HAp sensor in real time.

Four different functional monomer solutions containing 0.1% functional monomer (MDP, 4-META, GPDM or Phenyl-P), 2% ethanol and 8 mM HEPES were prepared (pH adjusted to 7.0 with NaOH). Frequency change and the shift of energy dissipation were recorded at a flow rate of 1 ml/min. The QCM-D chamber and liquid samples were temperature-stabilized to 37.0±0.1 °C.

Each of the four functional monomer solutions was injected after frequency and dissipation became stable with the control solution without functional monomer. After the reaction was completed, the control solution was again injected to wash the unreacted functional monomer on the HAp surface. Immediately after injection of the functional monomer solutions, the HAp-sensor frequency dropped significantly in all the groups. In the MDP group, along with the frequency drop, energy dissipation shifted sharply and even after the wash with the control solution. The frequency shift was leveled at a fixed position.

Frequency change and the shift of energy dissipation were material-dependent and depended on the design of the monomer structures. The adsorption behaviors of the functional monomers on HAp varied depending on the molecular structure. The chemical adsorption of chemical monomers on HAp, particularly MDP, may potentially improve the bonding interface and reduce the risk of secondary caries.

Monomers Interaction to Collagen Studied by Saturation Transfer Difference NMR
Hiraishi N., Otsuki M., Tagami J. Tokyo Medical and Dental University Graduate School, Japan

The interaction of adhesive monomers with collagen is not well understood at a molecular/atomic level. The saturation transfer difference NMR spectroscopy is a powerful method in drug delivery studies for screening ligands for their binding to proteins and to determine the ligand binding epitopes. The objective of this study was to examine the molecular/atomic level interactions of dental resin monomers with collagen model.

Saturation transfer difference NMR experiments were performed to investigate the binding interaction of three adhesive monomers: 2-Hydroxyethyl methacrylate (HEMA), 4-methacryloyloxyethyl trimellitate anhydride (4-META) and 10-methacryloyloxydecyl dihydrogenphosphate (MDP), with atelocollagen as a triple-helical peptide model. The ligands HEMA, 4-META and MDP were dissolved in deuterated dimethyl sulfoxide (d6-DMSO) to 20 mM and each one was added to the atelocollagen solution. Final concentration for saturation transfer difference NMR measurement was 4 mM. NMR experiments were performed at 298 K on 600 MHz and 800 MHz spectrometers equipped with a cryogenic probe (Bruker BioSpin Corporation). When the saturation transfer difference effect was detected, its epitope mapping of ligands binding to atelocollagen was obtained by normalizing the largest value to 100%. High saturation transfer difference intensities were detected on the protons in MDP, whereas they were not detected for HEMA and 4-META. The STD epitope mapping revealed that the intense saturation transfer difference signals were primarily associated with the aliphatic region in MDP.

The results imply that MDP has a relatively stable interaction with the collagen, because of the hydrophobic interactions between the hydrophobic MDP moieties and the collagen surface. HEMA and 4-META have not such hydrophobic regions and no intense saturation transfer difference signals were observed. Hydrophobic moieties allow the MDP monomer to form the monomer-collagen aggregate and may control collagen degradation, which accounts for the stable property of hybrid layers.
First Penn Periodontal Conference Exceeds Expectations

ON JUNE 23-28, 2013, Penn Dental Medicine presented its inaugural Penn Periodontal Conference, which drew more than 200 attendees from across the country and around the world. Interest was so great that the conference, originally scheduled to be held at the dental school, was moved to the Annenberg Center for the Performing Arts on Penn’s campus to accommodate more participants. The scientific gathering was a success on multiple levels, says Morton Amsterdam Dean Denis Kinane, who organized and hosted the event with Dr. Dana Graves, Professor, Department of Periodontics, and Vice Dean for Research and Scholarship.

“This was a conference that was timely and much needed, and had an impact that greatly exceeded expectations,” says Dean Kinane. “Our aim of encouraging a large body of both young and experienced dental and basic science researchers was admirably achieved. In addition, the impact on the discipline is already being felt in terms of new projects and publications.”

The conference featured presentations by leading researchers on the latest findings in periodontology, concentrating on four main topics: inflammation, microbiology, periodontal regeneration and repair, and the oral-systemic health connection. Other areas of discussion included innate and adaptive immunity, bone remodeling, oral medicine, disease specificity, epigenetics, stem cells, and clinical microbiology. Highlights included a keynote address by Dr. E. John Wherry, Director of Immunology and Associate Professor, Department of Microbiology, at Penn’s Perelman School of Medicine, titled “Altered Immunity when Pathogens Persist.” Invited speakers came from the United States, Europe, Asia, and South America. See selected abstracts on pages 52–53 for a flavor of the topics and research projects that were presented.

