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FOREWORD




This has been an exciting year which saw a new and higher level of maturity and growth in the Faculty's research enterprise. In its pursuit of research excellence, change is the only constant that drives the Faculty of Dentistry to lead in the area of dental and craniofacial research.

Together with the five leading research programmes, the Faculty has identified the need for three umbrella research units to be developed so as to empower the Faculty to grow in strength and research expertise. These research centers serve as incubators for the development of major research programmes leading the Faculty's research thrust in the life sciences.

Research partnerships are vital and essential for the Faculty's pursuit of research excellence. The Faculty continues to establish valuable research collaborations with top institutions and industry.

This Dentistry's Research Report will give you an overview of the research programmes, plans and achievements of the dental and craniofacial research work undertaken by staff and students. While developments in life sciences research are racing ahead, the Faculty's constant aim is to advance and apply scientific knowledge so that the community of patients will ultimately be the beneficiaries of the investments made in research.

Associate Professor Kelvin W.C. Foong
Vice Dean (Research)



FACULTY RESEARCH OVERVIEW

NUS Vision

Towards a Global Knowledge Enterprise

NUS Mission

Advance Knowledge and Foster Innovation,
Educate Students and Nurture Talent in Service of
Country and Society

Faculty Vision

To be a Dental Institution of International Distinction

Faculty Mission

To Improve Oral Health through Academic Excellence,
High Impact Research and Quality Clinical Service

Research Mission

To Improve Oral and Craniofacial Health and the Delivery of Care

Strategy 1:

Grow funding resources

Strategy 2:

Develop peaks of
excellence of high
impact research and
clinical techniques

Strategy 3:

Ensure sustainability
and robustness of
research programmes

Strategy 4:

Develop strong
support infrastructure
for research

3 Strategic Research Initiatives

Centre for Craniofacial and
Regenerative Biology

Dental Biophotonics
Programme and Biomaterials
Programme

Craniofacial Clinical
Research Unit

RESEARCH HIGHLIGHTS

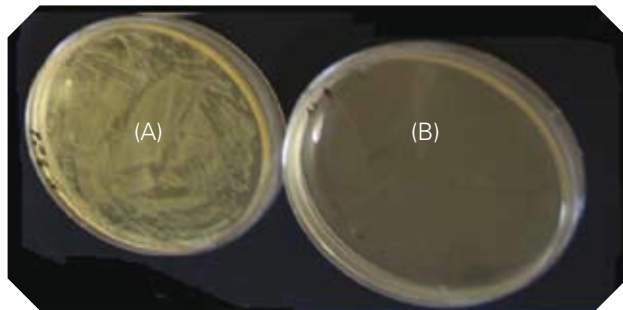
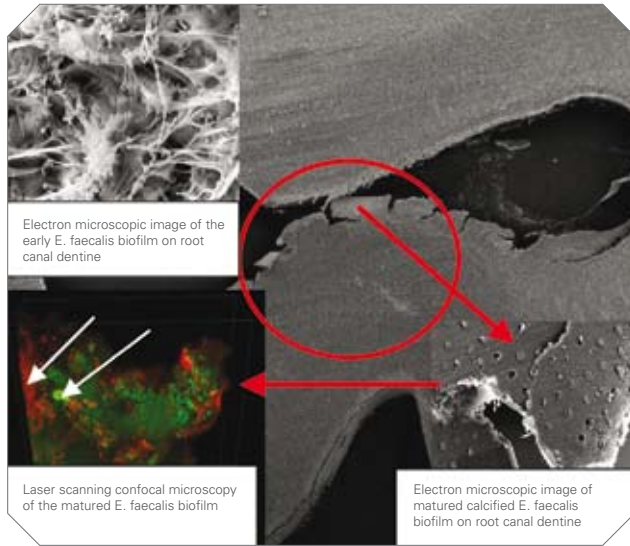
Novel Findings of Research Projects | Dr Anil Kishen

Ability of a bacterium to survive as calculus within the root canal

Enterococcus faecalis is the most predominant bacteria in teeth with failed root canal therapy. It is found to survive harsh conditions prevailing in the root canals of endodontically treated teeth.

