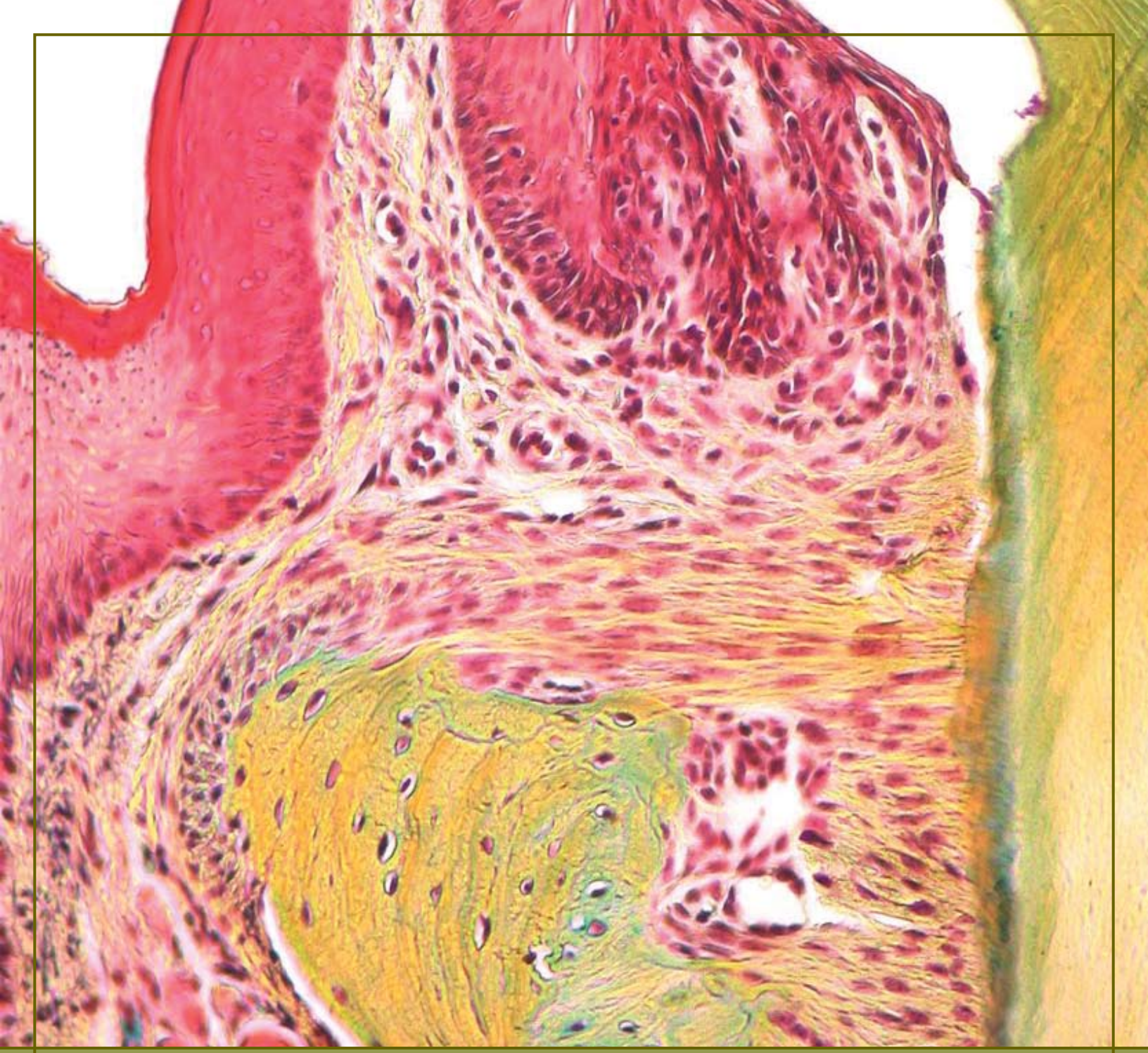


UBC FACULTY OF DENTISTRY

Research Day

JANUARY 29, 2008

> “To advance oral health through outstanding education, research, and community service.”

UBC FACULTY OF DENTISTRY MISSION STATEMENT

Table of Contents

MESSAGE FROM THE DEAN ›

Welcome to the first Research Day for the University of British Columbia Faculty of Dentistry. A yearly event to highlight the research accomplishments of the faculty has been one of our goals for several years. We are pleased that in 2008 we have achieved this objective and organized our first annual research event.

Research discovery is one of the five pillars of UBC's TREK 2010 vision and UBC is recognized internationally as an outstanding research-intensive university. The Faculty of Dentistry has an exceptional history of research achievement directly addressing the TREK 2010 objectives. One of the strategic objectives essential to our planning for the next five years is to amplify our research productivity. Research Day provides a forum to highlight our current research accomplishments and begin to define the future opportunities for new investigation.

Research in the health sciences is frequently initiated by a question derived from some aspect related to a patient presentation. Our curriculum is organized in a way to facilitate asking or eliciting these types of questions about patient presentations and empowering students to find the information necessary to make an evidence-based decision. The Research Day program is organized to use these types of patient-based questions to demonstrate the origin of basic biomedical research projects and the application of their findings through translation to new clinical therapies. Clinical problems or questions related to loss of teeth, loss of bone, and replacement of the dentition occupy a majority of the practice experience for dentists. These situations can present significant challenges for both the patient and the dentist. Considerable progress has been made in the past few years to develop new clinical approaches based on scientific discovery to manage these clinical problems in the best possible way. Thus, clinical questions arising from the loss of teeth, bone and their replacement have been selected as the focus for the presentations on this first Research Day.

The term "Bench to Bedside" has often been used to describe the necessary translation of basic research findings to patient applications. Examples of that process, however, have not often been presented in a comprehensive fashion. The goal of today's program is to demonstrate how the Faculty of Dentistry is making contributions in basic biomedical research that are leading to improved treatment options for patients.

The Faculty of Dentistry has established several basic biomedical research themes that have achieved international recognition. It is significant that the Faculty of Dentistry has two Tier I Canada Research Chairs, Professors Dieter Brömme and Christopher Overall, and their research achievements in basic processes of tissue degradation and bone resorption will open the day's program and highlight significant problems in oral health care. It is also significant that one of our alumni, Dr. Sonia Leziy, is an internationally-recognized expert in the clinical application of implants and she will close the program with the ultimate application of basic research discovery—new and improved approaches to patient care. Through this Research Day program, it should become apparent that basic research is a critical element for the improvement of patient care and that the UBC Faculty of Dentistry plays a leading role in these advances.

I would like to thank the outstanding set of speakers who have agreed to participate in this inaugural Research Day and to thank the members of the Research Day organizing committee, Ingrid Ellis, Viki Koulouris, Hannu Larjava, Ed Putnins, Laura Rosenthal, and Andrea Wink, who contributed so much to make this event a success.

I hope you enjoy the program. I know that I am looking forward to an exciting day of scientific advances leading to new and improved patient care applications.

Thank you for your participation.

Charles Shuler, D.M.D., Ph.D.
Professor and Dean, UBC Faculty of Dentistry

MESSAGE FROM THE ASSOCIATE DEAN OF RESEARCH › I would also like to welcome you all to the first Research Day of the Faculty of Dentistry at the University of British Columbia. I am confident that this new tradition will continue in the foreseeable future, exposing our students, staff members, part-time instructors and eventually the public to the variety of research topics addressed in our faculty.

Today, it is no longer acceptable to contain research and the researchers to silos with no information leaking to the outside world. This has become a mandatory process as our granting agencies require researchers to publicize their research findings. In addition, there is a wide lag between basic science findings and their applications to clinical practice.

We are making a conscientious effort to get the research that is performed in our faculty to the public domain. Research Day is one of the many ways we are planning to tackle this task.

The UBC Faculty of Dentistry Research Day is theme-based, focusing on one theme at a time and the theme will change every year, exposing the audience to new faces and new research and clinical problems that our researchers are trying to address. This year's theme focuses on implant therapy at a very broad level and combines information from basic science of tissue degradation and cell interactions with implants to clinical applications.

During the break in the middle of the day, you are welcome to visit the poster session where our undergraduate and graduate students, post-doctoral fellows and faculty members will present their research projects. During the poster session, you will be exposed to a larger variety of research topics investigated in our Faculty.

The 2008 Research Day theme revolves around clinical problems that Mrs. Istu Te is experiencing. She is attending a dental office and tries to ask many questions to make an informed decision as to how to proceed with her treatment and then improve her quality of life. These questions are highlighted at the beginning of each presentation. Her chief complaint is that she had an old problem with one of her front teeth for many years that recently became acute and caused her to see a dentist; she presented with an abscess. The tooth was pulled and during the tissue healing, the gums (gingiva) collapsed and now she presents with a large gap between her front teeth that needs to be restored.

THE CASE OF MRS. ISTU TE

Case Learning Objectives:

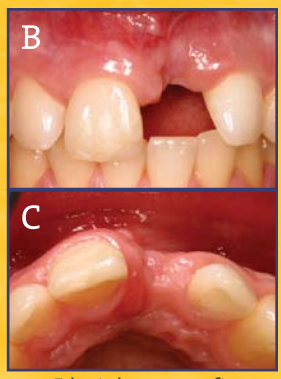
At the end of Research Day, participants are expected to be able to:

- describe the pathophysiology of soft and hard tissue degradation around natural teeth;
- understand the functions of metalloproteinases and cathepsins in the above processes;
- describe the clinical applications of bone augmentation for restoration of the alveolar ridge in implant placement;
- describe how the cells interact with various implant materials and surface topographies;
- explain the indications and limitations of immediate implant placement;
- understand the management of edentulous patients with or without implants;
- recognize the importance of proper management of anterior implant esthetics; and
- understand the principles of successful implant therapy at the anterior esthetic zone.

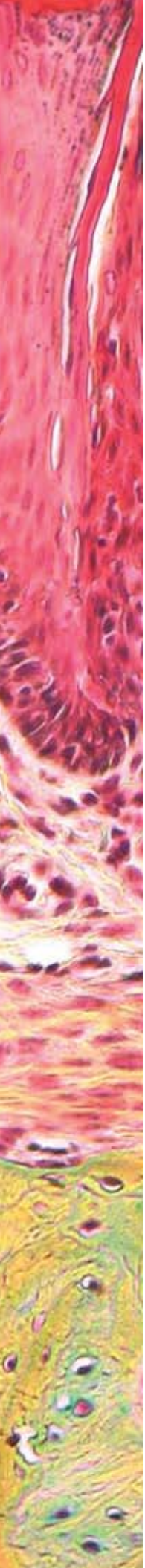
I hope you enjoy this Research Day and the Case of Mrs. Istu Te.

Hannu Larjava, D.D.S., Ph.D., Dip. Perio.
Associate Dean of Research and Graduate Studies

A. Endodontic problem with tooth #21 that lead to vertical fracture and hopeless prognosis



B.-C. Edentulous area after extraction of #21



Research Day Schedule

Tuesday, January 29, 2008
at the UBC Student Union Building Ballroom

IMPLANTS: *From basic science of tissue destruction to predictable esthetic implant placement*

7:30 – 8:00	**Registration & Continental Breakfast**
8:00 – 8:15	**Welcome** *Dr. Charles Shuler, Dean*
8:15 – 8:30	Case of 'Istu Te': **"I have a big hole in my gums after the tooth was pulled and cannot smile; why, and what can be done?"** Introduction of the Clinical Case *Dr. Hannu Larjava, Associate Dean of Research and Graduate Studies*
8:30 – 9:00	**"I was told that I lost my gum because of an infected tooth."** New roles for matrix metalloproteinases in controlling inflammation *Dr. Christopher Overall, Canada Research Chair in Metalloproteinase Proteomics & Systems Biology*
9:00 – 9:30	**"I was told that my bone shrunk away after the tooth was pulled."** Basic mechanisms of bone resorption *Dr. Dieter Brömme, Canada Research Chair in Proteases & Diseases*
9:30 – 10:00	**"Can I have implants? How do they interact in my jaw bone?"** Improving the implant surface by controlling cell behaviour using surface topography *Dr. Donald Brunette, Professor of Oral Biology*
10:00 – 10:15	**Coffee Break**
10:15 – 10:45	**"My upper tooth has to be pulled. Can I have an implant placed right away?"** Immediate implant placement in fresh extraction sockets in the esthetic zone *Dr. Tassos Irinakis, Graduate Periodontics Program Director*
10:45 – 11:15	**"What about the big hole? How can a metal root go in and look nice?"** Ridge augmentation *Dr. Ian Matthew, Oral & Maxillofacial Surgery Chair*
11:15 – 12:15	**"Some of my lower teeth are also bad. If I loose them all, can I have implants there as well?"** Managing edentulism with or without implant prostheses *Dr. Joanne Walton, Professor of Prosthodontics* *Dr. Ross Bryant, Assistant Professor of Prosthodontics*
12:15 – 1:45	**Research poster presentations** *by undergraduate students, graduate students, post-doctoral fellows, research associates and faculty members* **[box lunch provided]**
1:45 – 4:30	**"How will these new implants look?"** The science and art of aesthetic implant treatment: A blueprint for success *Dr. Sonia Leziy, Certified Specialist in Periodontics* **[3:15 – 3:30 Break]**
4:30 – 5:00	**Discussion; case wrap-up; poster prize winners** *Dr. Hannu Larjava, Associate Dean of Research and Graduate Studies*

PRESENTERS

Bios and Synopses

- Christopher M. Overall, *B.D.S., B.Sc. (Dent.)(Hons.), M.D.S. Ph.D.*
- Dieter Brömme, *Ph.D.*
- Donald M. Brunette, *Ph.D.*
- Tassos Irinakis, *D.D.S., M.Sc., Dip.Perio, F.R.C.D.(C.)*
- Ian Matthew, *Ph.D., M.Dent.Sc., B.D.S., F.D.S.R.C.S.(Eng.), F.D.S.R.C.S.(Ed.)*
- Joanne N. Walton, *D.D.S., Cert. Pros., F.R.C.D.(C.)*
- Ross Bryant, *D.D.S., Ph.D., F.R.C.D.(C.)*
- Sonia S. Leziy, *D.D.S., Dip.Perio*

CHRISTOPHER M. OVERALL, *B.D.S., B.Sc. (Dent.)(Hons.), M.D.S., Ph.D.*

Dr. Overall is a Professor and Tier 1 Canada Research Chair in Metalloproteinase Proteomics and Systems Biology at the University of British Columbia. He completed his B.D.S., B.Sc. (Dent)(Honours) and Masters degrees at the University of Adelaide, South Australia; his Ph.D. in Biochemistry at the University of Toronto; and was a MRC Centennial Fellow in his post-doctoral work with Dr. Michael Smith Nobel Laureate, Biotechnology Laboratory. He won the CIHR Award for Research Excellence in Oral Health, Institute of Musculoskeletal Health & Arthritis in 2002 and the 2002 CIHR Scientist of the Year, the University of British Columbia Killam Senior Researcher Award (Science) 2005, and was the Chair of the 2003 MMP and the 2010 Protease Gordon Research Conferences. On Sabbatical in 1997-1998 he was a Visiting Scientist at British Biotech Pharmaceuticals, Oxford, UK and in 2004-2005 he was a Visiting Scientist at the Expert Protease Platform, Novartis Pharma, Basel, Switzerland. He is the pioneer of Degradomics, with five Nature Review Papers on this, protease genomics, drug target validation, MMP therapeutics, and substrate discovery and has developed many new quantitative approaches to elucidate the protease and substrate degradomes.

New roles for matrix metalloproteinases in controlling inflammation

We discovered that chemokines are a new class of substrate for matrix metalloproteinases (MMPs) (McQuibban et al 2000, Science 289,1202-1206). Monocyte chemotactic protein-3 (MCP-3) was cleaved by MMP-2 to generate a potent receptor antagonist to block cell responses to a variety of chemokines in vitro. In vivo, this was manifest as a profound reduction in monocyte accumulation and by a 40% reduction in experimental peritonitis. Hence, MMPs also exhibit profound anti-inflammatory properties. We also identified MMP-8, the polymorphonuclear (PMN) leukocyte collagenase, as a critical mediator initiating lipopolysaccharide (LPS)-responsiveness in vivo. PMN infiltration towards LPS is abrogated in MMP8-null mice. MMP-8 cleaves LPS-induced CXC chemokine (LIX) at Ser4~Val5 and Lys79~Arg80 to increase bioactivity. However, with biochemical redundancy between MMPs 1, 2, 9, and 13, which also cleave LIX at position 4~5, it was surprising to observe such a markedly reduced PMN infiltration towards LPS and LIX in MMP8 -/- mice. Hence, rather than collagen, these PMN chemoattractants are important MMP-8 substrates in vivo; PMN-derived MMP-8 cleaves and activates LIX to execute an in cis PMN-controlled feed-forward mechanism to orchestrate the initial inflammatory response and promote LPS responsiveness in tissue. Through the activity of macrophage-specific MMP-12 we found that macrophages then dampen the LPS-induced influx of PMNs—so providing a new mechanism for the termination of PMN recruitment in acute inflammation. MMP-12 specifically cleaves and inactivates human ELR+ CXC chemokines (CXCL1, 2, 3, 5, and 8) at E-LR, the critical receptor-binding motif, or for CXCL6, carboxy-terminal to it. Furthermore, MMP-12 processed and inactivated monocyte chemotactic proteins CCL2, 7, 8, and 13 at position 4-5 generating CCR antagonists. We propose the macrophage, specifically through MMP-12, assists in orchestrating the regulation of acute inflammatory responses by precise proteolysis of ELR+ CXC and CC chemokines. So rather than extracellular matrix proteins as substrates, MMPs are critical regulators of innate immunity through processing of chemokines.

DIETER BRÖMME, *Ph.D.*

Ph.D. in Biochemistry from the Martin-Luther Universität Halle-Wittenberg/GDR in 1983 • Research Associate at the Institute of Biochemistry in Halle/GDR from 1983-1990 • Research Officer at the Biotechnology Research Institute in Montreal/QC from 1991-1993 • Senior Scientist with Khepri Pharmaceuticals, Inc. (later acquired by Arris/Axys Pharmaceuticals) in South San Francisco/CA from 1993-1997 • Doctor of Science from the Friedrich Schiller Universität Jena/Germany in 1997 • Associate/Full Professor at the Mount Sinai School of Medicine in New York from 1997-2004 • Full Professor and Canada Research Chair at the Faculty of Dentistry of the University of British Columbia in Vancouver, B.C. since 2004.

Basic mechanisms of bone resorption

Our skeleton is replaced every 7-10 years by a process called bone remodeling. Bone remodeling is a fine balance between bone resorption and bone formation. It happens on a major scale after bone fractures, tooth extraction, and other traumatic events but on a smaller scale throughout life to grow bone and to repair microfractures caused by everyday physical stress on the skeleton. Bone is primarily formed by osteoblasts and degraded by multinucleated osteoclasts. Osteoclast-mediated bone resorption can be subdivided into two processes: (1) demineralization and (2) resorption of the organic bone matrix, which consists of 90% type I collagen. During the demineralization step, osteoclasts acidify the underlaying bone, which leads to the dissolution of the inorganic, mostly phosphoapatite content of bone. The bone salts are responsible for the strength and hardness of the bone, whereas the collageneous matrix forms the scaffold of the bone and is responsible for its overall stability. The organic matrix is subsequently degraded by proteases secreted by the osteoclast. The result of this proteolytic action of the osteoclast is the formation of a resorption pit. The major proteolytic activity of osteoclasts is the cysteine protease, cathepsin K. Cathepsin K is the only known mammalian collagenase capable of cleaving inside the triple helical collages at multiple sites and to completely break down the collagen fibrils into small soluble pieces. To be active as a collagenase, cathepsin K forms specific complexes with bone-resident glycosaminoglycans. Other collagenases of the matrix metalloproteinase family appear to help in the "cleaning" of remaining collagen fibril remnants in the resorption pits prior to the invasion of osteoblasts, which will refill the pit with new bone. Excessive bone resorption is a major problem of aging and is mostly manifested in a disease called osteoporosis. Recent therapeutic efforts to slow down bone resorption are focused on the development of highly potent cathepsin K inhibitors which are presently in clinical phase II trials.