FILLING A VOID IN PERIODONTAL RESEARCH

In the past, explains Dr. Graves, those at the forefront of periodontal research attended the Gordon Conference on Periodontal Diseases, which is no longer held. “There was a need for a new, broad-based conference that explored the basic sciences related to periodontal disease, etiology, and treatment,” he says, and Penn Dental Medicine was eager to take the lead in filling that void.

“Our goal was to create a forum for investigators to meet, hear presentations by leading researchers in different fields of periodontology and to discuss research projects,” he says. The scientific program was structured to encourage interaction among participants. Presentations were scheduled in the morning and evenings so that the afternoons were free for attendees to talk about their research projects and attend the poster sessions. A total of 69 posters were presented.

Dr. Graves believes the success of the conference is due in large part to the internationally known, highly respected presenters, who drew a large audience throughout the weeklong meeting. “The response was overwhelmingly positive because of the quality of the speakers,” he says, “and also because the University provided such a rich environment for an international conference of this caliber.”

Adds Dean Kinane, “In less than two years, we plan to rekindle this wonderfully exciting conference. We hope it will continue to stoke the fires of high quality periodontal research and serve this discipline well into the future.”
**Detection of Undiagnosed Diabetes in the Dental Setting**

*By Evie Lalla, DDS, MS, Professor of Dental Medicine, Division of Periodontics, Section of Oral and Diagnostic Sciences, Columbia University College of Dental Medicine*

Type 2 diabetes often remains undiagnosed. Early identification, diagnosis, and treatment can limit the disease’s many serious oral and systemic complications and improve health outcomes. The purpose of the work presented was to evaluate approaches to identification of undiagnosed diabetes and prediabetes in dental patients and to assess outcomes at six months in those identified with hyperglycemia.

In total, 1,097 new dental patients who presented for care at Columbia with a self-reported risk factor for diabetes completed the study. All eventually received a diagnostic blood test to determine their actual diabetic status. The presence of ≥ 26% teeth with deep pockets or ≥ 4 missing teeth correctly identified 75% of prediabetic or diabetic individuals. The addition of a fingerstick blood test (HbA1c ≥ 5.7%) as part of the screening increased correct identification to 90%.

At a six-month follow-up visit, the vast majority of those identified as potentially diabetic or prediabetic in the dental office reported that they had followed our recommendation to visit a physician and had discussed study outcomes. Many reported changing diet and exercise habits. Only a small fraction of the prediabetic individuals progressed, based on a six-month HbA1c test, to or above the diabetes diagnostic cut-off. Almost 2/3 stayed in the prediabetic state and almost 1/3 improved. All diabetic patients had improved HbA1c levels.

This work underscores that dental professionals have the unrealized opportunity to assume an active role in identifying, among their patients who present with diabetes risk factors, those with undiagnosed hyperglycemia, and can have a positive impact on lifestyle and metabolic outcomes in such patients.

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**Modulation of Periodontal Regeneration by Inflammation and Biomechanical Loading**

*By James Deschner, DMD, PhD, Professor and Head of the Clinical Research Unit 208, Experimental Dento-Maxillo-Facial Medicine, University of Bonn*

Regeneration of periodontal tissues remains a major and often unpredictable challenge that may be due to a number of factors such as inflammation and occlusal loading. A better understanding of the interactions of regeneration factors with inflammatory and biomechanical signals may result in more powerful treatment strategies in the future. We therefore examined in vitro whether the response of periodontal ligament (PDL) cells to enamel matrix derivative (EMD) is modulated by inflammation or biomechanical loading.

Our in vitro studies revealed that EMD stimulated the proliferation, osteogenic differentiation, adhesion, wound fill rate as well as the synthesis of growth factors and matrix molecules. However, inflammatory factors or biomechanical loading reduced the beneficial effects of EMD on PDL cells.