Research in our laboratory has highlighted a distinct interaction of *E. faecalis* with root canal dentine. Our experiments have demonstrated different stages in the biofilm formation by *E. faecalis* under different environmental conditions. Further, the ability of *E. faecalis* to initially demineralise the dentine substrate, and later on formed calcified biofilm structures (like calculus) within the root canal dentine was revealed. The calcified biofilm structure housed both viable and dead cells and may be a potential cause of persistent endodontic infection.

The findings from this work has been published in *Journal of Endodontics* 2005 Dec;31(12):867-872 and *J Biomed Mater Res* 2006 May;77(2):406-15.



(A) Water (control) (B) Advanced Non Invasive Light Activated therapy

Culture plates showing bacterial growth from dentine biopsies after root canal disinfection with Advanced Non Invasive Light Activated therapy.

Using light to eliminate microbes in teeth

Persistence of bacteria after treatment is the main cause of failure of most dental treatment procedures.

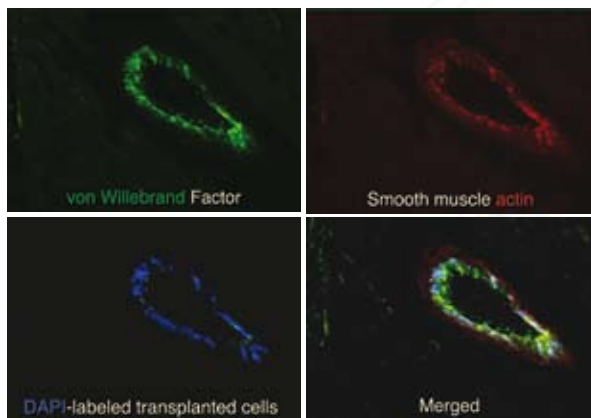
In Root Canal Treatment, the current practice is to use high concentrations of caustic chemicals such as sodium hypochlorite in combination with mechanical instrumentation to eliminate microbes in the root canals of teeth. However, anatomical complexities of the root canal and tubular nature of the dentine makes thorough disinfection of the root canal difficult. The inability of root canal medicaments to eliminate some bacterial species is also a shortcoming.

The light based therapy developed in NUS combines the advantages of photoactivated disinfection with the structural and optical characteristics of the dentine with biophysical characteristics of certain inert chemicals to eliminate bacteria within the anatomical complexities, dentinal tubules and in biofilm state. This method is effective with a broad range of microbial flora. It is an easy-to-use technique that does not necessitate excessive removal of tooth structure or application of caustic chemicals. The treatment duration is reduced, and the development of drug resistant bacterial strains can be evaded by this approach.

NUS has filed a US patent on this invention.

RESEARCH HIGHLIGHTS

Novel Findings of Research Projects | Dr Cao Tong



Endothelial Differentiation of hESC

Directed somatic differentiation of human embryonic stem cells into various progeny lineages for diverse clinical and non-clinical applications

Human embryonic stem cell (hESC)-derived somatic cells are the best source of human tissue and organ-forming cells that can be utilised for broad-ranging therapeutic and non-therapeutic purposes. The major applications are:

- The study of genetic and developmental mechanisms;
- Gene/protein delivery therapy to cure tissue and organ lesions;
- Cell-injection therapy for tissue and organ repair;
- Cell transplantation-based tissue and organ reconstruction and regeneration;
- The development of toxicity screening tests for biomaterials and drugs; food, household and personal care products;
- Environmental analysis of water, soil, air, and natural/artificial products and analysis of bio-chemical toxins and anti-toxin system;
- Disease study and drug discovery.

The Faculty of Dentistry stem cell group has successfully differentiated hESC into osteogenic, chondrogenic, endothelial and myocardial cells.

The immunogenicity and immuno-modulatory function of osteogenic cells differentiated from mesenchymal stem cells

Multi-potent mesenchymal stem cells (MSC) are reported to be immunoprivileged as well as immunosuppressive. Hence, they are ideal candidates for allogeneic transplantation to induce regeneration of diseased tissues and organs. However, it is not known whether MSC would retain their immunoprivileged and immunomodulatory properties after differentiating into the local cell types of the transplantation site.