DONALD M. BRUNETTE, *Ph.D.*

Donald Maxwell Brunette, Ph.D. (Medical Biophysics) is a Professor in the Department of Oral Biological and Medical Sciences, and a former Head of the Departments of Oral Biology and Oral Biological & Medical Sciences, as well as a former Associate Dean of Research and Graduate Studies in the Faculty of Dentistry at the University of British Columbia. A founding member of the Medical Research Council (MRC Canada) Group in Periodontal Physiology directed by Dr. A.H. Melcher at the University of Toronto, Dr. Brunette has published over 90 articles in refereed journals and has won awards from the International Association of Dental Research, Association of Canadian Faculties of Dentistry (W.W. Wood Teaching Award) and the American Medical Writers Association (for the first edition of Critical Thinking). His research has been continuously supported by MRC/CIHR for over 30 years and has encompassed several fields, including citation analysis and clinical studies of breath odour, but is mainly concerned with cell-biomaterial interactions. He serves as a consultant to three biomaterial-related journals as well as to the American Dental Association's Council on Scientific Affairs and has been a member, chair or scientific officer of grant evaluation committees of the Canadian Institutes of Health Research as well as the National Science Foundation (USA).

Improving the implant surface by controlling cell behaviour using surface topography

Commercially-available dental implants vary widely in their surface properties, with each manufacturer touting the advantages of their systems. This diversity of available choices indicates that an optimum surface has yet to be developed, and improved surfaces will be required as dental implants are placed in more and more demanding situations. It is clear that surface properties, including topography and chemistry, are of prime importance in establishing the response of tissues to biomaterials. Our objective is to develop principles of cell response to topography that could be used to design surfaces for tissue interaction on implanted devices. We have studied the effects of topography on cell behaviour using microfabricated surfaces produced by techniques used in the microelctronics industry as well as those produced by industrial processes in implant fabrication such as grit blasting or acid etching. Microfabrication techniques have enabled the production of precisely-controlled surfaces in silicon (Si) with features designed to affect cell behaviour. The surfaces originally produced in Si or titanium (Ti) can be replicated in epoxy, and coated with Ti and used as substrata for cell culture or implanted in vivo. Processes relevant to implant performance that have been found to be affected by surface topography include epithelial and fibroblast locomotion and protease production, fibroblast gene activity, connective tissue attachment, cell signaling, osteoblast differentiation, and cytokine secretion by macrophages. There is a good correlation between the effects of the surfaces in vivo and in vitro for some processes such as direction of cell migration and bone formation. Surface topographic features can act synergistically to achieve their effects. Only a few of the many possible topographies that can be produced by microfabrication techniques have been investigated, and there is considerable potential for optimizing cell responses to implanted devices by topographic control of cell behaviour.

TASSOS IRINAKIS, *D.D.S., M.Sc., Dip.Perio., F.R.C.D.(C.)*

Dr. Anastasios (Tassos) Irinakis completed his dental degree in Athens, Greece. After working in private practice he continued his education at the University of British Columbia where he received his specialty training in Periodontics and Implant Surgery. He was awarded the "McAnulty Memorial Prize" for Excellence in Periodontics in 2001. His postgraduate education led to a Diploma in Periodontics and a Masters degree in Oral Biology. He continued to obtain his Fellowship with the Royal College of Dentists of Canada.

Dr. Irinakis currently works at UBC as a Clinical Associate Professor in the Division of Periodontics & Dental Hygiene. He is the Director of Graduate Periodontics & Implant Surgery. He has established a Bone Grafting & Implant Clinic at UBC where he offers his services weekly. He is a Periodontal Consultant for Vancouver General Hospital and for the College of Dental Surgeons of British Columbia. He also maintains part-time private practice, performing a variety of periodontal and implant surgeries in Vancouver and Coquitlam, B.C. and Calgary, Alberta, Canada.

Dr. Irinakis was recently awarded the "2005 Educator Award" from the American Academy of Periodontology. He serves the Academy as a member of the Review Panel for the Journal of Periodontology. He has also founded an Institute for Continuing Dental Education, i.e. I.D.E.A.S.; Institute for Dental Education & Advanced Surgeries (www.dentalideas.ca). Dr. Irinakis lectures actively in study clubs, conferences and hands-on courses for dental professionals nationally and internationally.

Immediate implant placement in fresh extraction sockets in the esthetic zone

We are commonly faced with the dilemma between a conservative approach and an assertive response when evaluating a compromised or failing tooth. Should we proceed with complicated endodontic therapy or should we consider extraction and restorative rehabilitation with and implant? This presentation will focus on the second approach and provide insight in order for the clinician to respond appropriately to such cases with a successful diagnosis and treatment plan. Key factors will be briefly mentioned on when to proceed with socket preservation (and bone grafting and delayed implant placement) and when to proceed with immediate implant placement in fresh extraction sites. On one hand, the practitioner can extract the tooth and fill the socket with grafting material to preserve the architecture of the socket and proceed with delayed implant placement at a later time. On the other hand, it may be prudent and desirable to immediately place an implant into a fresh extraction socket at the time of tooth removal, thus saving the patient money and time. Advantages and challenges of each procedure will be mentioned, along with tips to allow easier decision making. Esthetic considerations are always a crucial determining factor and helpful guidelines will be offered throughout this presentation.

IAN MATTHEW, *Ph.D., M.Dent.Sc., B.D.S., F.D.S.R.C.S.(Eng.), F.D.S.R.C.S.(Ed.)*

Dr. Ian Matthew is a certified specialist in oral surgery within the European Union, and is currently Chair, Division of Oral Surgery at the UBC Faculty of Dentistry. His principal interest in the field of implantology is in the provision of a "hands-on" educational forum for undergraduates, general practice residents, graduate periodontics residents, and graduate dentists. Dr. Matthew has over 20 years experience in implantology using Straumann ITI implants, and more recently, the Nobel Biocare implant system.

Ridge augmentation

Dental implants require adequate bone substrate to achieve osseointegration. Bone loss occurs naturally following tooth extraction, oral cancer, or facial trauma. Bone grafting can augment bone at implant sites with inadequate bone structure due to previous extractions, gum disease or injuries. Research into osteoporosis has provided a greater insight into a condition which is prevalent among the population and can also impact on implant placement. Distraction osteogenesis, an alternative to ridge augmentation with grafted bone, is based on the pioneering work of Ilizarov, and is of particular value in restoring large jaw defects.

Graft selection is based on the clinical findings and other factors such as clinician training, graft availability, cost, personal preference, and patient choice. It is possible to augment a small defect using synthetic graft materials based on hydroxyapatite, the basic inorganic substrate of bone. Cadaveric bone graft material from a tissue bank is also available. However, the gold standard is the patient's own bone harvested from a local or distant site. Maxillary sinus grafts are also performed as an alternative to ridge augmentation, to replace bone in the posterior upper jaw. A resorbable membrane may be indicated to protect the bone graft and encourage bone regeneration (guided tissue regeneration).

Major bone grafts are typically performed to repair more extensive jaw defects. This bone is harvested from various sites depending on the size of the defect: the hip (iliac crest), lateral knee (tibia), and skull (cranium). These procedures are routinely performed in an operating room and may require a hospital stay. Techniques in pain control now permit the patient to have the surgery as an out-patient and return home the same day.

The pursuit of technical excellence in bone grafting relies heavily on meticulous pre-operative planning, aided by advanced radiology techniques and software, for example Nobel Biocare's NobelGuide. The aim of this presentation is to illustrate the key points involved in treatment planning for bone grafting procedures. The objectives are to describe indications for bone grafting, choices and selection of graft material, clinical and radiological requirements for treatment planning, and grafting techniques for ridge augmentation. Research into grafting techniques will also be covered.

JOANNE N. WALTON, *D.D.S., Cert. Pros., F.R.C.D.(C.)*

Dr. Joanne Walton completed her dental education at the University of Alberta and practiced general dentistry for four years before specializing in prosthodontics at Walter Reed Medical Center in Washington, D.C. After six years in full-time prosthodontic practice, including two years as a part-time clinical instructor at the University of British Columbia Faculty of Dentistry, she became a full-time faculty member at UBC, maintaining a part-time prosthodontic practice. Since joining UBC, Dr. Walton has conducted research related to both implant prosthodontics and dental education. She has collaborated extensively with Dr. Michael MacEntee to examine prosthodontic outcomes with implant-retained overdentures, currently completing the first clinical trial to compare patient satisfaction, treatment costs and prosthodontic maintenance with dentures retained by a single implant to those retained by the standard two implants.

Managing edentulism with or without implant prostheses – Part I

Today's presentation focuses on results of the clinical trials conducted by Drs. Walton and MacEntee investigating patient satisfaction, prosthodontic maintenance, altered sensation, implant angulation, and implant treatment choices, all related to implant overdentures (IOD) in an older population. Recognizing that many edentulous patients are satisfied with conventional dentures, the overall goal of this research has been to provide sound evidence for clinicians seeking the least expensive, least invasive treatment alternatives for those patients who may be struggling with conventional complete dentures.

ROSS BRYANT, *D.D.S., Ph.D., F.R.C.D.(C.)*

Dr. Bryant is a clinician, researcher and educator in the ELDERS (Elders' Link with Dental Education, Research and Service) Group at the University of British Columbia, with teaching responsibilities in implant dentistry and fixed and removable prosthodontics. His research interests, and presentations and publications, focus on quality of life assessment and management of the biological and psychosocial impact of tooth loss, oral prostheses and dental implants. He treats patients in the Oral Implant Clinic at the UBC Specialty Clinic, and he has for several years served on the executive of the B.C. Society of Prosthodontists and the Dental Specialist Society of B.C.

Managing edentulism with or without implant prostheses - Part II

Being unable preserve the remaining lower dentition begs an open discussion of treatment options with the patient, including a conventional denture, and either a fixed or removable implant prosthesis. However, the problem remains that it is not clear what the optimal strategy is for management of edentulism – with or without implants. This presentation reviews evidence of biological and psychosocial outcomes for managing complete tooth loss in adults. The biological outcome of implants depends on selection of patients with stable general and oral health and adequate bone status. Unfavorable jawbone condition can impair implant success, particularly in the atrophic edentulous maxilla. However, aging itself does not seem to detract from oral implant success, despite age-related systemic illness including osteoporosis. Generally, both implant prostheses and complete dentures are associated with favorable physiological and psychosocial outcomes. Interestingly, edentate older adults may prefer the ease of cleaning associated with removable compared to fixed prostheses, whereas this may not be the case for younger adults. Substantial differences also exist in the initial fiscal costs of the various options, and some efforts are being made to reduce costs to improve accessibility. However, there is no consensus on how or even whether to assess the long-term cost-benefit comparing the various options, particularly when considering the impact on quality of life of patients. It is generally accepted that tooth loss diminishes quality of life through impaired oral function and appearance and the resulting impact on psychological and social experiences. It is also increasingly clear that conventional dentures can be acceptable substitutes for many individuals with missing teeth. Indeed, contrary to current opinions, elders with or without implants can use very positive language to describe their quality of life outcomes, suggesting factors other than the physical impairment can be influencing how individuals adapt positively to tooth loss. For some, oral implants can offer the hope of stable artificial teeth with improved satisfaction. The scientific challenge in managing adults with terminal dentitions or edentulism in at least one jaw remains the need to distinguish the influence of patient-mediated expectations on the physiological and psychosocial outcome of treatment.

SONIA S. LEZIY, *D.D.S., Dip.Perio.*

Sonia S. Leziy received her dental degree from McGill University. Her post-graduate degree in periodontics was completed at the University of British Columbia in 1993. Dr. Leziy is a Fellow of the Royal College of Dentists of Canada, a Fellow of the ICOI, and a member of the British Columbia Society of Periodontists, the Canadian Academy of Periodontists, the American Academy of Periodontists and is past president of the British Columbia Society of Periodontists. Dr. Leziy is a member of the advisory board of the Journal Spectrum Dialogue, a member of the Nobel Biocare Global Scientific Committee and a member of the Nobel Biocare NobelKnowledge web expert panel. She is an assistant clinical professor and sessional lecturer at the University of British Columbia and co-mentors the VIP study club, a Vancouver chapter of the Seattle Study Club. She has published and lectures internationally on implants and aesthetics/periodontal plastic surgery. Dr. Leziy maintains a full-time private practice with Dr. Brahm Miller (prosthodontist) and fellow periodontists Dr. Priscilla Walsh and Dr. Andrea Csiszar, specializing in periodontics and implant surgery.

The science and art of aesthetic implant treatment: a blueprint for success

Conventional concepts in aesthetic restorative treatment generally focus on modifying tooth form and colour. Today, it is unquestionably recognized that the interplay with the surrounding gingival framework plays an equally important role in the aesthetic outcome of treatment. An understanding of how to control the tissue architecture around implant restorations is a key element to a successful aesthetic outcome.

This presentation will focus on the following key subjects:

- Treatment planning considerations in the esthetic zone: from extraction through restoration.
- Engineering hard and soft tissues.
- 3D implant positioning and design-influence: impact on tissue architecture.
- Provisionalization as the final ‘surgical’ step.
- Inter-implant papilla: surgical considerations for enhanced esthetics.

POSTER ABSTRACTS

Poster Competition Judges

- Dr. Dieter Brömme
- Dr. Ross Bryant
- Dr. Virginia Diewert
- Dr. Leeni Koivisto
- Dr. Anthony McCullagh
- Dr. Gethin Owen
- Dr. Steve Pelech, *Faculty of Medicine*
- Dr. Clive Roberts
- Dr. Ravi Shah, *Chair of Poster Competition*
- Dr. David Sweet
- Dr. Doug Waterfield
- Dr. Chris Wyatt

1. Effect Of Implant Surface Roughness On The NFkB Signaling Pathway In Macrophages

Ali TA*, Brunette DM, Waterfield JD
Department of Oral Biological & Medical Sciences, The University of British Columbia, Vancouver, Canada

OBJECTIVES: The aim of this study is to examine the effect of implant surface topography on activating the NFkB signalling pathway in Macrophages. The further understanding of the signalling pathways will lay a solid foundation for the development of methods for controlling inflammation in the form of down regulating the inflammatory response and up regulating the healing and in turn Osseointegration.

METHODS: Murine macrophage-like cells (RAW 264.7 cell line) were used in this study. They were cultured on epoxy replicas of Smooth, Acid Etched and SLA surfaces. The macrophages were analysed for their ability to both adhere and translocate NFkB to the nucleus under a number of experimental conditions [with and without serum, LPS and membrane cholesterol].

RESULTS: A. Macrophage Activation: 1. Different surface topography causes activation of the NFkB pathway differently. The Smooth surface showed the highest level of activation. 2. Addition of the suboptimal concentrations of LPS mildly enhanced the response by signalling through the Toll receptor. 3. Triggering of the macrophages occurred in the absence of fetal calf sera although to a lesser extent. This indicates that components of sera were partially responsible for activation of the NFkB pathway. 4. Disruption of the lipid rafts in the membrane through removal of the cholesterol content affected the triggering and signalling of the NFkB pathway. It appears that it may be concentration dependent. B. Adherence: 1. Smooth surfaces bound more macrophages in the 30 minute assay. 2. Serum components were also found to increase binding of macrophages to the various test surfaces. 3. Removal of cholesterol did not affect the ability of macrophage to bind their respective surfaces.

CONCLUSIONS: This in vitro study has demonstrated that surface topography modulated activation of the NFkB signalling pathway in a time-dependent manner. Further research will be required to determine mechanisms regulating specificity and selectivity of NFkB function, as well as its role in different cell types.

2. Influence In The Quality Of Life And Efficacy Of Support Therapy For TMD As An Adjunctive Therapy For Oral Appliance Treatment

Cunali PA[1], Almeida FR[2]*, Garbuio S[1], Santos CD[1], Nascimento LS[1], Valdrighi NY[1], Tufik S[1], Bittencourt LRA[1]
[1] *Federal University of São Paulo – UNIFESP, Brazil;* [2] *Faculty of Dentistry, The University of British Columbia, Vancouver, Canada*

OBJECTIVES: Pain in the mastication muscles and/or in the temporomandibular joints (Temporomandibular Dysfunction-TMD) can be a contra-indication of Oral Appliance (OA) therapy or can lead to non-compliance of OA as a treatment for Obstructive Sleep Apnea Syndrome (OSAS). The quality of life is reduced in OSAS patients and can be worsened if the patient happens to also suffer from Temporomandibular Dysfunction (TMD). Support therapy (ST), in the means of jaw exercises, is the first choice of treatment for TMD. The aim of the study is to follow a population with pre-existing TMD symptoms and evaluate the influence of ST on the patient's quality of life and to assess the efficacy of ST in reducing pain symptoms related to TMD during OA therapy.

METHODS: Patients with mild to moderate OSAS and TMD symptoms who were referred to OA therapy have been included in the study. The patients were divided in two groups: support therapy (ST) and placebo therapy (PT). The study was double blinded and patients were randomized prior to performing ST or PT. Quality of life (SF 36) and the Fletcher & Luckett sleep questionnaire were used prior and after 120 days of therapy for all patients. TMD symptoms were scored following the Research Diagnostic Criteria for Temporomandibular Disorders – RDC. The RDC was score as presence or absence of pain related to TMD prior treatment and after OA titration. OA compliance was assessed one week after insertion and after titration.

RESULTS: Fifteen patients received ST and 14 patients received PT. Both groups showed significant reduction in the AHI. After titration, SF 36 showed a significant improvement in 5 of its 8 domains in the ST group (pain, limitation of emotional aspects, mental sanity $p<0.05$; general state of health and vitality $p<0.01$); while the PT group showed a significant improvement in 3 out of the 8 domains (physical limitations, social aspects $p<0.05$ and vitality $p<0.01$). The Fletcher & Luckett questionnaire showed a significant improvement in the ST group only. At 2/3 advancement, a higher number of patients without pain was observed in the ST group (12) when compared to the PT group (5) which continued at maximal advancement of the OA (ST=11 and PT=4) ($p<0.01$). ST also proved to be significantly efficacious in the reduction of pain intensity caused by TMD towards the end of the treatment period ($p=0.01$). Compliance to OA after titration was significantly higher in ST (86%) when compared to PT (63%) ($p<0.05$).

CONCLUSIONS: Patients with OSAS and TMD wearing OA had higher improvement in quality of life, quality of sleep and reduced craniomandibular pain when ST was used as a supportive adjunctive therapy. Results demonstrate that non-indication of the OA in TMD cases should be re-examined, and that jaw exercise may be decisive in OA compliance.

3. Differential Response Of Fibroblasts And Osteoblasts To A Roughness-Gradient

Baharloo RB[1]*, Zink C[2], Yokoyama T[1], Spencer ND[2], Brunette DM[1]
[1] *Faculty of Dentistry, The University of British Columbia, Vancouver, Canada;* [2] *Laboratory for Surface Science and Technology, Department of Materials, ETH, Zürich, Switzerland*

OBJECTIVES: To examine the effect of titanium surfaces with roughness gradient on the behaviour of different cell types.

METHODS: Multi microcolonies of green rat dermal fibroblast cells (GDF), rat calvarial osteoblast cells (RCO), and pig periodontal ligament epithelial cells (PLE) were stamped on the surfaces with a wide range of roughness values (Ra=~1μm-6μm). The responses of the microcolonies of cells were studied using epifluorescent light microscopy, confocal laser scanning microscopy, scanning electron microscopy, and live cell imaging up to day-7 post culture.

RESULTS: RCO in contrast to GDF and PLE microcolonies exhibited a preference to move towards increasing roughness. Parameters such as microcolonies' projected area, microcolonies' direction of migration along gradient, and cell polarity in different regions of the gradient will be reported.

CONCLUSIONS: This study shows that a roughness gradient has the potential to differentially affect different cell types leading to the possibility of designing implant surfaces of varying roughness that are specialized for specific cell types.

ACKNOWLEDGEMENTS: We would like to thank the Canadian Institutes of Health Research for funding and Mr. Leon Cheng for technical assistance.