Our findings suggest that critical PDL cell functions are reduced in an inflammatory environment and biomechanical loading. Therefore, an efficient anti-infectious and anti-inflammatory periodontal treatment before the application of EMD may be critical to ensure the full regenerative capacity of the periodontal ligament tissue. Furthermore, occlusal loading of EMD-treated teeth, at least immediately following surgery, may be minimized to obtain optimal regenerative healing results.
Molecular Inhibition of Bone Formation by NF-kB
By Cum-Yu Wang, DDS, PhD, Associate Dean of Graduate Studies, Dr. No-Hee Park Endowed Chair in Dentistry, Chair of the Division of Oral Biology and Medicine, UCLA School of Dentistry

The purpose of this work is to investigate whether oral inflammation may inhibit bone formation and mesenchymal stem cell function by activating nuclear factor-kappa B (NF-kB), a master regulator of inflammation and infection. Although it has been long known that pro-inflammatory cytokines from periodontal or periapical diseases inhibit bone formation and repair, the underlying mechanism is not clear. Using a mouse model, our group at UCLA found that inflammatory mediators inhibited bone-forming cell function and bone formation in vivo. In contrast, the inhibition of NF-kB significantly enhanced bone formation.

Mechanistically, we found that NF-kB activation led to the degradation of the key molecules that promoted bone formation. By inhibiting NF-kB with a small molecule inhibitor, we enhanced the function of mesenchymal stem cells, bone regeneration, and bone repair in vivo. Our results suggest that targeting NF-kB may have dual benefits in enhancing bone regeneration and repair and inhibiting oral inflammation and bone loss. This may be important in a number of oral treatments including endodontics, periodontics, and oral surgery.

The Influence of Vitamin D and Parathyroid Hormone on Periodontal Regeneration
By Jill Bashutski, DDS MS, Clinical Assistant Professor, Division of Periodontics, Department of Periodontics and Oral Medicine, University of Michigan School of Dentistry

Teriparatide is a commercially available form of the first 34 amino acids of parathyroid hormone and is FDA approved for the treatment of osteoporosis. It is unique because it promotes bone growth as opposed to most other bone regeneration therapies, which typically prevent bone loss. Regenerating bone around teeth that is lost due to periodontal disease is unpredictable and thus, there is a critical need for the development of new therapies to encourage periodontal regeneration.

Teriparatide is a promising therapeutic candidate since numerous studies have validated its ability to successfully improve bone quality in osteoporotic patients and there are numerous similarities between osteoporosis and periodontitis. A double-masked, placebo-controlled study was conducted in order to evaluate the effects of teriparatide in conjunction with periodontal surgery on craniofacial osseous regeneration in patients with advanced periodontal disease. In this study, 40 adult patients with a severe vertical infrabony defect received an open flap debridement surgical procedure along with daily self-administered injections of teriparatide (20 µg) or placebo control, 1000 mg calcium and 800 IU of Vitamin D for six weeks. Patients were then followed for one year post-operatively.

Teriparatide administration resulted in significantly greater probing depth reduction, clinical attachment gain, and radiographic alveolar bone defect resolution than patients who received placebo, and these results were sustained for one year. The use of a systemic anabolic agent like teriparatide provides an exciting new avenue of therapeutic potential for periodontitis patients.

These findings are significant since this may support the development of a more predictable and less invasive treatment for bone lost due to periodontal disease. Furthermore, the results of this study support the idea that a systemic medication can have positive effects in the oral cavity and so there may be the potential for expanded applications, such as promoting dental implant success or treating other craniofacial defects.
Student Research Day Celebrates Achievement with Poster Presentations

PENN DENTAL MEDICINE’S Student Research Day, held May 9, 2013, was a celebration of the broad range of research projects conducted by Penn Dental Medicine DMD students during the past year. This inaugural event brought together for the first time the work of students who benefit from three of the School’s dynamic curricular opportunities: the Summer Research Program; the School’s honors degree programs in research, community health, and clinical care; and the Bridging the Gaps community externship.

“Each year there is a significant increase in the level of sophistication and attention to detail in the research projects and poster presentations. I believe this is a testament to the quality of the students we are attracting to our programs,” says Dr. Joseph DiRienzo, Assistant Dean for Student Research and Director of the Summer Research Program.

The event, held in the Fonseca Gardens courtyard behind the School’s Robert Schattner Center, centered on a poster session. Students from all three programs presented poster displays on projects conducted throughout the past year and also submitted abstracts of their work, which were included in an abstract booklet (view online at www.dental.upenn.edu/StudentResearchDay2013). A total of 86 posters were presented, including 15 from Summer Research Program participants, 13 from Bridging the Gaps, and 58 from the three honors degree programs combined. Students shared highlights of their projects with fellow students, faculty, and staff.

“Making a poster presentation offers students an experience similar to a professional meeting, which is an important part of all of these programs, so we were pleased to offer all of our student researchers this opportunity,” says Dr. Kathleen Boesze-Battaglia, Director of the research honors program.