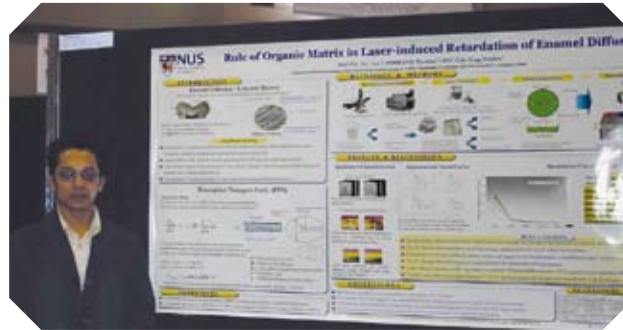
This study sought to investigate this question with a novel New Zealand White rabbit osteogenesis model. Results showed that osteogenic cells differentiated from MSC (DOC) in vitro did not express the MHC class II molecule, were incapable of inducing allogeneic lymphocyte proliferation in mixed lymphocyte culture or generating CTL, were inhibitory in ongoing lymphocyte proliferation, and secreted anti-inflammatory cytokines (IL-10 and TGF- β). There was a significantly higher secretion of IL-10 by DOC than that by MSC, while there was no significant difference between the TGF- β secretion of MSC and DOC in vitro.

However, after IFN- γ treatment, TGF- β secretion by DOC significantly decreased despite the increased production by MSC. Four weeks after local DOC implantation, despite MHC class II expression, second-set allogeneic skin rejection showed similar survival to first-set allogeneic skin rejection and DOC appeared to function as osteoblasts.

In conclusion, DOC retained their immunoprivileged and immunomodulatory properties in vitro, but the latter was lost following transplantation.

RESEARCH HIGHLIGHTS

Novel Findings of Research Projects | A/P Stephen Hsu



The role of organic matrix in laser induced caries prevention was presented at the 84th IADR General Meeting held in Brisbane from 27 June to 1 July 2006. The presentation won the SEA Division Travel Award.

From the invisible to the visible

The cariology research team has, at the micron level, applied two fluorescence techniques, namely FRAP (Fluorescence Recovery After Photobleaching) and Fluorophores Transport Study, to quantify site-specific diffusion in lased and normal enamel with or without organic matrix (OM) and to elucidate the mechanism involved in laser-induced caries prevention. Both techniques confirmed that OM plays an essential role in the diffusion process. Enamel showed a time-dependent two-phase diffusion pattern, with site-specificity and with significantly lower diffusion coefficient at subsurface enamel. These two techniques may be useful for evaluating diffusion-related phenomenon in dental tissues and facilitate clinical application of laser on caries prevention.

At the population level, the team has surveyed 1782 preschoolers in Singapore to profile the current disease patterns. They have identified the caries risk factors/ indicators, and successfully constructed promising risk assessment/prediction models. Both "any-risk model" and "high-risk model" were constructed with multivariate regression. Without salivary tests, the sensitivity and specificity reached 86% and 69%, while with salivary tests, the sensitivity and specificity reached 82% and 86%, respectively. The results may help identify the high risk group of pre-schoolers in Singapore for early intervention and serve as a diagnostic tool to facilitate quality treatment planning and minimal intervention for individual patients and clinical teaching.

Effect of Foundation Restorations on the Load Fatigue Performance of Full Gold Crowns



Principal Investigator: A/P Jennifer Neo
Total Project Value: \$51,150

RESEARCH HIGHLIGHTS

New Research Projects Approved In Financial Year 2005 - 2006

Aims:

- To determine whether: the presence of cores (in vital teeth) to increase preparation height will result in higher number of cycles to preliminary failure.
- To determine whether: the presence of post-cores (in endodontically treated teeth) to increase preparation height will result in higher number of cycles to preliminary failure.
- To determine whether: a critical tooth height exists at which the placement of foundation restorations (cores and post-cores) results in no significant difference in the number of cycles to preliminary failure.

Abstract:

The success of a cast restoration depends largely on adequate resistance and retention form. Resistance form is defined as those 'features of a tooth preparation that enhance the stability of the restoration and resist dislodgement along an axis other than the path of placement'. Factors that affect the resistance of a crown include auxiliary preparation features, total occlusal convergence, occluso-cervical (OC) dimension and luting cement. A recent review on the principles of tooth preparation proposed that 3 mm be the minimum OC height for premolars to possess adequate resistance form. However this number was based on theoretical calculations and monotonic load-to-failure studies.