4. Lessons Learned From Oral Cancer Patients – Experiences From Detection To Diagnosis

Biggar H[1]*, Poh CF[1], Hislop TG[2], Bottorff J[3], Rosin MP[4]
[1] *Faculty of Dentistry, The University of British Columbia, Vancouver, Canada;* [2] *B.C. Cancer Control Research, B.C. Cancer Agency, Vancouver, Canada;* [3] *The University of British Columbia Okanagan, Kelowna, Canada;* [4] *Simon Fraser University, Burnaby, B.C.*

OBJECTIVES: The prognosis of oral cancer is poor (50-60% five-year survival rate) and has shown minimal change over 3 decades, largely due to late stage detection. This has resulted in a significant impact on survival and quality of life. Understanding the process to early detection and diagnosis is key to improving outcome. The objective is to collect information from patients who have diagnosed high-risk oral lesions (severe dysplasia/carcinoma in situ) or invasive cancer relating to their experiences from first detection of an oral lesion to the diagnostic workup. The goal is to identify factors that impact on the severity of high-risk oral lesions at diagnosis.

METHODS: An interview-style questionnaire has been developed to collect both qualitative and quantitative data on patients' experience. Here we report data from a pilot study of 18 patients, all of which were diagnosed within the previous 12 months. All patients are participating in the Oral Health Study at BCCA.

RESULTS: Among the patients interviewed, 11 (61%) had invasive cancer and 7 (39%) a preinvasive lesion. Patients with preinvasive lesions all reported seeing both dental and medical professionals at least once per year prior to diagnosis in contrast to only 5 (45%) of individuals with invasive cancers (P = 0.04). Of 9 patients that self-identified their initial lesions, 8 had an invasive cancer. The chief complaint for these lesions was pain or presence of non-healing ulcers (6/9; 67%). In contrast, 9 patients had their initial lesions identified by health professionals (HPs), 8 during screening by dental professionals and the other by a physician for a health problem (N=1). Only 3 (33%) of the latter cases showed invasive lesions (P = 0.05). All lesions initially identified by HPs had no symptoms. On average, the time lag between the initial identification to biopsy was 5.3 + 4.9 months. Two patients (both asymptomatic) showed a delay of > 12 months from initial detection by a HP to biopsy. The main reason for this delay was a choice for watchful waiting rather than immediate biopsy by the HPs.

CONCLUSIONS: These results suggest dental health professionals can play an important role in early identification of high-risk oral lesions at an asymptomatic and preinvasive stage. They also draw attention to the importance of increasing oral cancer awareness in both patients and health professionals.

ACKNOWLEDGEMENTS: Research is supported by NIDCR grant R01DE13124 and CIHR & MSFHR grants to CFP.

5. Chromosomal Instability In High-Risk Oral Premalignant Lesions – A Tissue Microarray Study

Chen E[1,2*], Zhu Y[1], Zhang L[3], Rosin MP[1,2], Poh CF[2,3]
[1] *Simon Fraser University, Burnaby, B.C.;* [2] *B.C. Cancer Agency, Vancouver, Canada;* [3] *Faculty of Dentistry, The University of British Columbia, Vancouver, Canada*

OBJECTIVES: To characterize patterns of CIN in samples on a unique tissue microarray of oral premalignant lesions (OPLs) that contains samples of varying histological grade and with known outcome (i.e. progression to carcinoma). As a first step in this pilot study, heterogeneity of chromosome patterns in tissue on the array was determined using centromere probes from two chromosomes.

METHODS: The study involved a tissue array comprised of 64 oral premalignant lesions. As an internal control, the array contains 3 non-dysplastic lesions. A dual color probe set of CEP11 (Orange) and CEP7 (Green) was used for fluorescence in situ hybridization (FISH) analysis. These chromosomes have shown frequent CIN in earlier studies with oral squamous cell carcinoma.

RESULTS: On average, 209 + 22 non-overlapping nuclei were evaluated from each tissue. Thirteen (20%) of the dysplasia samples had cells with 3 or more CEP7 or CEP11 signals; seven samples had more than 10% of nuclei showing such change. Striking differences was observed among OPLs. One case (a low-grade dysplasia that later progressed to cancer) showed very heterogeneous patterns of CEP7:CEP11 signals, possibly reflecting an active process of instability in the tissue: patterns seen included (0:3), (1:3), (1:4), (2:3), (2:4), (3:0), (3,1), (3:2), (3:3), (4:0), (4:2), (4:3) and (4:4). Other samples showed small numbers of cells with alterations to signal numbers and fewer patterns of alteration (none of the aforementioned patterns). Another indication of heterogeneity was the fraction of cells in which the number of centromere signals on the two chromosomes differed by ≥ 2 (e.g. 2:4, 1:3, etc.). Eleven (17%) cases showed such patterns of alteration, with 5 over 10% of nuclei showing such change.

CONCLUSIONS: Levels of CIN in OPLs are varied, with some samples showing considerable heterogeneity in patterns of chromosomal alteration. Further studies will expand upon these observations to look for associations with outcome.

ACKNOWLEDGEMENTS: Sponsored by NIDCR R01 DE13124, CIHR MOP-77663 and MSFHR grants.

6. The Structural Requirement Of Elastinolytic Activity In Human Cathepsin V

Chen N-H[1*], Brömme D[1,2]
[1] *Department of Biochemistry & Molecular Biology, Faculty of Science, The University of British Columbia, Vancouver, Canada (UBC);*
[2] *Department of Oral Biological & Medical Sciences, Faculty of Dentistry, UBC*

OBJECTIVES: Despite sharing an amino acid sequence identity of over 80% and very similar subsite specificities only cathepsin V (cat V) has a potent elastase activity whereas cathepsin L (Cat L) lacks it. The objective of this research is to identify the presence of an exosite in Cat V that binds to elastin and contributes to its elastinolytic activity.

METHODS: Chimera mutants containing different proportions of Cat V and Cat L were generated by PCR, cloned and expressed in the Pichia pastoris system. The expressed enzymes were purified by FPLC and subjected to activity assay using a synthetic substrate and elastin derivatives. Finally, the HPLC profile of elastin degradation were also obtained.

RESULTS: We found that all mutants were comparably to their wild-type enzymes active towards a synthetic substrate, and that mutant 1 (M1; containing ~75% of Cat V) demonstrated a potent elastinolytic activity, whereas mutant 2 (M2; containing ~50% of Cat V) and mutant 3 (M3; containing ~25% of Cat V) were only weakly active. Also, HPLC profiles of both wild type Cat V, Cat L and all mutants showed that M1 exhibited similar, if not identical, elastin cleavage pattern as Cat V. These results directed us to further dissect the potential region of amino acids 53 to 117 in Cat V. Mutant 4 (M4; containing ~50% of Cat V in the potential region) and mutant 5 (M5; containing only ~15% of Cat V in the potential region) both displayed elastinolytic activity and generated identical cleavage pattern as shown by HPLC.

CONCLUSIONS: The result suggested that the region of amino acid 112 to 118 in Cat V seemed to be associated with elastin degradation. Further sequence and structural analysis, and mutant constructions targeting that region will elucidate amino acid residue responsible for the elastinolytic activity in Cat V.

7. A Creative Global Solution To Offering Baccalaureate-Level Dental Hygiene Education

Craig BJ*
Faculty of Dentistry, The University of British Columbia, Vancouver, Canada

OBJECTIVES: To develop an innovative, flexible and adaptable baccalaureate-level educational model that graduates dental hygienists with a 4-year degree and offers Canadian and international dental hygiene diploma/certificate/associate degree graduates access to an advanced educational opportunity.

METHODS: A multiple-admissions model was created with 4 entry points into the program using creative resource strategies. Each option has defined admission criteria and graduation eligibility requirements. The two options for degree completion allow learners to fulfill degree requirements through distance education without the more traditional residency requirement. Three admission options were implemented in 2002 and the fourth option commenced in September 2007. Surveys of graduates and current students were conducted to better understand the reasons for selecting the program.

RESULTS: To date program enrollment since 1992 has increased from 5 degree completion students to 193 students eligible to register in courses in all four admission options as of September 2007. Survey data revealed that 68% of current degree completion students reside outside the UBC catchment area and enrolled in the Program because of online course access and part-time study opportunities. Ninety percent of degree completion students are part-time and have up to 5 years to complete requirements to graduate.

CONCLUSIONS: Graduate numbers have more than doubled in the past 4 years. Twenty-five percent have gone on to graduate studies - Masters and doctoral. This model could be adapted to a variety of educational contexts globally.

8. Establishment Of A Community Partnership To Facilitate Oral Cancer Screening In A High-Risk Community

Currie BL[1]*, Poh CF[1], Hislop G[2], Bottorff JL[1], Zhang L[1], Rosin MP[3]
[1] *Faculty of Dentistry, The University of British Columbia, Vancouver, Canada;* [2] *B.C. Cancer Agency, Vancouver, Canada;*
[3] *Simon Fraser University, Burnaby, B.C.*

OBJECTIVES: To explore possible approaches that would facilitate an oral cancer-screening program in a high-risk community in the Vancouver DTES, a community that is characterized by poverty and an elevated exposure to known risk factors (tobacco and alcohol) associated with oral cancer.

METHODS: A screening clinic was established in partnership with a pre-existing community dental clinic in the Vancouver DTES. Patients attending the clinic for regular dental care were invited by the staff dentist to participate in a free oral cancer screening. Demographics, information on known risk factors and medical history were collected by interview-style questionnaires followed by a full head and neck evaluation using conventional technique and a novel translational tool (fluorescence visualization) to enhance visualization of oral lesions.

RESULTS: A total of 284 patients attended this drop-in clinic over a 2-year study period. Among these patients, 204 (72%) were invited by the staff dentists for screening – 200 (98%) of these accepted the invitation. The remaining 28% of individuals were deemed ineligible for the study for a variety of reasons including severe psychological problems, drug and/or alcohol intoxication and/or lack of willingness to wait for the screening exam. Of the 200 screened patients, most were smokers (86%) and regular consumers of alcohol (83%) and often immuno-compromised. Strikingly, 2 oral cancer and 8 precancers were identified.

CONCLUSIONS: The study is an example of capacity building through a community partnership to approach a hard-to-reach high-risk community. The screening activity identified a significant disease burden in this community and an urgent need to expand this initiative to create a more comprehensive strategy to outreach this community for not only screening, but also diagnostic work-up and treatment.

9. Preliminary Activities For Community Oral Health Research With Immigrant Children

Dabiri D*, Carino KMG, Harrison RL
Division of Pediatric Dentistry, The University of British Columbia, Vancouver, Canada

OBJECTIVES: Conducting a comprehensive community-based dental health survey of young immigrant children presents numerous challenges. The overall goal of this study was to document prevalence of caries and dental treatment needs among Filipino immigrant children in metro Vancouver. The objectives of this first phase of the research were to develop survey protocols (including those for subject recruitment), validate the clinical indices, and recruit and train volunteers.

METHODS: Protocols were tested in a series of "trial surveys" utilizing small, convenience samples of parents and children. Materials required for the final surveys were identified. The International Caries Detection and Assessment System (ICDAS) was adopted as the criteria for measuring dental caries. The trial surveys provided opportunity for (a) intra-examiner calibration, (b) training of the recorder, and (c) refinement of the dental chart. A logo, designed by DD, complemented the project slogan: Healthy Teeth, Happy Families. Information dissemination primarily involved flyers and posters distributed to community centers, libraries, Filipino stores and parenting groups. All materials were continuously evaluated and re-designed based on community feedback. Volunteers were recruited and trained in a series of workshops.

RESULTS: 20 children were examined in the trial surveys. The ICDAS system, though complex, proved workable for recording caries in very young children. The logo, used on all project-related materials, increased visual recall of the research project. The most successful means of subject recruitment was "face-to-face" (i.e. personal invitation). 11 volunteers were recruited and trained to assist with surveys.

CONCLUSIONS: Prior to launching a community-based child dental health survey, time must be devoted to 1) refining all protocols, 2) calibration of examiners, 3) identifying successful techniques for subject recruitment, and 4) training and maintenance of a reliable group of volunteers. The survey proper has now begun and is over 80% complete.

ACKNOWLEDGEMENTS: We acknowledge the dedication of our project's volunteers. This research was supported by a grant from the S. Wah Leung Endowment Fund. Ms. Dabiri was funded by the Network for Oral Research Training and Health (NORTH) Canadian Institutes of Health Research (CIHR) training program.

10. Social Isolation, Body-Image And Oral Health Among Elderly Women

Donnelly L*, O'Connor D, MacEntee MI
Faculty of Dentistry, The University of British Columbia, Vancouver, Canada

OBJECTIVES: Oral health of elders in residential care (RC) facilities is generally poor, but to what extent it affects their body-image and social behaviors is unknown. A positive body-image increases social contacts and improves health, well-being and quality of life. Literature on relationships between body-image and aging among elderly women does not explore the role of oral health. The objective of this study was to begin to investigate the relationship between overall body image and oral health among elderly women who reside in a RC facility.

METHODS: Open-ended interviews with a purposefully selected group of four older women were conducted and the narratives analyzed using a constant comparative method involving an iterative technique. A second interview with the participants was conducted to check trustworthiness of my interpretations.

RESULTS: Four themes emerged; 1) social interactions are influenced by the environment; 2) body-image is influenced by health and the social context; 3) the importance of a "nice smile"; and 4) priorities in life and health.

CONCLUSIONS: Relationships between social isolation, body-image and oral health among institutionalized elderly women can have multiple influences that depend on life-priorities, however, the information emerging from the interviews was not saturated which indicated that more interviews are needed to conclude this phase of the study. Further study is underway with a larger more diverse sample of elders to expand the context in which these observations occur.

11. Expression Of Integrin αvβ6 and TGF-β In Scar-Free Vs. Scar-Forming Wound Healing

Eslami A[1*], Gallant-Behm CL[2], Wiebe C[1], Hart DA[2], Honardoust D[1], Häkkinen L[1], Larjava H[1]
[1] Faculty of Dentistry, The University of British Columbia, Vancouver, Canada; [2] Faculty of Medicine, The University of Calgary, Calgary, Alberta

OBJECTIVES: Integrins are key mediators of TGF-β activation in vivo. The αvβ6 integrin can activate two isoforms of TGF-β, fibrogenic TGF-β1 and anti-fibrogenic TGF-β3. Expression of epithelial cell integrin αvβ6 is induced during wound healing but its function in wounds remains unclear. In the present study, we investigated the potential for αvβ6-mediated activation of TGF-β during wound healing by studying the spatio-temporal co-localization of αvβ6 integrin with the molecules involved in TGF-β activation in human gingival wounds. In addition, we compared the expression and localization of αvβ6 integrin along with its ligands, TGF-β1 and TGF-β3 in scar-free gingival versus scar-forming skin wounds in red Duroc pigs.

METHODS: Full-thickness excisional wounds were created in the gingiva of human volunteers, and in the gingiva and skin of red Duroc pigs. Wounds healing rate was clinically and histologically assessed at different time points up to 60 days after wounding. Immunohistochemical analysis and real-time PCR were used to assess the localization and expression of β6 integrin, TGF-β1 and TGF-β3.

RESULTS: The αvβ6 integrin was found to colocalize with both TGF-β1 and TGF-β3 in the wound epithelium of human gingiva. Analysis of the pig wounds showed that basal keratinocytes of the clinically healed gingival wounds continued to express αvβ6 integrin and TGF-β3 while their expression was negligible in scar-forming skin wounds.

CONCLUSIONS: The spatio-temporal colocalization of αvβ6 with TGF-β1 and TGF-β3 in human gingival wounds demonstrates a potential mechanism to regulate the activity of TGF-β isoforms by αvβ6 integrin during wound healing. Prolonged expression of αvβ6 integrin along with anti-fibrogenic TGF-β3 in the gingival wound basal epithelium may be important in protection of gingiva from scar formation.

ACKNOWLEDGEMENTS: Supported by the Canadian Institutes of Health Research and the Arthritis Society.

12. Frequency Of Cluster, Migraine And Tension Headaches Symptoms In Sleep Disordered Breathing Patients

Fastlicht S*, Mehta S, Almeida FR, Lowe AA
Faculty of Dentistry, The University of British Columbia, Vancouver, Canada

OBJECTIVES: Migraine, tension, and cluster headaches are frequently related to sleep. Reports of headache prevalence in OSA subjects range between 15% to 50%. When sleep disordered breathing (SDB) is treated successfully, headaches generally improve which suggests a possible relationship between SDB and headache symptoms. Migraines have been known to occur during sleep or after daytime naps and may be triggered either by lack of sleep or by excess sleep. Migraine patients will often manage the headache by going to sleep. Tension headaches, the most common but least studied, are often managed by sleep regulation. Cluster headaches which occur in attack clusters followed by pain free intervals occur at night during sleep.

METHODS: A series of 150 consecutive SDB patients diagnosed by in hospital overnight polysomnograms elected to pursue oral appliance therapy in the Dental Sleep Apnea Clinic at The University of British Columbia. All patients completed intake MIDAS questionnaires to evaluate headache frequency, type and severity.

RESULTS: Out of the 150 patients (21-77Y), some 72 suffered from headaches and 78 did not. Patients that suffered from headaches were younger (47.5 vs 50.9Y) but females with headaches were older (mean of 52.0F vs. mean 46.7M). Females also exhibited a higher incidence of headaches than males (31/50F vs. 41/100M). The perception of pain or severity of the headaches was higher in women. Overall, headache severity correlated with a higher RDI ($p<0.05$) and an increase in the HI ($p<0.05$). Of those individuals who reported headaches, 79.2% experienced morning headaches. A higher incidence of nausea, sensitivity to light, sensitivity to sound and smell was observed in females, while no significant difference was identified between the sexes for vomiting or tearing of the eyes. Alleviating factors were medication, silence, rest and a dark room. Of the individuals who suffered with headaches, 37.5% reported conjunctival injection, 29.2% had rhinorrhea, 16.7% experienced facial sweating while 13.9% reported ptosis. Headache duration was between one to six hours in 50.7% of the patients.

CONCLUSIONS: Features associated with migraine, tension and cluster headaches were observed in a population of SDB patients who presented at the Dental Sleep Apnea Clinic at The University of British Columbia. Females exhibited a higher incidence of headaches and reported greater severity than males. Headache severity correlated with a higher RDI and an increase in the HI. Of the individuals who reported headaches, 79.2% experienced morning headaches. A higher incidence of nausea, sensitivity to light, sensitivity to sound and smell was observed in females. While the interaction between headaches and OSA remains controversial, our findings suggest that headaches are frequent in OSA patients. Clinicians involved with OSA therapy might consider incorporating questions about headaches on their intake questionnaire. Headache investigations could become a part of routine practice for clinicians who treat sleep disorders. Further study is required to evaluate whether headaches improve with oral appliance therapy for SDB.

13. Absence Of αvβ6 Integrin Is Linked To Initiation And Progression Of Periodontal Disease

Ghannad F[1]*, Nica D[1], Garcia MI[1], Grenier D[2], Johnston S[1], Eslami A[1], Koivisto L[1], Jiang G[1], Putnins EE[1], McKee MD[3], Häkkinen L[1], Larjava HS[1]
[1] *Laboratory of Periodontal Biology, Faculty of Dentistry, The University of British Columbia, Vancouver, Canada;* [2] *Faculty of Dentistry & Medicine, Laval University, Montreal, Canada;* [3] *Faculty of Dentistry and Department of Anatomy & Cell Biology, McGill University, Montreal, Canada*

OBJECTIVES: Integrin αvβ6 is mostly absent from adult epithelia but its expression is induced in wound healing, cancer and certain fibrotic disorders. In the present study, we investigated the hypothesis that αvβ6 integrin-mediated TGFβ1 activation in the junctional epithelium (JE) plays a major protective role in inflammatory periodontal disease.

METHODS: Expression of αvβ6 integrin and its ligands was studied in normal and regenerating JE of human and murine gingiva using immunohistochemistry. Cytokine and bacterial regulation of αvβ6 integrin expression in cultured keratinocytes was studied using real-time PCR. Bone loss around molars of wild-type FVB and β6 integrin knockout mice was assessed using morphometry and high resolution radiographs. Specific antibodies against β6 integrin were used to block αvβ6 integrin-mediated TGFβ1 activation in a rat model of periodontal disease initiation.