Previously, students in the honors degree programs presented their projects at a separate event from the Summer Research Program and Bridging the Gaps participants. Having work from all three programs presented at one event added depth and breadth to the proceedings, noted Dr. Francis Mante, advisor to the School’s Vernon Brightman Research Society. Board members of the Vernon Brightman Research Society (Penn Dental Medicine’s chapter of the National Student Research Group, a subset of the American Association for Dental Research) helped to organize the day’s program.

The participating students represented programs that enrich and expand the academic opportunities available at Penn Dental Medicine. The Summer Research Program allows students to engage in a basic laboratory or clinical research project full-time during July and August with a faculty preceptor. Bridging the Gaps, also held over the summer, is an interdisciplinary externship program that teams healthcare and social service students from throughout Penn as well as other Philadelphia-area universities to provide services for underserved and economically disadvantaged residents at sites throughout the region. The honors degree program—the newest of the initiatives (entering its fourth year with the 2013-2014 academic year)—enables exceptional students to earn a DMD degree with honors in one of three areas—research, clinical dentistry, and community health.

The posters from the School’s Summer Research Program and Bridging the Gaps were judged by a team of independent faculty members. This year’s winners in clinical and basic science research include the following (read abstracts of their work on page 55):

**SUMMER RESEARCH PROGRAM**
First place: Kang I. Ko (D’15), as the first-place winner, Ko represented Penn Dental Medicine in the ADA/DENTSPLY Student Clinician Research Program at the ADA Annual Session in New Orleans, October 31 – November 3, 2013; Second place: William S. Konicki (D’15), as the second-place winner, Konicki presented his poster at the Hinman Student Research Symposium in Memphis, Tenn., October 25-27, 2013; and Third place: Snow Feng (C’14).

**BRIDGING THE GAPS**
First place: Wenting Guo (D’15); Second place: Eunice Chay (D’15); and Third place: Laurel Lee (D’15).

“The School of Dental Medicine research community is proud to have such accomplished students representing our research enterprise on Student Research Day and at national meetings,” adds Dr. DiRienzo.
Diabetes Reduces Mesenchymal Stem Cells Through Altering Apoptosis and Proliferation

Kang I. Ko (D’15) was awarded first place for this study, conducted with faculty preceptor, Dr. Dana Graves, Professor, Department of Periodontics

This work tested the hypothesis that diabetes reduces the number of mesenchymal stem cells and that this occurs through a mechanism involving diabetes-enhanced inflammation. Mesenchymal stem cells are multi-potent stem cells that can differentiate into osteoblasts, hence, they are indispensable to bone formation. It is well known that bone formation is reduced by diabetes, but the reasons for this have not been conclusively established.

Diabetic mice had a 40% reduction in mesenchymal stem cells. This was due to two primary causes: significantly increased cell death and significantly reduced mesenchymal stem cell proliferation. When inflammation was reduced by treatment with a TNF blocker, the mesenchymal stem cell number was restored to normal levels.

This study revealed that the inflammatory environment, which is enhanced by diabetes, adversely affects mesenchymal stem cells by increasing their cell death and reducing their proliferation. This may indicate that anti-inflammatory treatment could enhance bone formation in diabetics by preserving mesenchymal stem cells.

Inheritance of Amelogenesis Imperfecta and Modifier Genes in Transgenic Murine Models

William Konicki (D’15) was awarded second place for this study, conducted with faculty preceptor, Dr. Carolyn W. Gibson, Professor, Department of Anatomy & Cell Biology

Transgenic mice of varying backgrounds were used to simulate genetic diversity in human families affected by X-linked amelogenesis imperfecta (AI). It was hypothesized that much of the noted variation in clinical phenotype between members of the same sibing group is due to individuals’ unique complements of modifier genes rather than variations in the mutated alleles themselves. We predicted that crossing mouse backgrounds could generate something akin to what is seen in families’ clinical presentation.

This work has the possibility of contributing to the growing body of knowledge of how X-linked amelogenesis imperfecta is clinically manifested once inherited. Furthermore, it would investigate the appropriateness of mouse models for this disease and explore various methods of describing the severity of AI in the models. Various methods including visual inspection, immunohistochemistry, image analysis, and microCT were used to show that mouse strains with induced knockout mutations to Amelx (gene coding for amelogenin) had the smallest volumes and qualities of enamel. Mice with a mixed background displayed phenotypes somewhere between our positive and negative controls. In addition, the C57BL/6 strain of mice containing knockout mutations appeared to have diminished densities of both enamel and dentin. The wild-type mouse strain FVB, often chosen for transgenic experiments, displayed a short, richly pigmented and inconsistently dense dentition.