RESULTS: In the present study, we observed that αvβ6 integrin is constitutively expressed in the healthy epithelium linking gingival epithelium to the tooth enamel (i.e. junctional epithelium). Its expression was, however, downregulated in human periodontal disease. Remarkably, integrin β6 knockout mice developed classical signs of spontaneous, chronic periodontal disease with inflammation, epithelial down-growth, pocket formation and bone loss around the teeth. Integrin αvβ6 acts as a major activator of TGFβ1, a key anti-inflammatory regulator in the immune system. We found that TGFβ1 was expressed in the healthy junctional epithelium together with αvβ6 integrin and that an antibody that blocks αvβ6 integrin-mediated activation of TGFβ1 initiated inflammatory periodontal disease in a rat model.

CONCLUSIONS: Thus, αvβ6 integrin is constitutively expressed in the epithelium sealing the gingiva to the tooth, and it plays a central protective role against inflammatory periodontal disease via TGFβ1 activation.

ACKNOWLEDGEMENTS: This study was supported by a research grant from the Canadian Institutes of Health Research.

14. Surface Topography Modulates Src Phosphorylation And Subsequent Macrophage Signaling

Ghrebi SS[1]*, Hamilton DW[2], Waterfield JD[1], Brunette DM[1]
[1] *Department of Oral Biological & Medical Sciences, The University of British Columbia, Vancouver, Canada;*
[2] *Schulich School of Medicine & Dentistry, The University of Western Ontario, London, Canada*

OBJECTIVES: The geometry of implant surface topography alters cell behaviour. Macrophages are among the first cell types to attach to implants and play a critical role in inflammatory responses and wound healing. The mode and type of macrophage activation modulate their secretory profile. Available data shows that rough surface topography increases pro-inflammatory cytokines (IL-1, IL-6, and TNF-α) secretion by macrophages stimulated with suboptimal concentration of LPS. The control of cytokine secretion involves several signaling pathways. One such pathway involves focal adhesion kinase (FAK). A phosphorylated tyrosine in FAK provides specific binding sites for Src family kinases. Src is important in expression of pro-inflammatory cytokines IL-1 and TNF-α through MAP kinase signaling pathway. Our objective was to study the effect of different implant surface topographies on signalling cascades involved in macrophage activation.

METHODS: Macrophages (RAW 264.7) were seeded on Titanium-coated epoxy replicas of polished, blasted, etched, and blasted & etched (SLA) surfaces. Immunocytochemistry and Western blotting techniques were used to analyze the effect of these surfaces. Phospho-FAK, Src and ERK1/2 were tested and PP1; a Src specific inhibitor was used.

RESULTS: Immunostaining showed that rough surfaces increased macrophage Src phosphorylation at two and three days. ERK1/2 phosphorylation was increased at one day but decreased by day three compared to macrophages on polished surfaces. Western blotting analysis showed that all surfaces activated ERK1/2 in macrophages. Activation appeared to be down regulated on rough surfaces at three days when compared to polished [t-test, $p<0.05$]. In contrast, SLA appeared to increase ERK1/2 activation at one day but this was not significant. The PP1 Src kinase inhibitor reduced ERK1/2 phosphorylation on all surfaces at all time points [t-test, $p<0.05$].

CONCLUSIONS: These results suggest that implant surface topography modulates signalling pathways, which are known to control cytokine release and thus influence wound healing around implants.

ACKNOWLEDGEMENTS: Funded by a New Emerging Team Grant from the Canadian Institutes of Health Research.

15. Molecular Scrutiny Of Primary And Successional Tooth Development In Squamates (Reptilia)

Handrigan G[1]*, Buchtová M[2], Tucker A[3], Leung K[1], Richman JM[1]
[1] Department of Oral Health Sciences, Life Sciences Institute, The University of British Columbia, Vancouver, Canada; [2] Academy of Sciences, Brno, Czech Republic; [3] Craniofacial Development & Orthodontics, Kings College London, London, UK

OBJECTIVES: Research by our group considers the molecular regulation of primary and successional tooth development. Our specific goals include: 1) To compare gene expression between developing poly- and mono-phyodont dentitions; 2) To identify key molecules in tooth replacement; and 3) To infer developmental bases for variation in tooth number.

METHODS: For this work, we are studying the snakes Python and Elaphe, and the lizard Pogona. All three are polyphyodont and present a much longer dental lamina than the mouse. Reptile dental laminae grow in a characteristic direction and show asymmetry in both tooth-budding and cell proliferation. To understand the molecular basis for this, we have studied the gene Sonic hedgehog (Shh), which controls dental epithelial ingrowth in mammals. We cloned Python Shh and surveyed its expression during squamate odontogenesis. Furthermore, using reptile jaw explant and slice cultures approaches, we tested the gene's role in tooth development in both gain- and loss-of-function experiments.

RESULTS: In snakes, Shh is expressed in the presumptive dental epithelium and, at later stages, in the oral epithelium. This expression domain persists throughout the prehatching period in Python, but is prematurely lost in Pogona, which forms relatively fewer teeth. In both species, Shh is expressed in primary and generational enamel organs, but, surprisingly, is missing from the generational rudiment. Shh loss-of-function experiments led to shorter laminae that lacked their characteristic angulation and asymmetry in cell proliferation. In contrast, Shh gain-of-function produced longer laminae, further confirming that the gene drives dental epithelial ingrowth.

CONCLUSIONS: Our data reveal a clear role for Shh in squamate tooth development, but suggest it may be acting differently in primary versus successional odontogenesis. Furthermore, variation in tooth number correlates with the temporal persistence of oral Shh expression.

ACKNOWLEDGEMENTS: This work is funded by NSERC/MSFHR fellowships to GRH and an NSERC operating grant to JMR.

16. Regulation And Function Of A BMP Receptor Antagonist In The Face

Higashihori N*, Song Y-P, Richman JM
Department of Oral Health Sciences, Life Sciences Institute, The University of British Columbia, Vancouver, Canada

OBJECTIVES: 1) To map expression of a decoy receptor for Bone morphogenetic protein, Bambi in the developing face. 2) To identify growth factors that regulate the expression of Bambi in the lip fusion zone. 3) To test the function of BAMBI in a retroviral over expression experiment.

METHODS: A chicken Bambi probe was used in wholemount in situ hybridization to map expression in several stages of chicken embryos. To target growth factors in the face, microscopic beads were first soaked in either Bone morphogenetic protein-7, Noggin, Fibroblast growth factor-2 or retinoic acid and then implanted into the 4.5 day chicken embryo face. The full length human BAMBI open reading frame was cloned into RCAS (an avian retrovirus). Live virus was injected into the face of embryos.

RESULTS: During early development, expression of Bambi was limited to the endoderm. There was little expression within the embryo proper until organogenesis stages. From 3.5 days and onwards, Bambi expression almost perfectly overlapped with known expression patterns for BMP4, particularly in the face. Bead implant experiments showed that Bambi was strongly upregulated by BMP7 and retinoic acid but downregulated by Noggin (a BMP antagonist) and FGF2. The main phenotype caused by BAMBI over-expression was a selective loss of intramembranous bone in 50% of injected specimens (12/23).

CONCLUSIONS: Our data point to retinoids and BMPs as being major positive regulators of Bambi expression but that retinoic acid is more involved with ectodermal than mesenchymal expression. Furthermore, FGF2 represses Bambi expression and therefore may help to restrict Bambi to certain regions of the face. This result also demonstrates a novel point of intersection between the FGF and BMP pathways. The virus phenotypes suggest that BAMBI may prefer to interact with BMPR1a (ubiquitously expressed) rather than BMPR1b (more highly expressed in cartilage). This is the first demonstration of a selective difference in affinity for type I BMP receptors by BAMBI.

ACKNOWLEDGEMENTS: This work was funded by CIHR grants to JMR. JMR is a Michael Smith Foundation for Health Research Distinguished Scholar.

17. Expression Of Small Leucine-Rich Proteoglycans And Transforming Growth Factor-β In Human Oral Mucosal Wound Regeneration

Honardoust D*, Eslami A, Larjava H, Häkkinen L
Department of Oral Biological & Medical Sciences, Faculty of Dentistry, The University of British Columbia, Vancouver, Canada

OBJECTIVES: The hallmark of scar formation is excessive accumulation of abnormally organized collagen in response to increased activity of transforming growth factor-β (TGF-β). Remarkably, wound healing in human oral mucosa rarely results to scar formation. Thus, understanding the mechanisms involved in oral wound healing may provide important information about the biological processes that regulate scar formation. The small leucine-rich proteoglycans (SLRPs), decorin, biglycan, fibromodulin, and lumican, are extracellular matrix (ECM) molecules that interact with type I collagen and regulate collagen fibrillogenesis. SLRPs also bind to TGF-β inhibiting its biological activity. Our aim was to analyze the expression of SLRPs and TGF-β during human gingival wound regeneration.

METHODS: Expression of SLRPs, TGF-β1, TGF-β3 and collagen deposition and organization were analyzed in frozen sections from full-thickness, excisional human gingival wounds (collected 3-60 days after wounding) by immunohistochemical and histochemical techniques.

RESULTS: Expression of the studied molecules were spatio-temporally regulated in distinct wound cells and ECM. Strongest upregulation for all of the molecules except lumican occurred from day 7 to 28 after wounding. After 60 days, expression of lumican remained still reduced while the expression of decorin, fibromodulin and TGF-β3 were still upregulated. Gradual increase in expression of SLRPs correlated with maturation of collagen in the wound ECM. Expression of fibromodulin, lumican and TGF-β1 and -3 were spatio-temporally upregulated also in the wound epithelium.

CONCLUSIONS: Expression of SLRPs is spatio-temporally regulated in parallel with increased expression of TGF-β and collagen maturation at different stages of wound healing suggesting that SLRPs collaborate to regulate collagen organization and TGF-β activity in wound regeneration.

ACKNOWLEDGEMENTS: Supported by the Canadian Institutes of Health Research.

18. Craniofacial Development Studies In The Richman Lab

Hosseini S*, Higashihori N, Geetha-Loganathan P, Nimmagadda S, Handrigan G, Richman JM
Department of Oral Health Sciences, Life Sciences Institute, The University of British Columbia, Vancouver, Canada

OBJECTIVES: Our laboratory is working on three main research themes: mechanisms of cleft lip, jaw identity, and evolution and development of amniote teeth. The most common group of craniofacial anomalies is orofacial clefts; however it is also common to see discrepancies in the size and shape of the jaws and problems with tooth number. Our lab uses oviparous species such as chicken, emu and snake to study signalling involved in jaw patterning and tooth formation. The long-term goal is to prevent human jaw and tooth deformities through a better understanding of the molecules involved.

METHODS: Our approach is to first map expression of genes at several different stages in the embryonic face. These patterns of expression then are used to plan our experimental approaches to test in the embryo. In the gain-of-function experiments, we overexpress the signals using RCAS vectors or by injecting cells that express those signals or beads soaked in purified proteins. In the loss-of-function experiments, we block signalling pathways by using dominant-negative RCAS constructs, by injecting cells expressing antagonists or by applying beads soaked in antagonists.

RESULTS: In the Cleft Lip project, we have identified novel requirements for FGF signalling but these FGF dependent regions are not near the zone of fusion. Instead FGF dependence is greatest near the top of the nasal slit and when blocked, the embryos develop cleft lip. We are now working on the Wnt pathway to see which Wnts are expressed in the face and whether other growth factors regulate their expression. In the Jaw Identity project we have used a microarray approach to identify genes that are involved in specifying frontonasal mass identity. Several of these genes are now being followed up with functional studies. In the Reptile Project we have found that Sonic hedgehog is expressed within the odontogenic band, the first region of epithelium fated to make teeth. Interestingly this band is similarly present in birds even though they do not have teeth. Our data suggests conservation of the early signals is present in dentate and edentate reptiles but that later steps in tooth morphogenesis are blocked or not supported in birds.

CONCLUSIONS: Our data provide an explanation for how abnormalities in signalling could cause facial defects and failure to form primary or secondary teeth.

ACKNOWLEDGEMENTS: This work was funded by CIHR and NSERC grants to JMR. G. Handrigan is a MSFHR and NSERC Postdoctoral Fellow. JMR is a MSFHR Distinguished Sholar.

19. Oral Health Beliefs And Treatment Needs Of LTC Chinese Seniors

Hui N*, O'Connor D, MacEntee MI
Department of Oral Health Sciences, Faculty of Dentistry, The University of British Columbia, Vancouver, Canada

OBJECTIVES: To explore the oral health beliefs, knowledge and treatment needs of Chinese seniors living in a long term care facility in Vancouver Chinatown.

METHODS: We used open-ended, semi-structured interviews with 7 Chinese elders living in a long-term care (LTC) facility in Vancouver's Chinatown, and we analyzed transcripts of the interviews by a constant comparison of the interviews and emerging themes.

RESULTS: Three major themes emerged during our analysis: self-diagnosis; oral health knowledge; cost of dental treatment.

CONCLUSIONS: Chinese elders living in a LTC facility are aware of oral health problems but their knowledge of oral healthcare and dental services is relatively poor. Apparently, they avoid seeking dental services because of the cost of dental treatment. Clearly now there is need for further study of traditional health beliefs and practices to improve the oral healthcare of this population, and to inform dental professionals about culturally competent care for Chinese elders.

20. Application Of Fluorescence Visualization In Surgical Treatment Of High-Grade Preinvasive Oral Lesions

Kung A[1]*, Poh CF[1,2], Durham S[3], Anderson D[3], Zhang L[1], Rosin MP[1,3]
[1] *Faculty of Dentistry, The University of British Columbia, Vancouver, Canada;* [2] *B.C. Cancer Agency, Vancouver, Canada;*
[3] *Simon Fraser University, Burnaby, B.C.*

OBJECTIVES: Recurrence following excision of high-grade dysplasia/carcinoma in situ (HGL) implies the presence of subclinical change at the margins not apparent at surgery, resulting in incomplete excision. Fluorescence visualization (FV) has a demonstrated ability to identify clinically unapparent oral lesions. The objective of this study is to assess the efficacy of intraoperative FV in detecting high-risk occult tissue extending beyond clinical boundaries of HGL.

METHODS: Lesions were delineated under OR illumination and with FV in 35 patients: 22 with HGL and 13 cancers. Geographic mapping within excised tissue was used to co-localize histology with clinically apparent lesion, loss of autofluoresence (FVL) only margins and surgical margins.

RESULTS: FVL was apparent in all 35 lesions. FVL extended beyond clinical boundaries in 95% of HGL. Extension around the lesion perimeter was uneven (1-25 mm) similar to observations in cancers. 35% (13/37) of FVL/clinically negative biopsies from HGLs showed high grade dysplasia; in 5 cases, this change went beyond 10-mm, the conventional margin for cancer. In contrast, none of 35 biopsies from surgical margins, located in areas without FVL or clinical change had HGL and only 4 had mild dysplasia.

CONCLUSIONS: Integrating FV in surgery might provide a useful tool to better manage HGL through identification of subclinical field change.

ACKNOWLEDGEMENTS: Sponsored by NIDCR R01 DE17013, CIHR MOP-77663 and MSFHR grants.

21. Assessment Of PSP Sensors Used At UBC Oral Health Centre

Lam H*, Nouri R, Harrison RL
Division of Pediatric Dentistry, The University of British Columbia, Vancouver, Canada

OBJECTIVES: The aim of this study was to evaluate the fate of Photo-Stimulated Phosphor (PSP) sensors used in digital radiology and to evaluate qualitatively and quantitatively the different types of damages seen on these sensors during their first year of use at the UBC OHC.

METHODS: Damaged PSPs used during one academic year were collected; visible damage was categorized quantitatively. PSPs were repackaged, exposed to x-rays; scanned into Romexus. Resulting JPEG files were transferred into Adobe Photoshop and converted to TIFF files. Radiological damage was assessed; artifact radio-opacity was quantified and compared with radio-opacity of tooth structure using a step wedge as reference for standardization.

RESULTS: Out of 834 PSPs, only 363 (44%) were still in circulation, i.e. not missing (47%) or damaged (9%) by the end of first year of use. 41% of Size-1, 64% of Size-2 PSP sensors were missing. 10% of Size-0 films, 6% of Size-1 films, and 13% of Size-2 films were damaged. Qualitative assessment of damage revealed that scratches, clamp marks, folds and bite marks were most common types of damage. The most prevalent damage was scratches likely caused during the scanning process, return of the sensors in a cup, or during the sterilization and repackaging process. Quantitative assessment of all types of damage proved that, other than pen-mark damage that may result in radio-opacity darker than enamel, all other damage would most likely lead to radiolucencies that could result in mis-diagnosis of radiographic anomalies.

CONCLUSIONS: Loss of the PSP sensors was a significantly more serious problem than damage to the sensors. A bar-coding or tracing system should be used to diminish accidental loss of sensors in any clinical setting. Users should be trained to avoid "non-bite" damage to sensors. Protective means e.g. sponges or sleeves for PSP sensors should be developed to avoid bite-mark damage.

ACKNOWLEDGEMENTS: Special thanks to Ms. Neala Welburn, Dr. Fernanda Almeida, Dr. Andrea Esteves and Ms. Kathy Pitt. This project was Burroughs-Wellcome Summer Student Research.

22. Oral Cancer Screening – Empowering Oral Health Professionals To Save Lives

Laronde DM[1]*, Williams PM[2], Hislop TG[3], Poh CF[4], Ng S[2], Rosin MP[1,3]
[1] *Simon Fraser University, Burnaby, B.C.;* [2] *B.C. Cancer Agency, Vancouver, Canada;*
[3] *B.C. Cancer Research Centre, Vancouver, Canada;* [4] *Faculty of Dentistry, The University of British Columbia, Vancouver, Canada*

OBJECTIVES: To develop, implement and evaluate an education module, to study current oral cancer screening practices, to identify factors that influence this behavior and to gain information on the use of autofluorescence visualization (FV) in the community. Oral cancer screening is a noninvasive, quick and painless skill that all dental personnel are taught, yet less than 30% of people surveyed had ever been screened. More than 60% of oral cancers are diagnosed at a late stage where 5-year survival is poor.

METHODS: 10 dental practices from the Vancouver area participated in a workshop on oral cancer screening which reviewed etiology, epidemiology, clinical risk factors, FV and included a clinical training session. Knowledge and practice of oral cancer screening was assessed by quiz and questionnaire. Dental offices screened adults 21 years and older for 4 months collecting risk habit information, completing extraoral, intraoral and FV exams. Focus groups of the participants were conducted at the conclusion of the study.

RESULTS: 1511 were screened using FV. 42 patients with a loss of fluorescence (FVL) were referred for reassessment. 35 were reassessed by a study facilitator. 26 were found to be known confounders for FV or had resolved by reassessment. 9 lesions were referred for an oral medicine workup: 2 mild dysplasias, 2 lichen planus, 1 denture epulis, 1 is in follow-up and 3 have yet to be seen. 7 patients were referred without reassessment by the facilitator: 2 lichen planus and 5 were known confounders or normal tissue. 4 themes resulted from the focus groups: the need for mandatory oral cancer screening education, the need for screening guidelines and protocols, the need to present strategies for dialoguing with patients and the need to increase awareness among both professionals and the public.

CONCLUSIONS: Educational modules should address guidelines and patient communication skills and should integrate clinical sessions.

ACKNOWLEDGEMENTS: Supported by NIDCR grant R01DE13124 and a scholarship from the Michael Smith Foundation for Health Research to DML.

23. A Community Dental Prenatal Program: An Insider Evaluation

Lin DL*, Harrison RL, Aleksejūnienė J
Division of Pediatric Dentistry, The University of British Columbia, Vancouver, Canada

OBJECTIVES: A community dental public health program in Vancouver has been providing clinical hygiene services and oral health counseling to a limited number of high-risk, low income pregnant women for over 20 years. To enable future program decision-making, an evaluation of this program was undertaken with the following objectives: 1) to describe program and clients; 2) to determine whether program activities have been implemented as intended; and 3) to assess the program's effectiveness.

METHODS: The evaluation, undertaken by the resident dental hygienist, had two phases. Phase 1: Evaluability assessment, descriptive and process evaluation (retrospective chart reviews, semi-structured interviews, appointment statistics, and field observations). Phase 2: A short and medium-term outcomes evaluation with a convenience sample who attended over a 1-year period. Data, collected by questionnaires, semi-structured interviews, clinical indices, field observations, and appointment statistics, was analyzed with a combination of univariate and bivariate analyses.