The results of these experiments indicated that the experimental model of AI was legitimate. The expected trend of mixed-background mice displaying less severe phenotypes, compared to those of a single background, correlates clinically to family members’ varying penetrance of modifier gene complements resulting in different phenotypes even when the X-linked mutation to amelogenin is shared by all. The unexpected hypodensity seen in the dentin of the KO C57BL/6 mouse strain may hint at an unexplored link between amelogenesis and dentinogenesis. Amelogenin is expressed in dentin, though at one thousandth of the level found in enamel. The data obtained with the FVB mice identifies what might be a challenge for workers using this mouse in transgenic experiments. The strain appears to have several inherent idiosyncrasies that previous studies may have taken for granted.

This work generated a successful mouse model of x-linked amelogenesis imperfecta, provided inroads in identifying modifying genes affecting expression of the disease, raised questions about the interplay between amelogenesis and dentinogenesis in a certain commercial strain of mouse, and highlighted a few developmental quirks of one strain that may confound the outcomes of other studies.

The Effect of Musashi Expression on the Self-Renewal and Differentiation of Mesenchymal Stem Cells

Snow Feng (D’15) was awarded third place for this study, conducted with faculty preceptor, Dr. Christopher Lengner, Assistant Professor, Department of Animal Biology, School of Veterinary Medicine

The effect of Musashi (Msi) gene expression on stem cell differentiation and proliferation had never been studied in mesenchymal stem cells (MSC). The purpose of the research was to identify whether Msi induces differentiation or maintenance of MSCs. Msi is a translational regulator of cell fate and has been demonstrated in many stem cell compartments and aggressive tumors but it has never been studied in MSC.

The effect of Musashi (Msi) gene expression on stem cell differentiation and proliferation had never been studied in mesenchymal stem cells (MSC). The purpose of the research was to identify whether Msi induces differentiation or maintenance of MSCs. Msi is a translational regulator of cell fate and has been demonstrated in many stem cell compartments and aggressive tumors but it has never been studied in MSC.

MSC have the ability to differentiate into osteoblasts, chondrocytes and adipocytes. Therefore, they serve as an important reservoir for self repair of bone tissue. Understanding the mechanism Msi plays in MSC differentiation will provide greater insight into connective tissue regeneration. Manipulation of Msi activity may enable strategies for expansion of undifferentiated MSC in vitro.
There were no obvious differences between the number of colonies formed by Msi-deleted cells compared to that of a wild-type control. Reduced colony formation was observed by Msi+/doxycycline resistant cells compared to that of the control. These results were completely opposite those obtained with intestinal stem cells. There were no obvious differences in colony number between Msi+/tamoxifen resistant and control cells. Reduced colony formation was observed with Msi-induced cells compared to that of the control cells. This observation is completely opposite of what was observed with intestinal stem cells. There were no obvious differences in colony number of Msi-deleted cells compared to that of control cells.

At the histological level, both Msi-induced and -deleted cells were able to differentiate into the tri-lineage when cultured in specific differentiation media and no differences were observed compared to the control cells. Understanding the roles that Msi plays in MSC differentiation will increase understanding of connective tissue regeneration and improve methods for expansion of undifferentiated MSC in vitro.

BRIDGING THE GAPS PROJECT WINNERS

The following abstracts summarize the experiences of three Student Research Day prizewinners in their community externships through the Bridging the Gaps program.

**Working for Change**

Wenting Guo (D’15) was awarded first prize for her project at The College of Physicians of Philadelphia, with Caroline Fortin, Penn’s School of Social Policy and Practice

Guo and Fortin worked with the College of Physicians of Philadelphia staff and 13 high school students in the Teva Summer Internship Program, which focused on sexually transmitted disease and violence education and prevention in Philadelphia communities. The program’s activities included workshops; writing and filming public service announcements about HPV; field trips to Children’s Hospital of Philadelphia, local gardens and community building projects; and resource gathering. Guo and Fortin assisted in the various program activities, compiled lessons on STIs, developed pre- and post-evaluations of the program, chaperoned trips, and hosted lunchtime discussions.

**Sudanese Women’s Group**

Eunice Chay (D’15) was awarded second place for her project at HIAS and Council Migration Service of Philadelphia, with Ijeoma Chinwuba, Penn’s Perelman School of Medicine

Chay and Chinwuba facilitated a biweekly women’s group for recently resettled Sudanese refugee women living in Northeast Philadelphia. Each meeting focused on a particular health topic or life skill, such as family planning, nutrition, oral health, and financial literacy. Learning activities took place in clients’ homes as well as at various sites in the community, such as health clinics and grocery stores. Guest speakers were invited to present on pregnancy, personal safety and women’s health. Individually, Chay assessed the need for improved access to pediatric dental care by identifying community resources and patterns of utilization. In addition, both Chay and Chinwuba served as liaisons between patients and medical and dental clinics, as well as between the clinics and HIAS, by acting as patient escorts, scheduling appointments, securing interpretation services, and communicating messages and health information between patients and their caseworkers at HIAS.

**Laying Down Roots in West Philadelphia**

Laurel Lee (D’15) was awarded third place for her project with Earth’s Keepers, Inc. (EK), an urban farm in Southwest Philadelphia, with Nicole Oakman, Penn’s Perelman School of Medicine

Lee and Oakman worked with high school students at Earth’s Keepers (EK) to grow, harvest, and sell fresh organic produce. They also led discussions and hands-on exercises related to nutrition, food sovereignty, health, cooking, and guidance counseling. The interns’ work culminated in the production of a colorful mural on the side of the garden’s greenhouse. Lee noted, “Seeing the interest people in the community have to come to the farm to volunteer, ask questions, or purchase fresh produce reinforces my belief that food can bind a community, and reaffirms the importance of having local farms within otherwise food-poor neighborhoods.”
ON MAY 31, 2013, Penn Dental Medicine held its annual faculty research retreat, bringing together the School’s basic science and clinical faculty, as well as postdoctoral fellows and students, for a day of exchange with colleagues across disciplines. The meeting, held this year at the Hill Pavilion within Penn’s School of Veterinary Medicine, reflects the quality and diversity of research carried out at the School, and provides opportunities for information sharing, networking, and discussions on future collaborations.

“The goal of our annual retreat is to create a forum in which our basic and clinical science faculty can take time out together to share their latest research activities with one another,” says Dr. Ellis Golub, Professor, Department of Biochemistry, and Chair of the Research Retreat Organizing Committee.

In preparation for the retreat, faculty, postdoctoral fellows, and students are asked to submit abstracts of their research from the past year for consideration by the School’s Faculty Senate Research Committee. This year, from more than 60 abstract submissions, seven faculty projects were selected for the day’s program of presentations and five abstracts from postdoctoral fellows were chosen for oral poster presentations. Poster presentations of many of the faculty research project submissions were also on display for discussion.

Those faculty projects presented included the following (see abstract briefs on several of the research presentations, page 58):

- **Mechanical Signal Transduction Pathways Associated with the Sarcoglycan Complex**, Dr. Elisabeth Barton, Associate Professor, Department of Anatomy & Cell Biology
- **The Role of Genipin, a Phytochemical from the Terpenoid Family, in Osteoblast, Matrix and Mineral Characteristics**, Dr. Patricia Miguez, Assistant Professor, Department of Periodontics
- **A Virally Encoded Small Peptide Regulates the Switch of Kaposi’s Sarcoma-associated Herpesvirus from Latent to Lytic Life Cycle**, Dr. Yan Yuan, Professor, Department of Microbiology
- **Sensory Feedback for Dental Caries Detection and Removal**, Dr. Margrit P. Maggio, Assistant Professor of Clinical Restorative Dentistry
- **Antimicrobial peptides activate human mast cells via MAS-Related gene (MrgX2 and MrgX3): Cross-regulation by LPS**, Dr. Hydar Ali, Professor, Department of Pathology
- **Classification and Treatment of Dental Implant Postsurgical Pain Employing Intranasal Ketorolac**, Elliot V. Hersh, Professor, Department of Oral & Maxillofacial Surgery/Pharmacology
- **Characterization and Treatment of Dental Implant Postsurgical Pain Employing Intranasal Ketorolac**, Elliot V. Hersh, Professor, Department of Oral & Maxillofacial Surgery/Pharmacology

In addition to these and the oral presentations by postdoctoral students (see the winning student abstracts, page 59), the retreat featured an annual tradition, The Joseph L. Rabinovitz Memorial Lecture, presented this year by Dr. Ali Naji, M.D., PhD., J. William White Professor of Surgery and Director, Kidney/Pancreas Transplant Programs, Hospital of the University of Pennsylvania. Dr. Naji’s lecture focused on his work in developing procedures for pancreas transplants in the treatment of Type I diabetes. A key part of this work involves developing protocols for immune suppression which will protect the transplanted tissue from the host’s immune system without depriving the recipient of the ability to fight off infections.