RESULTS: Phase 1: Stakeholders' goals were identified; a logic model and organizational flowchart were developed. Chart review (N=123) revealed mean client age of 27 years; 28% Canadian-born; 48% had other children; 78% were concerned about "bleeding gums"; and 63% had visible tooth decay. 28% of women referred to the program never made an appointment. Unfamiliarity of clients with the dental "experience", language barriers, and clinic time restraints affected implementation of program's activities. Phase 2: Outcomes in clients (N=61) demonstrated significant improvements ($P<0.05$) in clinical indices, oral health knowledge and skills, and dental care for clients' children. However, 69% of clients never obtained the other dental services that they needed.

CONCLUSIONS: Evaluation revealed positive knowledge, behavioural and clinical outcomes despite language barriers, limited resources, and ill-defined program goals. However, lack of affordable and accessible comprehensive dental services resulted in considerable unmet dental needs and resulted in discrepancies between program intent and program reality.

ACKNOWLEDGEMENTS: This research was partially supported by a grant from the Canadian Dental Hygienists Association. The authors would like to acknowledge the clients and staff at the North Community Health Office Dental Clinic and the Evergreen Healthiest Babies Possible Program for their participation and help. Special thanks to Phil Feeley for his help with the data.

24. Reduced Scar Formation In Oral Mucosa Compared To Skin

Mak K[1]*, Manji A[2], Gallant-Behm CL[3], Wiebe C[1], Hart DA[3], Larjava H[1], Häkkinen L[1]
[1] *Laboratory of Periodontal Biology, Faculty of Dentistry, The University of British Columbia, Vancouver, Canada;*
[2] *University of Western Ontario, London, Canada;* [3] *University of Calgary, Calgary, Alberta*

OBJECTIVES: Scar formation following skin injury can have devastating consequences causing discomfort and functional and esthetic concerns. Interestingly, wound healing in oral mucosa appears to proceed faster than in skin and results in less scar formation. Our long-term goal is to find out the biological mechanisms that lead to better wound healing in oral mucosa and use this information to prevent scar formation in skin. In the present study, we hypothesized that oral mucosa is resistant to scar formation in red Duroc pigs that are prone to hypertrophic-like scar formation in skin. To this end, we compared wound healing in oral mucosa and skin in these animals.

METHODS: Identical (15 x 27 mm), full-thickness, excisional wounds were made in the gingiva of hard palate and dorsal skin of red Duroc pigs. Standardized images were obtained at different stages of healing to quantitate wound contraction rate and scar formation and wound biopsies were collected for histological analysis. Clinical and histological scar formation were quantitated using a scar assessment scale. The numbers of key wound healing cells were quantitated using immunostaining and image analysis.

RESULTS: Gingival wounds showed significantly less wound contraction and had clinical and histological scar assessment values significantly lower than skin wounds 60 days after wounding. The numbers of macrophages, mast cells and blood vessels were significantly lower in gingival wounds as compared to skin 60 days after wounding. The number of myofibroblasts increased strongly during wound healing in both skin and gingiva and remained significantly elevated at day 60, with gingiva having significantly more myofibroblasts than skin.

CONCLUSIONS: Gingival wounds displayed significantly less clinical and histological scar formation than skin and this was associated with significantly reduced inflammatory reaction at the late stage of wound healing. Despite of presence of more myofibroblasts, gingival wounds showed significantly less contraction than skin wounds.

ACKNOWLEDGEMENTS: Supported by grant #77550 from the Canadian Institutes of Health Research and the Arthritis Society.

25. Neuropathic Pain And Implants: Case Report

Mehta SA*
Orofacial Pain Clinic, Faculty of Dentistry, The University of British Columbia, Vancouver, Canada

OBJECTIVES: The International Association for the Study of Pain defines neuropathic pain as "pain initiated or caused by a primary lesion or dysfunction in the nervous system". Acute postoperative pain may activate peripheral nerve fibers and the pain experienced may have a direct relation to the extent of the injury. While estimates of chronic pain range between 2% to 40% of adults depending on how the question is asked and what definitions are used, the true incidence of neuropathic pain is unknown. Dental endosseous implants can result in ongoing pain to peripheral trigeminal fibers. This case report illustrates neuropathic pain associated with dental implant placement and the associated frustrations with diagnosis, management and effect to quality of life.

METHODS: A case report of an individual presenting to the University of British Columbia's Orofacial Pain Clinic with pain after dental endosseous implant is reviewed. Patient suffered ongoing chronic pain lasting greater than six months with onset after implant placement.

RESULTS: Patient underwent multiple consultations with multiple medical and dental providers with several diagnoses. Medication trial prior to consultation included multiple antibiotics, anti-inflammatories, analgesics, muscle relaxants, anti-anxiety agents, anti-depressants as well as oral appliance therapy. Levels of impact to overall quality of life were reviewed at initial examination and after trial to pain management. Pain numeric scales were utilized to record pain at time of initial consultation and during time of management.

CONCLUSIONS: Dentists placing and restoring endosseous implants should be aware of complications to such treatment including the possibility to neuropathic pain onset. Patients experiencing ongoing refractory pain after dental implant placement may require further investigation and intervention with dental providers knowledgeable about neuropathic pain. Individuals suffering these forms of pain may experience huge impact to quality of life as well as increased costs associated with multiple healthcare visits.

26. Dental Negligence Across Canada

Moore B*, MacDonald D
Faculty of Dentistry, The University of British Columbia, Vancouver, Canada

OBJECTIVES: The self-regulatory bodies governing the practice of dentistry vary across Canada by province. In British Columbia, the College of Dental Surgeons of BC fills this role. In times of failure of the dentist-patient relationship, when remediation is sought beyond which the regulatory body can achieve a resolution, proceedings are generally expressed as negligence in a court of law. With regulatory bodies and courts differing across Canada by province, the aim of this study was to investigate the distribution of such cases. It must be noted emphatically that these distributions are indicative of the desires of the patients to litigate and likely other reasons which will not be explored – they are not to be interpreted as differing regional levels of professional negligence.

METHODS: The Canadian Legal Information Institute (http://www.CANLII.org), an online database of Canadian legal documents, was used to isolate and analyze negligence cases relating to the practice of dentistry and medicine. It was necessary to exclude motor vehicle accidents for the purposes of the research. An example of a search would be: "dentist /7 patient AND negligence OR malpractice NOT vehicle". The '/7 patient' refines the search to include only court documents containing dentist and patient within 7 words of each other.

RESULTS: As a result of the research, it was determined that there are indeed certain provinces where patients are more inclined to litigate than others. British Columbia was found to have the greatest proportion of Canadian dental and medical negligence cases heard in court, when adjusted for population, at 27% and 43%, respectively. In contrast, Ontario was found to have the smallest proportions at 8% for dental cases and 7% for medical cases. Furthermore, the distribution of dental negligence cases across Canada was observed to be quite similar to that found for medical negligence cases.

CONCLUSIONS: Clearly, there exists a difference in the number of negligence cases being heard in courts across Canada and these findings certainly warrant further investigation.

ACKNOWLEDGEMENTS: We are grateful to Mary Mitchell , UBC Law Librarian, for her invaluable assistance.

27. Characterization Of Marimastat-FITC: A Modified Matrix Metalloproteinase Inhibitor

Munsie S*, Harwig C, Perrin D, auf dem Keller U, Overall CM | *Centre for Blood Research, The University of British Columbia, Vancouver, Canada*

OBJECTIVES: This study tests marimastat that was modified by adding a fluorescent probe (FITC) to see if it is still an efficient MMP inhibitor, is able to bind specifically to MMPs and to determine if Marimastat-FITC binds to MT1-MMP overexpressed on the surface of cultured cells.

METHODS: Enzyme Kinetics assay of MMP-2 with Marimastat-FITC inhibitor, polyarcylamide gel analysis of MMP-2 incubated with Marimastat-FITC and incubation of Marimastat-FITC in human MDA cells overexpressing MT1-MMP.

RESULTS: Results showed that Marimastat-FITC is an effective MMP inhibitor with an IC50 of 7nM (compared to the unmodified Marimastat: 6nM), Marimastat-FITC specifically binds MMP-2 on polyacrylamide gels and effectively binds MT1-MMP in cell culture (human MDA-MB-231 cells).

CONCLUSIONS: MMPs, a family of proteases known to cleave many elements of the extracellular matrix as well as various inflammatory-related proteins, are implicated in periodontal disease, arthritis and cancer metastasis. Modified MMP inhibitors such as Marimastat-FITC may be useful tools for imaging MMPs in future studies of these conditions.

ACKNOWLEDGEMENTS: Funding for this project was provided by the Canadian Breast Cancer Research Alliance (CBCRA).

28. Microarray Analysis Identifies New Targets Of Retinoic Acid And Noggin

Nimmagadda S*, Buchtová M, Geetha-Loganathan P, Richman JM
Department of Oral Health Sciences, Life Sciences Institute, The University of British Columbia, Vancouver, Canada

OBJECTIVES: Previously we identified Retinoic Acid and Noggin as two molecules that can transform the maxilla into the midline of the face. This striking phenotype was due to a localized increase in retinoic acid and blocking of BMP signalling with Noggin. We have since carried out a microarray analysis of the genes differentially expressed in the presence of RA and Noggin, RA+Tris, Noggin+DMOS and control Tris+DMSO. The objective of this study is to validate the gene expression changes seen on the chicken genome chips with in situ hybridization studies and then to follow the most promising of these genes with functional studies.

METHODS: Beads soaked in RA and Noggin are applied to the maxillary region of 2.5 day chicken embryos. Following 16h of treatment, embryos are collected and in situ hybridization carried out. Genes that are upregulated on the array are cloned into RCAS retroviruses and then over expressed in 2.5 day chicken embryos. Effect on gene expression and skull morphogenesis is analyzed.

RESULTS: In general, genes strongly upregulated following RA Noggin treatment are also upregulated in wholemount in situ analyses. For example, transcription factor Tbx22 and enzyme PI15 are both increased around the RA Noggin beads. In addition Tbx22 is upregulated by Noggin+DMSO or RA+Tris. PI15 is also upregulated following RA-Noggin bead implants. Interestingly expression is more strongly upregulated around the RA bead. Embryos injected with PI15 have various skeletal defects including fusion between the upper and lower jaws. Tbx22 injected embryos also have skeletal defects in addition to duplication of the midline comb. We are currently testing whether PI15 and Tbx22 are part of the same molecular pathway.

CONCLUSIONS: Our data provide evidence for novel functions for both Tbx22 and PI15 in specifying jaw identity and controlling facial skeletal morphogenesis.

ACKNOWLEDGEMENTS: This work was funded by Canadian Institutes of Health Research grants to JMR. JMR is a Michael Smith Foundation for Health Research Distinguished Scholar.

29. Expression Pattern Of Id2 During Murine Palatal Fusion

Oda R[1]*, Cui X-M[2], Schmid D[2], Yamashiro K[1], Shuler CF[1]
[1] *Department of Oral Biological & Medical Sciences, Faculty of Dentistry, The University of British Columbia, Vancouver, Canada;*
[2] *Center for Craniofacial Molecular Biology, School of Dentistry, University of Southern California, Los Angeles, USA*

OBJECTIVES: Transforming growth factor (TGF)-β3 is known to regulate the disappearance of murine medial edge epithelium (MEE) during palatal fusion. TGF-β3 null mutant mice (TGF-β3-/-) have a phenotype characterized by cleft palate. Overexpression of Smad2 in the MEE is capable of rescuing the cleft palate in TGF-β3-/- mice, however the downstream effects of activated Smad2 have not yet been determined. The Inhibitor of DNA binding (Id) proteins are negative regulators of basic helix-loop-helix transcription factors and involved in cellular differentiation and proliferation. It has been reported that Id1 is expressed in both palatal mesenchyme and epithelium. The sites of expression and timing of expression suggest that Ids might be involved in mechanisms related to palatogenesis. The purpose of this study was to examine Id2 expression during murine palatal fusion.

METHODS: Expression of Id2 at mRNA and protein levels was examined by RT-PCR, in situ hybridization and immunohistochemistry.

RESULTS: Id2 mRNA was present in the palatal shelves before and during normal palatal fusion. By whole-mount in situ hybridization, the antisense probe specifically hybridized to Id2 transcripts in the tips of horizontal palatal shelves, the site of the MEE. Immunohistochemistry demonstrated an absence of the nuclear staining of Id2 protein in vertical palatal shelves at gestation day E13. Intense nuclear staining specific for Id2 was clearly identified in the MEE cells when the horizontal palatal shelves remained in contact (E14, E14.5). The pattern of Id2 gene expression and localization of the Id2 protein was coincident with the appearance of phospho-Smad2 in MEE cells.

CONCLUSIONS: The temporal and spatial localization of Id2 indicates that it may be a downstream signaling target of the TGF-β3/Smad2 signaling pathway and play an important role in the regulation of MEE disappearance during murine palatal fusion.

ACKNOWLEDGEMENTS: Supported by NIDCR grant R01 DE16296.

30. 3D Comparison Of Cardiac Development In Kyoto And Carnegie Human Embryos

Park J*, Diewert VM
Department of Oral Health Sciences, Faculty of Dentistry, The University of British Columbia, Vancouver, Canada

OBJECTIVES: To compare the stages of cardiac development in Kyoto embryos to that in Carnegie embryos documented in the literature. To reconstruct 3D images from normal serially-sectioned Kyoto embryos of stages 16, 17 and 18.

METHODS: Photographs of serially-sectioned Kyoto embryos of stages 16-18 (Diewert Collection) were studied. WinSURF software was used to make 3D models of selected serially-sectioned Kyoto embryonic hearts. Fusion of atrioventricular (AV) cushions and formation of the interventricular septum were assessed in histological sections and 3D reconstructed images.

RESULTS: Stage 16 - 2 of 6 specimens have fused endocardial cushions and divided AV canals. All show evidence of beginning stages of fusion. Interventricular septum development slightly delayed. Stage 17 - Only 4 of 13 specimens have fused cushions. The muscular interventricular septum is more prominent but the muscular IVS is not fused to the cardiac cushions. Stage 18 - All (4/4) have fused AV cushions, separating the AV canal. Incomplete closure of secondary interventricular foramen in all specimens.

CONCLUSIONS: Heart development in Kyoto embryos appears delayed at stage 17. Fusion of facial prominences to form the upper lip is delayed in Kyoto embryos. Although heart and face development were delayed in stage 17 Kyoto embryos studied, by stage 18 normal Kyoto embryos were similar to Carnegie embryos on which most of the literature is based.

31. Versican Degradation By Macrophage Metalloproteinases MMP-7 And MMP-12 In Resolution Of Wound Healing

Pourmalek S*, Dean R, Overall CM, Roberts CR
Centre for Blood Research, The University of British Columbia, Vancouver, Canada

OBJECTIVES: The proteoglycan versican is a component of the provisional matrix laid down in the process of wound healing. Typically, fibroblasts migrate into the area of clot, adopt a myofibroblast phenotype, which includes increased versican production, and proliferate. They sysnthesize collagen in this versican-rich matrix. Return to normal tissue structure, at late stages of wound healing, involves degradation of versican and concomitant (myo)fibroblast apoptosis. Fibrosis involves excessive deposition of collagen, and versican and myofibroblasts persist in all forms of fibrosis studied. The mechanism of versican degradation, and whether versican degradation is mechanistically linked to cell apoptosis, are unknown. In pulmonary tissue remodelling and fibrosis, our data shows that macrophages localize to versican-rich fibroproliferative lesions. We hypothesized that macrophage metalloproteinases are involved in versican degradation, and could affect the balance between resolution and progression to fibrosis. Bronchiolitis obliterans organizing pneumonia (BOOP) is a condition where airspace lesions resolve; we have shown that macrophages are spatially and temporally associated with disappearance of lesions. In human BOOP, versican-associated macrophages express MMP-7 and MMP-12.

METHODS: We studied degradation of versican by purified and recombinant macrophage matrix metalloproteinases 2, 7 and 12.

RESULTS: A comparison of versican degradation by macrophage matrix metalloproteinases revealed that versican is cleaved efficiently by MMP-7 and MMP-12, but less rapidly and with fewer cleavage sites by MMP-2. An MMP-7 cleavage site was determined in the lectin like domain of the versican C-terminal region by N-terminal sequencing.

CONCLUSIONS: Disappearance of versican rich provisional matrix is concomitant with accumulation of macrophages that express matrix-degrading metalloproteinases, particularly MMP-7 and MMP-12.

ACKNOWLEDGEMENTS: This work was supported by operating grants from CIHR and the B.C. Lung Association, a Tonzetich studentship to SP, and a CFI grant to The UBC Centre for Blood Research.

32. Betel Chewing And Oral Mucosal Lesions In A Vietnamese Population

Priebe SL[1]*, Hong NT[2], Cuc TTK[2], Ngoc NTB[2]
[1] Faculty of Dentistry, The University of British Columbia, Vancouver, Canada; [2] Faculty of Odonto-Stomatology, University of Ho Chi Minh City, Vietnam

OBJECTIVES: Betel quid chewing is a habit consisting of a betel leaf, areca nut and slaked lime. A population sample from Vietnam where betel plants and areca palm trees are grown was studied. The objectives were to investigate the modalities of betel quid chewing and to determine the prevalence of oral mucosal lesions.

METHODS: Two groups, one of 152 chewers and the other of 137 non chewers were examined by 2 calibrated examiners.

RESULTS: The prevalence of oral mucosal lesions was significantly higher in chewers (80.4%) as compared to non chewers (37.2%), including betel chewer's mucosa (66%), oral submucous fibrosis (13%), lichen planus (5.2%), and leukoplakia (3.9%). Tobacco is added (81.7%).

CONCLUSIONS: Prevention and management of oral mucosal lesions should be addressed in health care programs of this region as well as a dental professional awareness of oral mucosal lesions in these populations in countries where they have immigrated to.

33. Testing A Model For Assessing Quality Of Dental Geriatric Programs

Pruksapong M*, MacEntee MI
Department of Oral Health Sciences, Faculty of Dentistry, The University of British Columbia, Vancouver, Canada

OBJECTIVES: Quality assessment in dental geriatrics is difficult because there are no widely accepted care objectives or quality indicators. We have proposed a model for assessing quality of oral healthcare services in long-term care facilities based on a combination of theoretical principles of quality assessment in general healthcare and empirical information specifically about dental geriatrics from an ethnographic case study of a university-based program in Vancouver. This study reports on the testing of the model when applied to another dental geriatric program in northern British Columbia. It aims to firstly, evaluate the feasibility and usability of the model; and secondly, explain how the model was revised following this application.

METHODS: The process and product of applying the assessment model was evaluated against a series of feasibility and usability criteria endorsed by leading quality management agencies. We applied the assessment model by conducting 15 interviews with participants in the program, made site-visits to the 5 facilities, and reviewed documents on the development and operations of the program.

RESULTS: The model was feasible because 1) the data required is available within the normal operational flow of the program; 2) the cost and time required for assessment is reasonable; 3) confidentiality is addressed; and 4) audit trails are available. However, the label and descriptors of some quality indicators were expanded to fit the different contexts. In addition, the usability of the model needs modification because it helps the assessment process but lacks mechanism to prompt improvement of the program without aids for building organizational capacity such as data collection forms and automated information system.

CONCLUSIONS: The original model, with minor modification provides a feasible and useful process for assessing the quality of community-based dental geriatric programs.

ACKNOWLEDGEMENTS: This study was support by the S. Wah Lueng Endowment Fund, UBC Faculty of Dentistry.

34. Role Of Cathepsin K In Atherosclerosis Progression

Samokhin A[1]*, Wong A[1], Saftig P[2], Brömme D[1]
[1] *Department of Oral Biological & Medical Sciences, Faculty of Dentistry, The University of British Columbia, Vancouver, Canada;*
[2] *Biochemisches Institut, Christian-Albrechts-Universität Kiel, Kiel, Germany*

OBJECTIVES: Stability and elasticity of blood vessels mainly depend on the presence and integrity of elastic and collagen fibers. Recent studies have shown that lysosomal cysteine proteinases such as cathepsins K, S, V and L represent the most potent elastinolytic and collagenolytic activities in mammalian tissues.

METHODS: To elucidate the role of cathepsin K, which exerts both a strong collagenolytic and elastinolytic activity, we analyzed the effect of cathepsin K-deficiency (ctsK-/-) on atherosclerosis progression in brachiocephalic arteries of atherosclerosis-prone ApoE-deficient mice on high fat diet (HFD).