“The retreat was inspiring and edifying for all attendees,” says Dr. Golub. “Each year, the research shared at our retreat grows in depth and diversity.”
SELECTED FACULTY RETREAT ABSTRACTS
Following are highlights of several of the research projects presented at the School’s annual faculty research retreat, held May 31, 2013.

Characterization and Treatment of Dental Implant Postsurgical Pain Employing Intranasal Ketorolac
Elliot V. Hersh, Professor, Department of Oral & Maxillofacial Surgery/Pharmacology

The purpose of this project was to characterize the nature of postsurgical pain following the placement of one to three implants. A secondary goal was to explore the analgesic efficacy and tolerability of intranasal ketorolac in this patient population. Twenty-eight patients 18-64 years of age who required the surgical placement of one to three dental implants and signed an IRB-approved informed consent participated in this open-label study.

Following surgery, patients self-administered 31.5 mg ketorolac nasal spray upon experiencing pain of at least a moderate intensity (≥40 mm on a 100 mm VAS). Pain intensity and pain relief were assessed for six hours, as were the onsets of first perceptible and meaningful relief. Patients were transitioned to a multi-dose take-home phase, administered the drug every six hours as needed and recorded dose frequency and adverse events over five days.

The results were as follows: Ninety-two percent (23/25) of subjects rated intranasal ketorolac as very good or excellent. Eighty percent (20/25) of subjects required additional doses of intranasal ketorolac and/or rescue medication at home and 54% (13/25) required dosing on an as-needed basis for three days. The results were as follows: Ninety-two percent (23/25) of subjects rated intranasal ketorolac as very good or excellent. Eighty percent (20/25) of subjects required additional doses of intranasal ketorolac and/or rescue medication at home and 54% (13/25) required dosing on an as-needed basis for three days.

Mechanical Signal Transduction Pathways Associated with the Sarcoglycan Complex
Dr. Elisabeth Barton, Associate Professor, Department of Anatomy & Cell Biology

Muscles respond to changes in mechanical load, and can respond by altering expression of genes to adapt properties to use needs. The sarcoglycan complex, which is lost from the muscle membrane in several Limb Girdle muscular dystrophies and Duchenne muscular dystrophy, is important for sensing muscle load.

The goal of this study was to identify the key steps in the signaling process associated with mechanical loading and to determine how signal transduction is altered in the absence of the sarcoglycan complex. Isolated extensor digitorum longus (EDL) muscles were subjected to 30 minutes of passive stretch (10% increase in resting length) or no stretch at all, and then rapidly frozen for biochemical analysis. Without stretch, the muscles from gamma-sarcoglycan null mice had elevated two important signaling proteins compared to unstretched wildtype muscles.

Passive stretch invoked increases in these two proteins in wildtype muscles, but in muscles from gamma-sarcoglycan null mice had a blunted response to passive stretch. Thus, the sarcoglycan complex appears to be important for appropriate mechanical signal transduction, and that impaired mechanical signal transduction underlies a significant part of the pathology associated with loss of sarcoglycans in the muscular dystrophies.

A Virally Encoded Small Peptide Regulates the Switch of Kaposi’s Sarcoma-Associated Herpesvirus from Latent to Lytic Life Cycle
Dr. Yan Yuan, Professor, Department of Microbiology

One key feature of Herpes viruses is they can remain dormant in a human host for many years, and then can become activated to the pathologic, lytic phase. How this transition is controlled is not well understood. Dr. Yuan presented evidence of a novel control mechanism which appears to function in Kaposi’s Sarcoma-Associated Herpesvirus (KSHV). It was previously known that one gene in the KSHV genome encoded the replication and transcription activator (RTA) that controls the switch of the virus between latent and lytic life cycle.

The present study found that a small RNA transcribed from the opposite DNA strand from that which encodes RTA encodes a small polypeptide which appears to bind to and stabilize RTA. As a consequence, expression of this small peptide facilitates KSHV gene expression and lytic replication. This finding revealed a novel mechanism of gene regulation in viral life cycle and provided a new paradigm for the biology of (apparently) noncoding RNAs.
RESEARCH RETREAT POSTDOC WINNING ABSTRACTS

Following are abstracts of the winning poster presentations by postdoctoral students at the School’s faculty research retreat, May 31, 2013.

The Role of MMP-13 in Skeletal Muscle Regeneration
Lucas R. Smith was awarded first place for this project, conducted in the lab of Dr. Elisabeth R. Barton, Associate Professor, Department of Anatomy & Cell Biology

Skeletal muscle requires timely expression of genes for satellite cell-based regeneration in coordination with extracellular matrix (ECM) remodeling. The ECM of skeletal muscle becomes pathologic in many muscle conditions, including muscular dystrophies and severe injury. Matrix Metalloproteinases (MMPs) are a family of enzymes responsible for breakdown of ECM components. We have identified one member of the MMP gene family, MMP13, which degrades fibrillar collagen during the resolution of muscle damage. To determine the timecourse of MMP expression and activity in regenerating muscle, cardiotoxin (CTX) injections were used to create reproducible muscle regeneration in adult mice.

Our results showed MMP13 expression is significantly increased in regenerating muscle. In unchallenged muscle, MMP13 null mice have no significant difference in histology or in active and passive mechanical properties compared to muscles of wild type mice. To determine the necessity of MMP13 expression in regeneration we injected CTX into MMP13 null mice and compared the resolution of damage to wild-type mice. Our results show trends for reduced muscle fiber size and vascularity of MMP13 null mice during regeneration following CTX injection. We compared fibrosis formation using sirius red staining and found that muscles from MMP13 null mice have similar collagen area, but that collagen is in a looser state compared to those from wildtype mice. Because satellite cells are an important component of muscle repair, we cultured primary myoblast (satellite cells) from MMP13 null and wild-type mice and found no change in proliferation, but reduced migration rates in the MMP13 null cultures. These data show that mice lacking MMP13 have decreased regenerative capacity within the muscle.

Understanding the role of MMP13 in muscle regeneration and fibrosis resolution may serve as a new therapy for muscle impairments that occur in nearly all muscle disorders.

FOXO1 Orchestrates the Wound Healing Response through Regulation of TGF-1 and Prevention of Oxidative Stress
Bhaskar Ponugoti was awarded second place for this project, conducted in the lab of Dr. Dana Graves, Professor, Department of Periodontics

Keratinocyte mobilization is a critical aspect of wound re-epithelialization, but the mechanisms that control its precise regulation remain poorly understood. We set out to test the hypothesis that FOXO1 has a negative effect on healing because of its capacity to inhibit proliferation and promote apoptosis.

We investigated our hypothesis by generating keratinocyte-specific FOXO1-deficient mice in vivo and by RNAi in primary cultures of dermal keratinocytes in vitro. Contrary to expectations FOXO1 deletion in keratinocytes delayed wound closure in vivo (P<0.05). Further analyses revealed that FOXO1 deletion reduced expression of the keratinocyte migration marker uPAR and increased cell death (P<0.05). Moreover, we show that decreased keratinocyte migration was due to a large decrease in TGF-1 expression while increased apoptosis was due a substantial increase oxidative stress when FOXO1 was deleted in vivo (P<0.05). To test whether the control of TGF-1 was functionally important, wounds in FOXO1 deleted mice were treated with recombinant TGF-1 and rescued the delayed wound healing phenotype. Lastly, we determined that FOXO1 directly regulated TGF-1 levels in vitro (P<0.05).

Our studies identify a novel function for FOXO1 in coordinating the response of keratinocytes to wounding through upregulation of TGF-1 and other factors needed for keratinocyte migration and protection against oxidative stress that inhibits migration. Treatment with FOXO1 agonists may represent a potential therapeutic target for the treatment of tissue repair by mobilizing keratinocytes for rapid wound epithelialization.
The Impact of Scholarly Activity

**AVERAGE H INDEX FOR DEPARTMENT FACULTY**

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*The h index indicates the quantity and quality of the researcher’s publications during their career and was developed to measure the impact of an individual’s scientific research output. The higher the number the better. Older researchers with longer careers will always have more than new or younger researchers.*

These lists were generated using the Scopus database, and the Author IDs found within that system. Articles published in journals that are not indexed in Scopus, are not included in the calculation. The articles that were included were published between January 2008 and December 2012 and the h index calculations were done in early 2013.

“The Penn Dental Medicine research enterprise continues to have a far-reaching impact across disciplines as evidenced by the number and frequency of faculty publications cited in the scholarship of other researchers. The impact of the research in the clinical departments demonstrates the breadth of research activities and is an important part of the School’s scholarship.”

—DR. DANA GRAVES, VICE DEAN FOR RESEARCH & SCHOLARSHIP

**TOP 20 FACULTY SCHOLARLY OUTPUT BY H INDEX & NUMBER OF PUBLICATIONS**

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