RESULTS: CtsK-/- mice had significantly less macrophages in tunica media while the number of smooth muscle cells was higher. After 8 weeks of HFD fat diet the collagen content in plaque areas and fibrous cap thickness were significantly higher in the ctsK-/- mice and they had smaller number of buried fibrous caps which are considered to be a hallmark of plaque rupture. Of note, ctsK-/- mice revealed a lower number of elastin fiber breaks which was also reflected by lower levels of serum desmosine. These differences resulted in smaller plaques areas after 16 weeks of HFD when compared to their cathepsin K expressing littermates. Higher plaque stability in ctsK-/- mice also correlated with a decrease in cell apoptosis. Immunohistochemical analysis has shown the presence of cathepsin K in macrophages and smooth muscle cells but significantly stronger staining for this proteinase was revealed in multinucleated giant cells. Cathepsin K-positive multinucleated giant cells were often seen attached to elastin fibers and in the vicinity of the fibrous cap.

CONCLUSIONS: Cathepsin K expression contributes to the destruction of elastin matrix of aortic wall that facilitates migration of smooth muscle cells from the media. The collagenolytic activity of cathepsin K contributes to plaque destabilization by weakening of the collagen-containing fibrous cap of atherosclerotic plaques.

35. Sleep Disordered Breathing Symptoms And Craniofacial Morphology In Children

Tsuda H*, Almeida FR, Fastlicht S, Chen H, Lowe AA
Faculty of Dentistry, The University of British Columbia, Vancouver, Canada

OBJECTIVES: Snoring in children may be an important sign of sleep disordered breathing (SDB), the consequences of which may include failure to thrive, behavioral disturbance, excessive daytime sleepiness, attention-deficit/hyperactivity disorder and reduced learning (Schechter, 2002). Adenotonsillar hypertrophy is the biggest risk factor and SDB children may exhibit craniofacial and/or dental arch abnormalities. Some orthodontic treatments (maxillary expansion and/or mandibular advancement) beneficially affect snoring and SDB. The aim of this study was to assess in children, by means of a standardized questionnaire and cephalograms from an orthodontic teaching clinic, the relationship between SDB symptoms and craniofacial morphology.

METHODS: All parents were asked to complete a SDB questionnaire (OSA 18, Franco, 2000) at the commencement of orthodontic therapy. The eighteen questions were scored on a graded scale as "none, hardly any, a little, some, a good bit, most of or all the time". Higher scores indicate a greater probability of disease and/or a reduced quality of life. The questions were divided into five domains: sleep disturbance, physical symptoms, emotional symptoms, daytime functions and caregiver concerns. The UBC cephalometric analysis included upper, lower and total face height, hyoid position, soft palate length, mandibular length, vertical airway length, overjet and overbite. Statistical analyses were performed with SPSS 10.0 with statistical significance as a 2-tailed P value less than 0.05. Spearman rank correlations ($R \geq 0.145$) were applied between the questionnaire scores and cephalometric variables. Unpaired student t-tests compared gender and continuous variables.

RESULTS: A total of 184 children (male 47.3%, mean age 10.18±1.91 years) completed the OSA questionnaire and the cephalometric analysis. The questionnaire suggested that only two children in the UBC orthodontic pool (1.1%) had a higher chance of exhibiting SDB. The mean score from the questionnaire was 26.2±9.4 (26.6±9.3 for Class I, 25.4±9.3 for Class II, Division 1 and 27.5±10.7 for Class II, Division 2 patients). Neither gender nor Angle molar classification revealed significant differences in the questionnaire scores except for aggression/hyperactivity between the genders. Loud snoring, mouth breathing and difficulty awakening were seen in more than 20% of the children. Snoring revealed a significant correlation with mouth breathing ($p<0.001$) but demonstrated no correlation with difficulty in awakening. A higher prevalence of snoring correlated with a lower hyoid position ($p<0.001$) and a longer airway ($p<0.05$). The higher incidence of mouth breathing and dysphasia were correlated with a lower hyoid position ($p<0.001$) and a greater interincisal angle ($p<0.05$). Frequent mouth breathing had a significant correlation ($p<0.05$) with upper incisor angulation. A high sleep disturbance probability ($p<0.05$) correlated with a low hyoid bone position, retroclined upper incisors and a deep overbite. Greater impairment of daytime function ($p<0.05$) correlated with a long soft palate, a high interincisal angle, more retroclined upper incisors and a deeper overbite.

CONCLUSIONS: The incidence of SDB in an undergraduate orthodontic teaching clinic appears to be relatively low at 1.1%. SDB symptoms were related to a low hyoid bone position, a long soft palate, an elongated airway, a high interincisal angle and a deep overbite. It appears that attributes of SDB in growing children may be directly related to specific craniofacial variables.

36. Cathepsin K Activity Dependent Regulation Of Osteoclast Actin Ring Formation

Wilson SR[1]*, Peters C[2], Saftig P[3], Brömme D[1]
[1] *Faculty of Dentistry, Centre for Blood Research, The University of British Columbia, Vancouver, Canada;* [2] *Albert-Ludwigs-Universität Freiburg, Institut für Molekulare Medizin und Zellforschung, Freiburg, Germany;* [3] *Biochemishes Institut, Christian-Albrechts-Universität Kiel, Kiel, Germany*

OBJECTIVES: Cathepsin K (catK) is responsible for the degradation of type I collagen in osteoclast mediated bone resorption. As collagen fragments can be biologically active, this study investigates their potential regulatory effect on osteoclasts.

METHODS: Soluble type I collagen, type II collagen, and bone powder were subject to degradation reactions by catK, L and MMP-1. Soluble collagen degradation products or GRGDS peptides were added to murine osteoclasts seeded on type I collagen substrate. Alternatively, the collagen substrate was predigested with catK or L. Wild type, catK and catL deficient osteoclasts were also treated with cysteine proteinase inhibitor LHVS and MMP inhibitor GM6001. After 24h, osteoclasts were stained with FITC-phalloidin and actin rings were counted as a percentage of total osteoclast number.

RESULTS: Osteoclasts treated with catK degraded type I collagen or bone demonstrated a lower percentage of actin rings. However, this was shown with neither undegraded collagen, nor collagen degraded by MMP-1 or catL. This inhibition could be partially abrogated by the presence of a vitronectin receptor blocking antibody. Both catK deficient osteoclasts and wild type osteoclasts treated with LHVS were found to have a lower basal level of active osteoclasts compared to untreated wild type cells. The number of actin rings was increased by seeding catK deficient osteoclasts on catK pre-digested type I collagen but not catL pre-digested collagen. MMP inhibition had no effect on osteoclast actin ring percentage in this study.

CONCLUSIONS: CatK is known to be the most efficient mammalian collagenase. These studies suggest it may release cryptic collagen fragments containing RGD sequences. These soluble fragments may interact with osteoclast integrin receptors disrupting the actin ring. In addition, uncovered RGD sequences in the collagen matrix may allow integrin binding of catK deficient osteoclasts. This is a novel regulatory role for catK and collagen fragments in bone resorption.

37. Seniors Oral Health: Are Treatment Recommendations Followed-Up?

Wong A[1]*, Matthews DC[2], Clovis J[2], McNally M[2], Filiaggi M[2]
[1] *Faculty of Dentistry, The University of British Columbia, Vancouver, Canada;* [2] *Faculty of Dentistry, Dalhousie University, Halifax, Nova Scotia*

OBJECTIVES: In 2005, seniors over the age of 65 from rural and urban areas, living independently and in various levels of care, were recruited from 9 sites in Nova Scotia. They were surveyed on their oral health and given an intra-oral examination. Treatment recommendations were made based on findings, and were provided to all participants and their dentists or doctors. To determine whether or not senior participants (SPs) followed-up with their treatment recommendations with an oral health care professional, a follow-up study was performed the summer of 2007.

METHODS: A short oral health questionnaire was developed and tested. SPs were interviewed by phone or in person if a private phone was not available. Interviews that could not be done by phone were conducted by proxies (family members or nurses).

RESULTS: Of the original 146 SPs, a total of 90 interviews were completed giving a response rate of 61.64%. 58 or 64.44% of the SPs interviewed had received dental treatment within the past two years.

CONCLUSIONS: Access to dental care had a major impact on follow-up. Treatment recommendations were followed-up at higher rates by SPs living independently in urban areas (n=3 sites; 80.00%, 80.00%, 83.33%), or in a rural area that had a local full-time dentist (n=1 site; 69.23%). Follow-up was very poor for those living in more rural areas with fewer amenities (n=2 sites; 41.67 and 42.86%) and rural long-term care (LTC) residents who did not have easy access to a local dentist (n=2 sites; 0.00% and 16.67%).

ACKNOWLEDGEMENTS: Michael I. MacEntee and the Network for Oral Research Training & Health (N.O.R.T.H.).

38. Accelerated Cutaneous Wound Healing In β6 Integrin-Deficient Mice Impaired By Dexamethasone

Xie Y[1]*, Gao K[2], Häkkinen L[1], Larjava H[1]
[1] *Department of Oral Biological & Medical Sciences, Faculty of Dentistry, The University of British Columbia, Vancouver, Canada;*
[2] *Dental Research Institute, School of Dentistry, The University of California, Los Angeles, USA*

OBJECTIVES: Integrin αvβ6 is an epithelial-specific receptor that is absent from healthy epidermis but expressed de novo in wound repair. Previous studies have indicated that αvβ6 integrin binds latent TGF-β1 and that binding results in release of active TGF-β1. αvβ6 integrin dependent activation of TGF-β1 has been shown to be the main activation mechanism of TGF-β1 in vivo and also been confirmed to be pivotal in mouse models of multiple epithelial organs including lung, kidney and liver, suggesting that this mechanism may be of general importance. The beneficial effects of TGF-β1 on wound healing have been well recognized, accumulating studies, however, indicated an anti-proliferative effect and pro-inflammatory response of TGF-β1 in wound healing. The function of αvβ6 integrin in cutaneous wound healing remains to be determined.

METHODS: Full-thickness, excisional cutaneous wound model impaired by dexamethasone treatment was established in β6 integrin-deficient (β6-/-) and wild-type (WT) mice. The wound area, granulation tissue formation, re-epithelialization and regeneration of basement membrane were evaluated. Keratinocyte proliferation, infiltration of inflammation cells and production of cytokines in wound site were determined.

RESULTS: Wound healing was significantly accelerated in dexamethasone-treated β6-/- mice compared with corresponding WT mice, characterized by an increased rate of granulation tissue formation, re-epithelialization and regeneration of basement membrane. Dexamethasone-treated β6-/- mice showed accelerated keratinocyte proliferation in both wound epithelium and hair follicles while the production of pro-inflammatory cytokines and TGF-β1 was reduced.

CONCLUSIONS: Our data strongly support that accelerated wound repair in dexamethasone-treated β6-/- mice is associated with a depressed anti-proliferative and pro-inflammatory effect of TGF-β1. Use of inhibitors of αvβ6 integrin for enhancing keratinocyte proliferation and downregulating inflammatory response may provide a specific target for future therapeutic intervention in impaired wound healing.

ACKNOWLEDGEMENTS: This work was supported by a grant from the Canadian Institutes of Health Research (CIHR).

39. Periodontal Regeneration Using Engineered Rat Bone Marrow Mesenchymal Stromal Cells

Yang Y[1]*, Rossi F[2], Putnins EE[1]
[1] *Faculty of Dentistry, The University of British Columbia, Vancouver, Canada (UBC);* [2] *Biomedical Research Center, UBC*

OBJECTIVES: Periodontal regeneration presumes simultaneous reconstitution of both hard (alveolar bone, cementum) and soft (periodontal ligament) connective tissues. To date bone marrow mesenchymal stromal cells (BM-MSCs) have demonstrated connective tissue regenerative potential. We hypothesized that rat BM-MSCs expanded *ex vivo* on a resorbable scaffold will support regeneration of lost periodontal tissues.

METHODS: BM-MSCs isolated from transgenic green fluorescent protein $(GFP)^+$ Sprague Dawley rats were expanded *ex vivo* on gelatin microcarrier beads prior to transplantation into surgically created rat periodontal defect. Control groups included control defect alone and defects treated with microcarrier beads alone. At three weeks all animals were sacrificed, jaws removed, decalcified and processed for histological examination.

RESULTS: At 3 weeks healing in all groups was uneventful. The percentage of new bone (50.6±18.5%) and number of perpendicular periodontal ligament fibers (5.2±1.8/100μM) were statistically greater in the beads plus cells group when compared to beads alone (26.4±4.6% new bone and 2.4±2.2/100μM new ligament) or defect alone (23.5±8% new bone and 1.1±0.6/100μM new ligament) groups. Mean cementum formation from the beads plus cells group was greater than both controls. Within all three-tissue compartments, we successfully tracked GFP^+ positive cells within new bone, cementum and periodontal ligament.

CONCLUSIONS: A novel rat bone marrow stromal cell expansion approach utilizing gelatin micro beads was applied to a rat jaw periodontal defect model. Significantly more alveolar bone, and functional periodontal ligament were regenerated and organized in the beads plus cells group. New cementum was deposited and anchored the new periodontal ligament fibers. We have demonstrated that both the newly formed periodontal hard and soft connective tissues may originate at least in part from the transplanted GFP^+ BM-MSCs.

ACKNOWLEDGEMENTS: This project was support by a Canadian Institutes of Health Research grant to Dr. Edward Putnins and Dr. Fabio Rossi.

RESEARCH LABORATORIES

Thank you to the following organizations for supporting our research.

CIHR IRSC
Canadian Institutes of Health Research
Instituts de recherche en santé du Canada

NIDCR National Institute of Dental and Craniofacial Research

Michael Smith Foundation for **Health Research**

The Arthritis Society

CDHA ACHD THE CANADIAN DENTAL HYGIENISTS ASSOCIATION L'ASSOCIATION CANADIENNE DES HYGIÉNISTES DENTAIRES

NSERC CRSNG

UBC Faculty of Dentistry
The University of British Columbia
www.dentistry.ubc.ca

Community and Educational Research Cluster

Scope of Interests

The research in this cluster relate to three of the four Canadian Institutes of Health Research themes: **health services research; social, cultural, environmental and population health;** and **clinical research,** and to a range of **educational studies.** The three domains are loosely interconnected and employ various quantitative and qualitative research methods and knowledge transfer.

Researchers

Faculty: Bonnie Craig, Mario Brondani, Ross Bryant, Chris Clark, Chris Wyatt, Joanne Walton, Jolanta Aleksejuniene, Chris Zed, Rosamund Harrison, Leandra Best, Ingrid Emanuels, Jim Richardson, Eli Whitney, Michael MacEntee (Coordinator). **Post doctoral fellows:** Khristine Carino. **PhD students:** Matana Pruksapong, Shiva Khatami, Leeann Donnelly. **MSc students:** Nita Chowdhry, Jessica Dubé, Nelson Hui, Diana Lin, Jana Sabo (leave of absence). **Visiting scholars:** Luciane Costa (Brazil), Tomoya Gonda (Japan).

Current Research Activities

Geriatrics

- Psychosocial and economic determinants of oral health in old age;
- Management of oral impairment and disability in residential care;
- Impact of oral ill-health on social isolation and frailty;
- Implementation of an assessment framework for building and monitoring community-based oral healthcare services;
- Identification, prevention and management of caries in frail elders;
- Construction and validation of psychometric instruments for assessing the impact of oral health and disability on quality of life;
- Economics of oral healthcare for frail elders in residential care;
- Oral healthcare and access to dental services as an indication of acculturation among elderly Chinese immigrants in Canada and Australia;
- Educating non-dental personnel about oral healthcare;
- Simplified complete denture technique for remote communities in Canada, South Africa and Thailand.

Implant prosthodontics

- Psychosocial assessment and rehabilitation of older adults with impaired dentitions and tooth loss;
- Clinical outcomes of oral implant treatment and impact on quality of life;
- Influence on oral implants of bisphosphonates treatments for osteoporosis;
- Long-term outcome of various attachment mechanisms on the maintenance and comfort of implant overdentures.

Pediatrics

- Improving the oral health of disadvantaged children from low income, immigrant and Aboriginal families by measuring the effectiveness of health promotion and prevention interventions, evaluating existing community oral health programs, and exploring barriers to good child oral health;
- Perspectives of general dentists in B.C. on the changing nature of care for child patients;
- Theory-based oral health behavior modification in adolescents.

Education

- Critical thinking in dental education;
- Assessing the educational environment for students in small group problem-based-learning sessions;
- Peer review in university education;
- Acquisition of clinical reasoning and related strategies by dental students;
- Influence of an electronic "personal response system" on student participation and evaluation in dental education;
- Student and faculty perceptions of a changed dental curriculum as a prelude to further curricular development.

Occupational health

- Studying occupational hazards to dental practitioner's general and mental health.

Please direct enquiries about any of the above studies to:

Michael MacEntee, *LDS(I), Dip. Prosth., FRCD(C), PhD,* macentee@interchange.ubc.ca

Coordinator, *Community and Educational Research Cluster*

Professor of Prosthodontics and Dental Geriatrics, *UBC Faculty of Dentistry*

iMatrix Research Cluster

iMatrix is an interactive research cluster within the Faculty of Dentistry at the University of British Columbia combining the research interests of 11 highly active laboratories in oral and biomedical sciences. Our research is supported by 26 grant awards and our findings have been published in more than 190 journal articles and book chapters within the last 5 years. We are located in the J.B. Macdonald Building and the Life Sciences Center at the main UBC campus. Highly motivated undergraduate and graduate students, post-doctoral fellows and other trainees as well as interested collaborators are welcome to contact our member laboratories.

Member laboratories:

Prof. Dieter Brömme
Lysosomal proteases and their role in health and disease

Contact: dbromme@interchange.ubc.ca

Prof. Don Brunette
Regulation of cell behavior on implant surfaces by substratum topography

Contact: brunette@interchange.ubc.ca

Prof. Virginia Diewert
Prenatal craniofacial morphogenesis relevant to cleft lip and cleft palate in humans and mouse models

Contact: vdiewert@interchange.ubc.ca

Assoc. Prof. Lari Häkkinen
Cell to extracellular matrix interactions in wound healing

Contact: lhakkine@interchange.ubc.ca

Prof. Hannu Larjava
Cell adhesion, integrins and signaling in wound healing and periodontal disease

Contact: larjava@interchange.ubc.ca

Prof. Chris Overall
Matrix metalloproteinase and inhibitor proteomics and protein engineering

Contact: chris.overall@ubc.ca

Prof. Ed Putnins
Disease pathogenesis and periodontal regeneration using mesenchymal stem cells

Contact: putnins@interchange.ubc.ca

Assoc. Prof. Joy Richman
Development of the face and teeth in the embryo

Contact: richman@interchange.ubc.ca

Assoc. Prof. Clive Roberts
Synthesis and degradation of proteoglycans in the cell biology of wound healing

Contact: clive.roberts@ubc.ca

Prof. Charles Shuler
Molecular regulation of palatal fusion

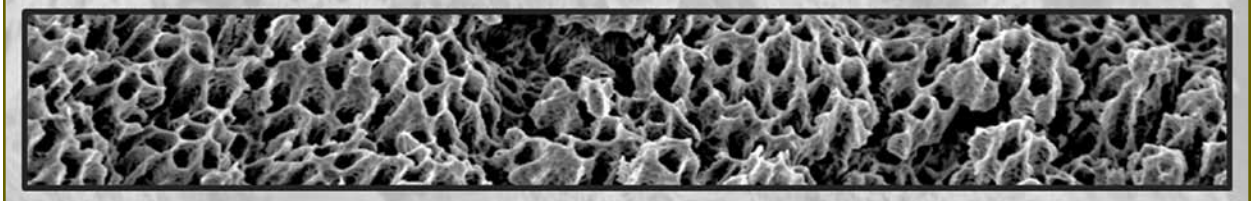
Contact: cshuler@interchange.ubc.ca

Assoc. Prof. Doug Waterfield
Adjuvant/MRL-lpr murine model of arthritis

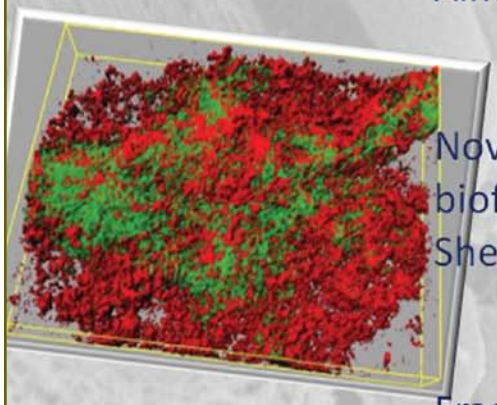
Contact: waterfld@interchange.ubc.ca

For more information, please go to: http://www.dentistry.ubc.ca/research

Clinical Research, Technology Transfer & Dental Materials Sciences Research Cluster

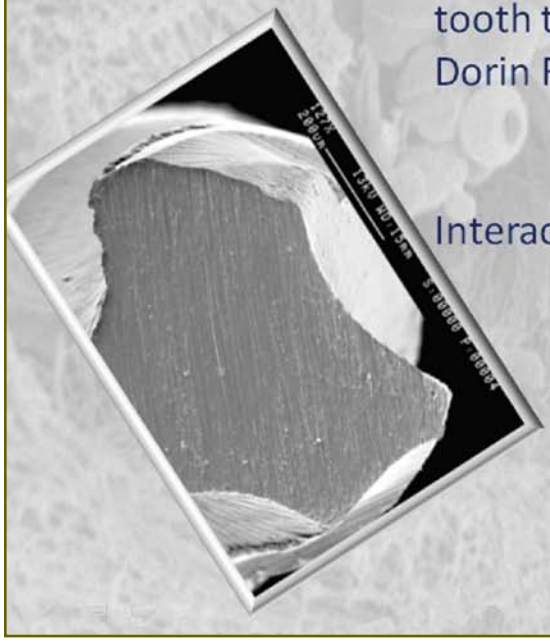


Dental sleep medicine: Alan Lowe, Fernanda Almeida, Sandra Fastlicht, Hiroko Tsuda.

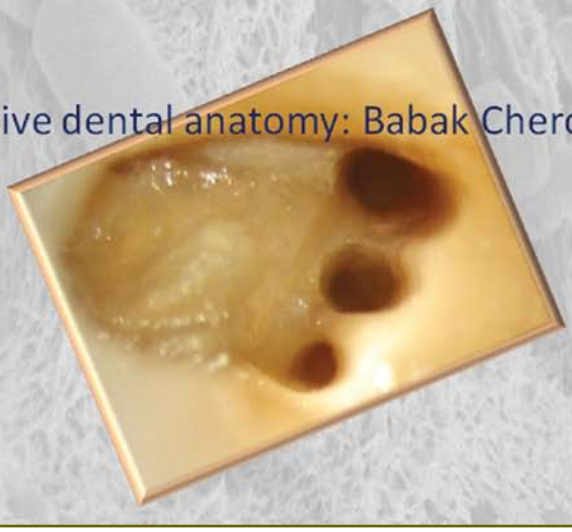


Novel strategies for eradication of dental biofilms: Markus Haapasalo, Wei Qian, Ya Shen, Fernanda Pappen.

Fracture mechanics and fatigue characterization of dental materials, hard tooth tissues, and dental adhesive interfaces: Dorin Ruse.



Interactive dental anatomy: Babak Cheroudi.



Please direct inquiries about any of the above studies to:

Markus Haapasalo, *DDS, PhD, DipEndo*

Coordinator, *Clinical Research, Technology Transfer &*

Summer Student Employment Opportunities

UBC Faculty of Dentistry students are invited to apply to these summer research opportunities:

The role of the transcription factor TBX22 *in facial development*

Genetics plays an important role in the etiology of clefting therefore there is a major effort to identify the genes and regions of the human genome that increase susceptibility to orofacial clefts. One approach is to look at syndromes with clefts since the causative genes are likely to play some role in face formation. Some of the genes that cause syndromes with clefts are IRF6 [14], MSX1 [19], PVRL1 [18] and *TBX22* [3]. In this project we are focusing on the T-box transcription factor, *TBX22* that is mutated in X-linked cleft palate and ankyloglossia (CPX, OMIM 303400). The protein product of the *TBX22* gene binds to target genes that contain a particular sequence of DNA and turns off or represses their transcription [1]. It is now known that in human CPX syndrome there are mutations in the sequence of *TBX22* that reduce the ability to bind to target genes [1]. All of the mutations are predicted to result in a loss of function. In this project the student will work out some of the downstream targets of *TBX22*. Embryos will first be injected with a retrovirus coding for *TBX22*, then collected 3 -4 days later. Fixed embryos will be hybridized to probes for different genes expressed in the face. The prediction is that places where the virus has incorporated will have altered gene expression. Such genes are likely targets of *TBX22*.

Funding: CIHR | **Supervisor:** Joy Richman, richman@interchange.ubc.ca | **Co-supervisors:** Norihisa Higashihori

Quality of student learning in PBL curriculum

When the PBL based curriculum was first introduced to UBC medical/dental faculties in 1997, both medical and dental students of the first and second years were integrated as one group for the PBL sessions. However, during the last four years, this practice has been changed where the dental students were separated from the medical students in their PBL sessions. Even though verbal feedback to date on this change has been positive for the most part, no attempt has been made so far to study the effect of this change on the quality of student learning. We (Dr. Karuna Karunakaran in collaboration with Dr. Leandra Best) performed a study last year through questionnaires distributed to students and tutors involved in the medical/dental PBL over the last four years. The proposed summer student will compile these results and compare the data to arrive at a conclusion to whether this change was overly successful. If the analysis of this study turned out to be novel, the student will also help us in writing a manuscript to submit to a peer reviewed dental/medical education journal.

Contact: Leandra Best, drlbest@interchange.ubc.ca

Oral sex, oral cancer, and oral health as related to HPV transmission

Dr. Brondani is looking for students who are interested in actively assisting in a qualitative (focus group) and quantitative (survey questionnaire) research study to investigate values and beliefs about oral sex, oral health and oral cancer among young and older gay men and women. Duties include helping to conduct a literature search on the topic, assemble the focus groups, and analyze the survey questionnaires and group discussion. No previous experience in research is necessary since this will be an opportunity to learn about different methods. However, being comfortable in reading/interacting with gay issues would be an asset. Other duties can be discussed with Dr. Brondani as well as the time commitment for this study.

Contact: Mario Brondani, brondani@interchange.ubc.ca

Community services and reflections as a tool to enhance learning

Dr. Brondani is looking for summer students who are interested in community service learning (CSL) to actively assist in a qualitative (focus group and field observation) research study. This study is aimed at investigating the use and value of reflections in the context of community service learning (CSL) and its impact on students' education. Duties include helping to conduct a literature search on the topic of reflection and CSL, analyze the group discussion, and

gather relevant information from community sites about health promotion activities. No previous experience in qualitative research is necessary since this will be an opportunity to learn. Other duties can be discussed with Dr. Brondani as well as the time commitment for this project.

Contact: Mario Brondani, brondani@interchange.ubc.ca

Effect of passive and active irrigation on predentin and smear layer on instrumented and uninstrumented parts of the dental root canal system

Cleaning and disinfection of the dental root canal system is a key part of successful endodontic treatment of infected teeth. Earlier studies have focused mainly on the effect of irrigating solutions on the smear layer which is created during instrumentation and consists of organic (collagen) and inorganic components of the root canal and dentin. New studies have indicated that large areas in various parts of the root canal system remain untouched by endodontic instruments and therefore do not have a smear layer. The effect of irrigating solutions on this part of the canal has been poorly studied. The aim of this project is to compare the effect of known and novel irrigating solutions on all parts of the root canal system using classical manual and new variable pressure irrigating systems. Scanning electron microscopy will be the main tool in the analysis of the effects of the irrigating solutions.

Funding: Vista Dental | **Supervisor:** Markus Haapasalo, markush@interchange.ubc.ca | **Co-supervisor:** Wei Qian

Cellular and molecular mechanisms of scar-free wound healing in gingiva

Wound healing is a complex process that often results in excess scar formation. For example, 67% of burn wound patients develop hypertrophic (HT) scars. This can have devastating consequences ranging from tissue disfigurement to organ dysfunction, emphasizing the need for better understanding and prevention of wound healing problems. Remarkably, gingival wounds resemble fetal wounds and heal by regeneration without scar formation. Understanding the mechanisms of gingival healing could provide valuable information about the factors that regulate scar formation. Our general hypothesis is that inherently different composition of the extracellular matrix (ECM) and/or phenotypically different cells that reside in gingiva or skin determine the outcome of the healing.

The hallmark of scar formation is the abnormal accumulation of ECM, including type I collagen, as a response to increased transforming growth factor-ß (TGF-ß) activity. The small leucine-rich proteoglycans (SLRPs) form a family of molecules that are important structural components in the ECM. We have shown that SLRPs decorin, biglycan, fibromodulin and lumican interact with type I collagen to coordinately regulate collagen fibrillogenesis in gingiva. SLRPs also bind to TGF-ß, reducing its activity. Recently, we demonstrated that decorin is also a signaling molecule that regulates cell growth. We hypothesize that differential expression of TGF-ß isoforms and their inhibitors, SLRPs, by fibroblasts in early gingival and skin wounds determine whether regeneration or HT scar formation results. SLRPs released from existing ECM also serve as signaling molecules and may regulate cell-ECM interactions, ECM turnover and organization. To study these processes, we use immunohistochemistry, electronmicroscopy, various cell culture and animal models, and biochemical and molecular biology tools.

Funding: CIHR | **Contact:** Lari Häkkinen, lhakkine@interchange.ubc.ca

Post-operative dental pain and/or discomfort following dental treatment of young children under general anaesthesia

A summer research student will be involved in data collection, both in person and by telephone, and in data entry for this project. This prospective cohort study will explore factors that influence the occurrence, extent, and severity of post-operative dental pain and/or discomfort in young children undergoing general anaesthesia (GA) for dental treatment. Such an investigation has not been done in a young population (<6 years) nor has post-operative dental pain and/or discomfort been correlated with types of dental procedures and other factors using a valid measurement. Our hypothesis is that post-operative pain or discomfort in young children who have had dental treatment under general anaesthesia is an unpredictable event. Data will be collected from 200 children and their parents attending two private GA facilities in Vancouver, BC, Canada. Children will be included in the study if they are between 3 and 6 years old, are in a good health but have tooth decay, and if their parents can communicate well in English, have a telephone at home and give informed consent. A nonprobability, consecutive-sampling technique will be used

to include children attending those two private units recruited during 6 months of data collection. Data will be collected through interviews, questionnaires, and observation using validated pain and emergence agitation scales. Parents will be followed-up 4 times by telephone: at 24 hours, 2 days, 1 week, and 1 month.

Investigators: Luciane Costa, luciane@interchange.ubc.ca, and Rosamund Harrison, rosha@interchange.ubc.ca

Early childhood caries and child-rearing practices among Filipino immigrants

A summer research student is requested to assist in the recruitment of study participants, to prepare supplies and materials for focus groups, to take notes during focus groups, and to do transcriptions. This study will be conducted to explore child-rearing practices in relation to increased susceptibility to early childhood caries (ECC) among Filipino immigrants in the Lower Mainland. This phase will compliment our ongoing quantitative survey that is documenting prevalence of ECC and treatment needs of preschool children in this immigrant community. Five focus group discussions (FGD) will be held in selected community centers. Participants will be Filipino mothers, grandparents, and professional child-care providers (n=40). The discussions will be audio taped, transcribed and analyzed following standard methods for qualitative studies. Results will be used in concert with the results of the quantitative study to help design culturally-specific oral health promotion initiatives for Filipino immigrants.

Investigators: Khristine Carino, kcarino@interchange.ubc.ca, and Rosamund Harrison, rosha@interchange.ubc.ca

Scarless oral wound healing

Alterations in wound repair, such as non-healing wounds and fibroproliferative disorders (hypertrophic scarring and keloids) are serious pathologic disorders that compromise the skin's biomechanical properties, resulting in tissue dysfunction. Often these disorders are associated with pain and cause not only cosmetic but also physical and psychological disabilities, thereby negatively impacting the quality of life. Interestingly, even the normal wound healing process in skin produces scars that can cause not only cosmetic concerns but also lack of or reduced function; nevertheless, in certain parts of the oral mucosal tissue, wound healing results in tissue regeneration with minimal or no scarring. Scar-free healing of oral mucosa has been explained by the moist environment, growth factors and cytokines in saliva, and the cell types present in the tissue itself. There is, however, no detailed information describing the differences in gene expression in normal healing of the oral mucosa compared to skin or fibroproliferative disorders. A number of cytokines and growth factors known to play key roles in wound repair and an imbalance in the synthesis and release of these cytokines, chemokines and growth factors at the wound site interfere with normal healing, as is seen in chronic diabetic ulcers or in over-scarring wounds. Thus, understanding the overall temporal and spatial relationships in the induction of key cytokines/growth factors and their receptors is essential to improving current therapies for wound treatment. For this project, the expression of cytokines and cell adhesion molecules will be investigated in specimens representing oral mucosa and skin using immunohistochemistry, PCR and ELISA techniques.

Funding: CIHR | **Supervisor:** Hannu Larjava, larjava@interchange.ubc.ca

A study in knowledge transfer

Background: The ELDERS group at UBC consists of three academics committed to the effective management of oral health in old age. They work with colleagues in several other faculties including geriatricians, nurses, psychologists, sociologists, social workers and statisticians and interact with various sectors of the community. The ELDERS group at UBC was one of the first to document the distribution of oral health problems in long-term care facilities, and to explore ways for managing the problems. We have investigated preventive strategies ranging from antibacterial agents to the education of care-aides.

Job Description: The ELDERS group web page was developed as a way to transfer knowledge about the research activities and results to a wide audience in Canada and abroad. It is used also as a way to arrange oral health care services and educational programs within the community. The research project for the summer student would be to revise and test the ELDERS web page to enhance its appeal and usefulness to meet the overall educational, research and service responsibilities of this inter disciplinary group.

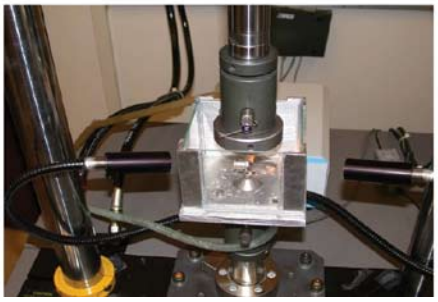
Supervisor: Michael MacEntee, macentee@interchange.ubc.ca

Bio Materials – UBC Faculty of Dentistry

http://www.dentistry.ubc.ca/research

Fracture mechanics and fatigue of bio-dental materials and adhesive interfaces

Dr. N. Dorin Ruse, MSc, PhD, MCIC
dorin@interchange.ubc.ca



The notchless triangular prism (NTP) specimen fracture toughness test

1. Dong, X., **Ruse**, N.D. "Fatigue crack propagation path across the dentinoenamel junction complex in human teeth" J Biomed Mater Res A 66A (1): 103-109, 2003.

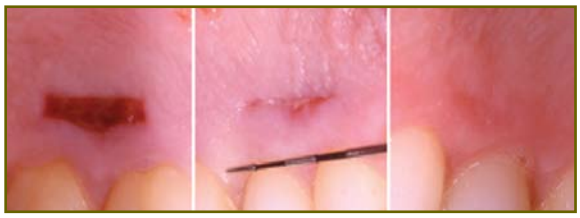
2. Iwamoto, N., **Ruse**, N.D. "Fracture toughness of human dentin" J Biomed Mater Res A 66A: 507-512, 2003.

3. Far, C., **Ruse**, N.D. "Effect of bleaching on fracture toughness of composite-dentin bonds" J Adhes Dent 5: 175-182, 2003.

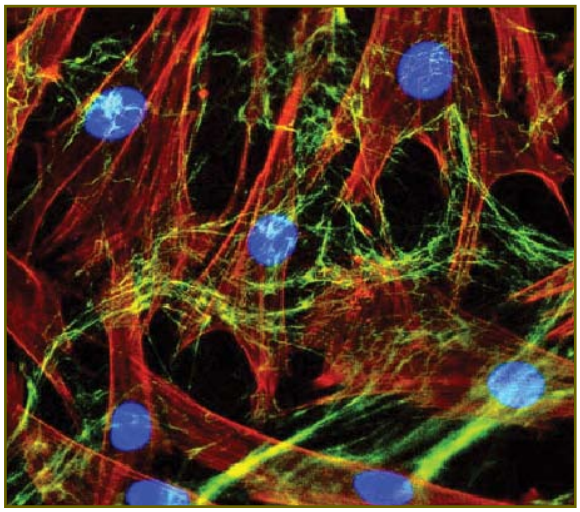
4. Muller, B., Pfrunder, F., Chiocca, L., **Ruse**, N.D., Beckmann, F."Visualizing the complex morphology of fatigue cracks in voxel-based 3D datasets" Mater Sci Tech 22: 1038-1044, 2006.

WOUND HEALERS WANTED!

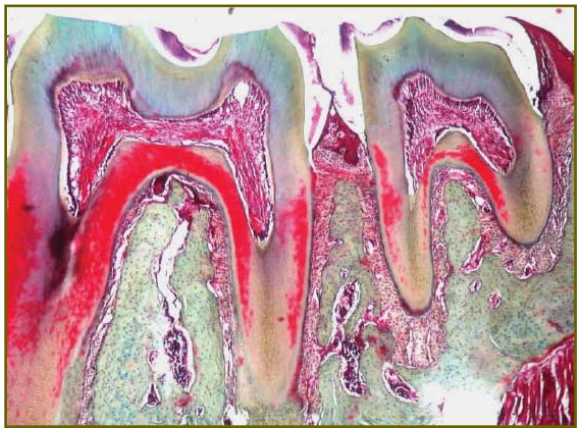
If you want to participate in our effort to understand and find novel ways to prevent wound healing problems and periodontal disease, join our enthusiastic research team.



We will accept highly motivated undergraduate and graduate students, postdoctoral fellows and other trainees to participate in these exciting projects. The projects will be individually tailored based on experience and time commitment.



Our laboratory is studying wound healing and periodontal disease at the molecular and cellular level using the latest in vitro technologies and human and animal models.



For more information, go to:

http://www.dentistry.ubc.ca/research/periodontalbiology/

Contact information

Dr. Hannu Larjava (larjava@interchange.ubc.ca)

Dr. Lari Häkkinen (lhakkine@interchange.ubc.ca)

University of British Columbia, Faculty of Dentistry,

Department of Oral Biological and Medical Sciences, Laboratory of Periodontal Biology

2199 Wesbrook Mall, Vancouver, B.C., Canada V6T 1Z3

Christopher M. Overall BDS, BSc(Hons), MDS, PhD, FCAHS

Professor, Canada Research Chair in Metalloproteinase Proteomics and Systems Biology

Research project summary • Proteases function as molecular switches in signalling circuits on the cell surface and in the extracellular milieu. In light of the many proteases that are encoded by the genome, and the even larger number of bioactive substrates, it is crucial to identify which proteases cleave a particular substrate and which substrates individual proteases cleave. We have developed innovative proteomic strategies to quantitate all components of proteolytic pathways: the proteases, inhibitors and substrates—a field we term "degradomics". Elucidating these degradomes will help us to understand the function of proteases in development and disease and to validate proteases as drug targets. By developing quantitative proteomic techniques of substrate discovery our understanding of the biological roles of matrix metalloproteinases in physiological processes and pathology has been revolutionized. Since 2000, interest in this innovative field has been reflected by five invited Nature Reviews on this and related topics, 73 invited plenary presentations at international meetings, 90 seminars at university departments and institutes, 76 publications, 9 invention disclosures, and current funding by a NIH and 5 5-year grants (2 CIHR, NCIC, CIHR and CBCRA Team Grants).

Research Theme One: Inflammation
(CIHR Grants MT-11633, MOP-37937)

A. Proteases: Proteomically identify and quantify protein expression levels of all MMPs and TIMPs in cellular model systems and in healthy versus inflamed connective tissues in mouse models and man.

B. Substrates: Proteomically identify the substrate repertoire (the substrate degradome) of the key MMPs in the 'protease degradome' (identified in A) in healthy and inflamed connective tissue cells eg periodontium.

C. Validation: Mechanistically dissect the roles of MMPs, bioactive substrates and cleavage products in homeostasis of connective tissues and in destructive inflammation in arthritis and periodontitis. Regulation of innate immunity and chemokine activity by proteases (MMPs, DDPs) are a major focus.

Research Theme Two: Cancer Metastases
(NCIC grant 015144; CBCRA grant 016508)

A. Analyze the protease degradome in breast cancer tumors, stroma, and metastases at the transcript and protein levels in mouse models of human metastases and murine tumors.

B. Discover novel bioactive protease substrates critical for the evolution of breast cancer metastases.

C. Validate the roles of MMP proteolysis of bioactive substrates in regulating metastases development.

D. Image proteases using activity based probes in vivo by microPET.

Research Theme Three: Proteolytic Regulation of Cholesterol
(CIHR Team Grant)

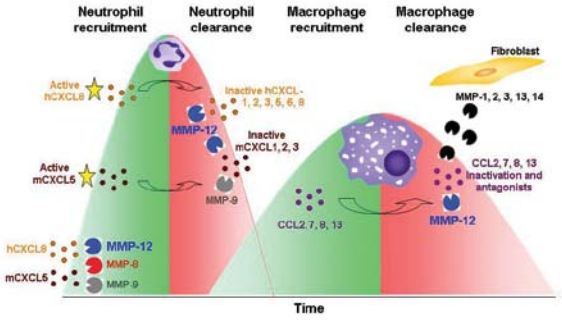
A. Proteomic and mechanistic analysis of the role of MMPs in the regulation of PCSK9 and the LDL receptor.

Trainees • Since 2000 I have supervised in my laboratory 17 Post-Doctoral scientists, 11 Ph.D. and M.Sc. students, 11 448/449 undergraduate student thesis projects, and 14 undergraduate Work/Study students. 7 of my UBC gradate students and 6 post-doctoral trainees have held local or international fellowships.

Funding • I have held 29 grants worth $8,841,574 in research operating funds as PI. I have contributed to $12,396,792 worth of funding as part of Research Teams, of which I have received $829,736. Current operating grants: $903,782 per year (CIHR, NCIC) and my trainees receive scholarships of a further $216,400 per year, plus I bring in $200,000 for CRC support. Not included is the Centre Grant from the MSRFHR and a CFI grant to acquire infrastructure for the Centre for Blood Research (co-applicant), $500,000 pa from the MSRFHR to fund the BC Proteomics Network that I am coleader.

Selected recent papers

1. **Overall, C.M.** and Kleifeld, O. 2006. Validating MMPs as Drug Targets and Anti-targets for Cancer Therapy. **Nature Reviews Cancer 6,** 227-239.
2. Tam, E.M., Morrison, C.M., Wu, Y., Stack, S., and **Overall, C.M.** 2004. Membrane Protease Proteomics: Isotope Coded Affinity Tag/Tandem Mass Spectrometry Identification of Undescribed MT1-MMP Substrates, **PNAS U.S.A.** 101, 6917-6922.
3. Vergote, D., Butler, G.S. Ooms, M., Cox, J.H. Silva, C., Hollenberg, M.D., Jhamandas, J.H., **Overall, C.M.** and Power, C. 2006. Proteolytic Processing of SDF-1alpha Reveals a Change in Receptor Specificity Mediating HIV-Associated Neurodegeneration. **PNAS U.S.A. 103,** 19182-19187.
4. **Overall, C.M.** and Blobel, C.P. 2007. In Search of Partners: Linking Extracellular Proteases to Substrates. **Nature Reviews Molecular Cell Biology 8,** 245-257.
5. Dean, R.A. and **Overall, C.M.** 2007. Proteomic Discovery of Metalloprotease Substrates in the Cellular Context by iTRAQ Labeling Reveals A Diverse MMP-2 Substrate Degradome, **Molecular Cellular Proteomics 6,** 611-623.
6. Tester, A.M., Cox, J.H., Connor, A.R., Starr, A.E., Dean, R.A., Puente, X.S., López-Otín, C., **Overall, C.M.**2007. LPS Responsiveness and Neutrophil Chemotaxis in vivo Require PMN MMP-8 Activity. **PLoS One,** Issue **3, e312,** 1-10. DOI number 10.1371/journal.pone.0000312.
7. Dean, R.A., Butler, G.S., Hamma-Kourbali, Y., Delbé, J., Brigstock, D.R., Courty, J., and **Overall, C.M.** 2007. Identification of Candidate Angiogenic Factors Processed by MMP-2 in Cell Based Proteomic Screens: Disruption of VEGF / HARP (Pleiotrophin) and VEGF / CTGF Angiogenic Inhibitory Complexes by MMP-2 Proteolysis. **Molecular Cellular Biology**, 8454-8465.
8. Fahlman, R.P., Chen, W., and **Overall, C.M.** 2007. Absolute Proteomic Quantification of Proteases and Proteolytic Processing in Complex Proteomes Using Proteolytic Signature Peptides. *Submitted.*
9. Butler, G.S., Dean, R.A., Tam, E.M., and **Overall, C.M.** 2007. Pharmacoproteomics of a Metalloproteinase Hydroxamate Inhibitor in Breast Cancer Cells: Dynamics of Matrix Metalloproteinase-14 (MT1-MMP) Mediated Membrane Protein Shedding. **Molecular Cellular Biology** *Conditional acceptance.*



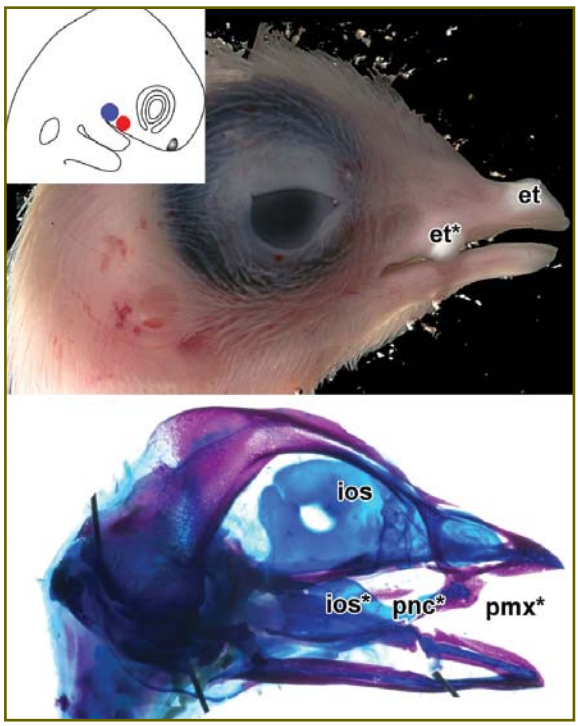
JOY M. RICHMAN | Craniofacial Development

Research topics: My lab studies craniofacial development in the embryo. Primarily I use chicken embryos but recently I have also started to work on snakes and lizards. The work covers three themes, Mechanisms of Cleft Lip (CIHR), Molecular Controls of Jaw Identity (CIHR) and Reptilian Tooth and Jaw Development (NSERC). Previously in the Cleft Lip project, two graduate students defined the roles of FGF and BMP signalling in lip fusion. In the next period we will work on the third major class of signalling protein, the Wnts and will determine which of these signals are the most important for promoting lip fusion. The other big focus in the next period will be on a gene that causes human clefting, *TBX22*. We have exciting new data to show that clefts can be induced in chicken embryos when this gene is delivered to embryos. These studies will reveal the identity of genes that could be involved in human clefting and ultimately lead to better diagnosis and prevention In the Jaw Identity project, we have carried out a microarray screen of the chicken genome to see which genes are causing the transformation of jaw identity. In the next few years we have several very promising candidates that will be followed up with functional studies. The aim is to see whether these novel genes are required or sufficient for setting up jaw identity. Finally in the third project, we are developing the snake and lizard models to study the signals that induce tooth replacement because these animals have many generations of teeth and we can have direct access to the embryos during development (because many reptilian species lay eggs, just like chickens). This is directly relevant to our understanding of how permanent teeth form in humans. We have already shown that it is not necessarily the same genes that make the primary set and replacement sets of teeth. The reptilian project is also studying evolution of teeth and in particular why some amniotes such as birds have lost their teeth. We are looking at expression of tooth specific genes in chickens and the most primitive birds, flightless Emus and Ostriches. The hypothesis is that more primitive birds will retain more of the molecules required to make teeth than more modern birds.

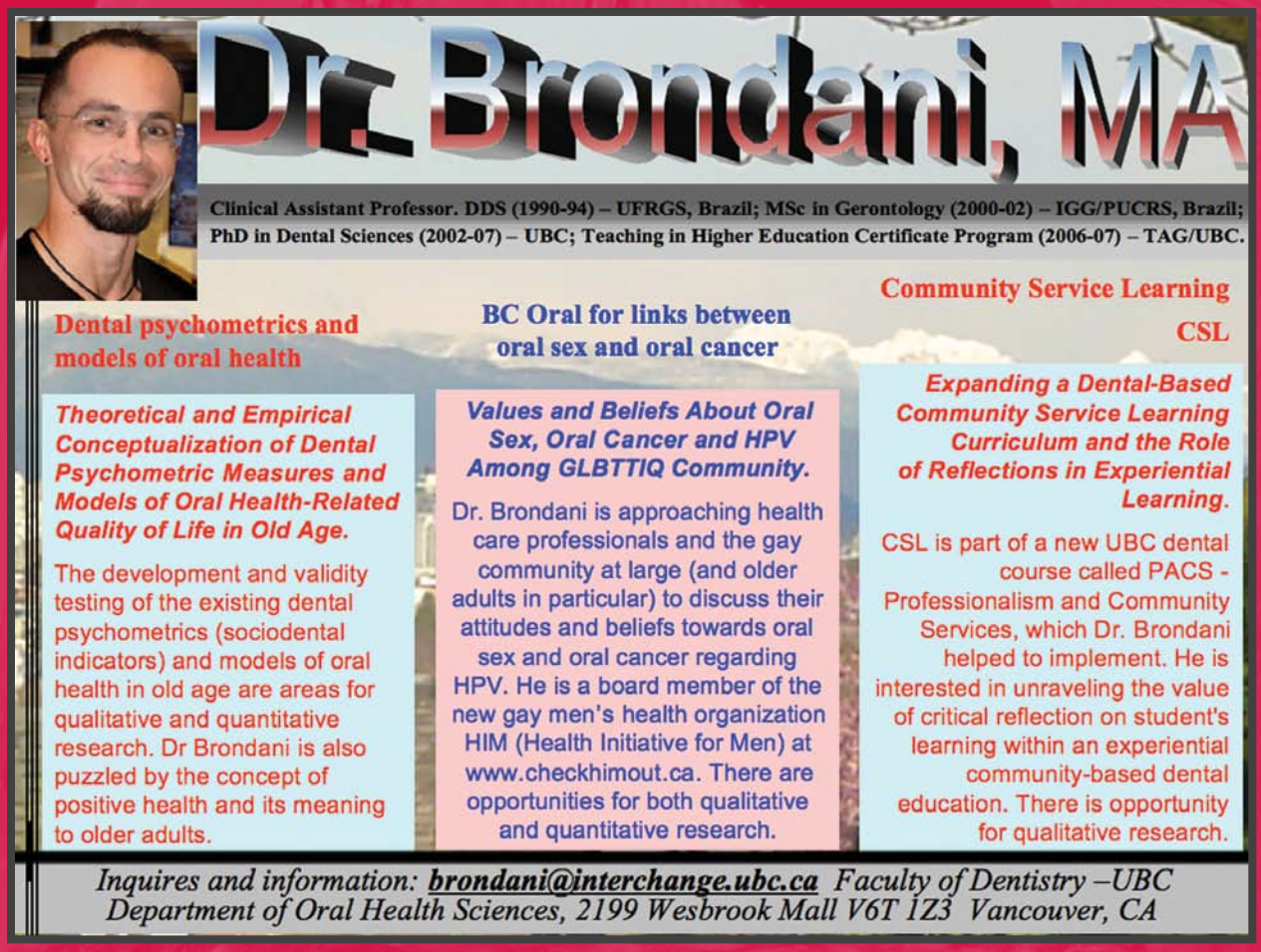
Lab statistics: My lab is in the Life Sciences Institute where I have 6 benches of space in addition to a tissue culture room (200 Sqf) and 3 other adjacent rooms (60 Sqf each). I have two offices, one for trainees and one for myself (150 sqf each). I currently have one graduate student from Dentistry, 4 post-doctoral fellows and 2 technicians. My work is most closely aligned with that of Dr. Shuler who works on mouse palate development.

Total number of publications within the last 5 years (published/accepted only): 11

Grants awarded within the last 5 years including total award $ amount: CIHR (1,343,328), NSERC (213,000), Alpha Omega (4,000)



Jaw duplication phenotype. Inset shows drawing of embryo with two beads, one soaked in Noggin (blue) and one in Retinoic Acid (red). Together they induce a complete change in identity visible from the outside of the beak. A second egg tooth forms (et). Looking Inside the same embryo shows that instead of maxillary bones, there is a large cartilage resembling the interorbital septum (ios), a prenasal cartilage (pnc) and premaxilla (pmx). All of these parts of the skeleton usually form in the centre of the face, not the side.


Dr. Brondani, MA
Clinical Assistant Professor. DDS (1990-94) – UFRGS, Brazil; MSc in Gerontology (2000-02) – IGG/PUCRS, Brazil;
PhD in Dental Sciences (2002-07) – UBC; Teaching in Higher Education Certificate Program (2006-07) – TAG/UBC.
Dental psychometrics and models of oral health
Theoretical and Empirical Conceptualization of Dental Psychometric Measures and Models of Oral Health-Related Quality of Life in Old Age.
The development and validity testing of the existing dental psychometrics (sociodental indicators) and models of oral health in old age are areas for qualitative and quantitative research. Dr Brondani is also puzzled by the concept of positive health and its meaning to older adults.
BC Oral for links between oral sex and oral cancer
Values and Beliefs About Oral Sex, Oral Cancer and HPV Among GLBTTIQ Community.
Dr. Brondani is approaching health care professionals and the gay community at large (and older adults in particular) to discuss their attitudes and beliefs towards oral sex and oral cancer regarding HPV. He is a board member of the new gay men's health organization HIM (Health Initiative for Men) at www.checkhimout.ca. There are opportunities for both qualitative and quantitative research.
Community Service Learning CSL
Expanding a Dental-Based Community Service Learning Curriculum and the Role of Reflections in Experiential Learning.
CSL is part of a new UBC dental course called PACS - Professionalism and Community Services, which Dr. Brondani helped to implement. He is interested in unraveling the value of critical reflection on student's learning within an experiential community-based dental education. There is opportunity for qualitative research.
Inquires and information: brondani@interchange.ubc.ca Faculty of Dentistry –UBC
Department of Oral Health Sciences, 2199 Wesbrook Mall V6T 1Z3 Vancouver, CA

NOTES ›

NOTES ›

Procera® Crown • Procera® Laminate • Procera® Bridge Alumina and Zirconia

The beauty of Procera® laminate is proven by the four-time Olympic gold medalist swimmer, Inge de Bruijn, from the Netherlands.

Procera® makes it easier to

deliver beautiful smiles

Procera® provides you and your patients with precision fit, strength, and unsurpassed lasting beauty. The core of our Easy Esthetics™ concept, Procera®, makes delivering beautiful smiles easier, quicker, and more profitable.

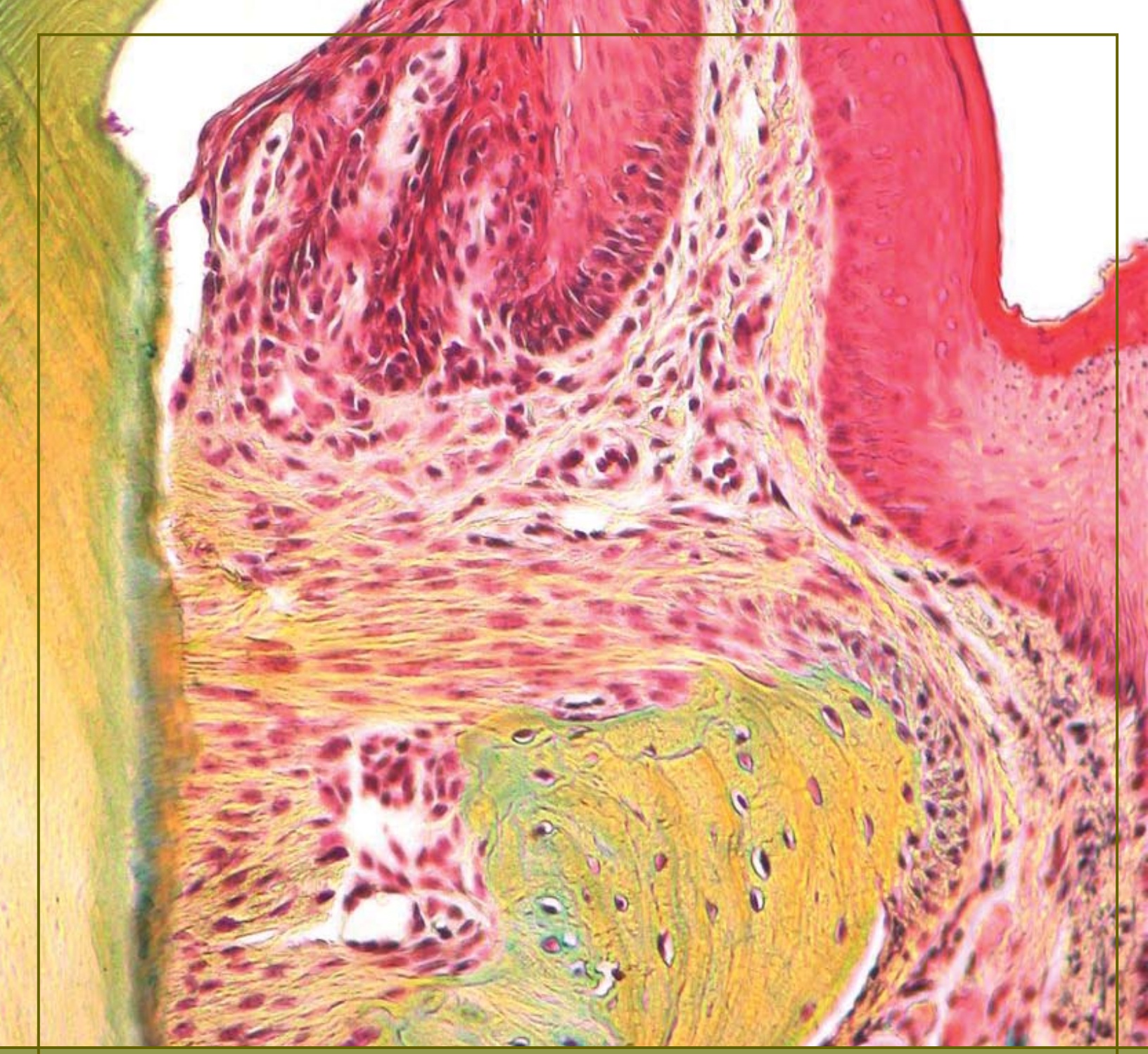
The Procera® lineup includes:

- **NEWS!** **Procera® Crown Zirconia 0.4** – Thinner core for increased esthetics, same Procera® Zirconia strength
- **Procera® Bridge Zirconia** – Full-arch lengths up to 14 units, with strongest zirconia available – 1200MPa flexural strength
- **Procera® Laminate** – Strongest laminate on the market – 700MPa flexural strength
- **Procera® Bridge Alumina** – Exceptional translucency and superior esthetics

Increase your patient satisfaction and your profitability.

Visit www.nobelbiocare.com for more information

Nobel Biocare™
making you smile™



Faculty of Dentistry

350 – 2194 Health Sciences Mall
Vancouver, BC
V6T 1Z3

www.dentistry.ubc.ca
Information: **(604) 822-5323**

The UBC Faculty of Dentistry Thanks the Following Research Day Sponsors:

Gold

Speaker sponsor

Nobel Biocare

Silver

Lunch sponsor

PLANMECA

Bronze

Coffee break sponsor

Wyeth Consumer Healthcare

Design by riveradesign.com