In most cases teeth in need of full coverage restorations have lost substantial tooth structure, thereby making it difficult to incorporate adequate resistance and retention form. Placement of foundation restorations has been advocated to replace lost tooth structure prior to crown fabrication. If the tooth to be restored is severely damaged, then crown lengthening and/or orthodontic extrusion must also be considered.

In spite of all this information no studies have been done to determine whether the presence of foundation restorations (cores and post-cores) can enhance resistance form. Most of the studies on cores focused on testing different materials, while those on post-cores focused on different configurations and ferrule heights ranging from 0-2 mm. It is therefore the aim of this study to determine whether foundation restorations increase the resistance form of a crown in terms of fatigue loading.

Clinical Relevance:

It is intended that this research shed light on the minimum occluso-cervical height necessary to achieve resistance form adequate for clinical success. If this is achieved, teeth with seemingly short occluso-cervical height may not need to undergo core placement, crown lengthening or orthodontic extrusion to gain additional ferrule. This would change the method of restoring teeth with short clinical crowns.



RESEARCH HIGHLIGHTS

Caries Risk Assessment for Children in Singapore - Adding Plaque pH as a Risk Indicator



Principal Investigator: A/P Stephen Hsu
Total Project Value: \$22,808

Aims:

- Characterise the plaque pH status of pre-school children in Singapore.
- Identify the association between plaque pH and other demographic, behavioral and biological factors.
- Determine the association between plaque pH and overall caries profile of children.
- Evaluate the predictive value of plaque pH in caries increment.
- Incorporate plaque pH in Caries Risk Assessment (CRA) models for a higher predictive accuracy.

Abstract:

Despite the decrease of dental caries rate in developed countries in the last few decades, caries remains as the single most common chronic childhood disease with the majority of lesions found in a minority of the children.

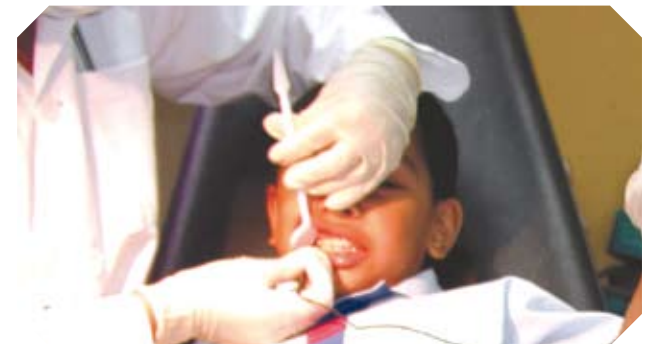
With the financial support of Academic Research Grant (ARF Grant R222-000-021-112), a large-scale longitudinal study aimed to establish a clinically useful CRA model for children in Singapore has been initiated by our team. The baseline survey confirmed a high prevalence rate in Singapore and a significantly polarised distribution of caries, indicating an important need for early prevention.

The association between plaque acidity and caries has been identified in some studies. As caries is a disease that involves multiple microbiological, dietary, salivary factors, and their interactions, plaque pH may serve as a direct and site-specific indicator thereby contributing to a more accurate predictive CRA model. Plaque pH measurement will be incorporated in the follow-up

survey, using a pH electrode on 30-60% (534-1069) subjects. The association of plaque pH with caries increment will be identified. Predictive CRA models, containing multiple risk factors including plaque pH, will be constructed and validated in this study.

Clinical Relevance:

In this study, with plaque pH and its interaction with other risk factors incorporated into the model, a computer-based caries risk assessment model with artificial intelligence will be further developed and validated. This model could be a clinically useful tool to target high risk patients for early detection of disease and cost-effective caries prevention at the individual and community levels. This locally-developed CRA model may contribute significantly to caries control and cost control among children in Singapore in addition to its potential commercial value.



RESEARCH HIGHLIGHTS

Intra-Radicular Causes of Persistent Endodontic Infection



Principal Investigator: Dr Anil Kishen
Total Project Value: \$178,500

Aims:

- Investigate the survival strategy of *E. faecalis* as a biofilm in root canal.
- Examine the inflammatory potential of the intra-radicular biofilm.
- Determine the effects of fluid leakage on the GP-dentine interface.
- The effects of cyclic masticatory loads on bacterial penetration.

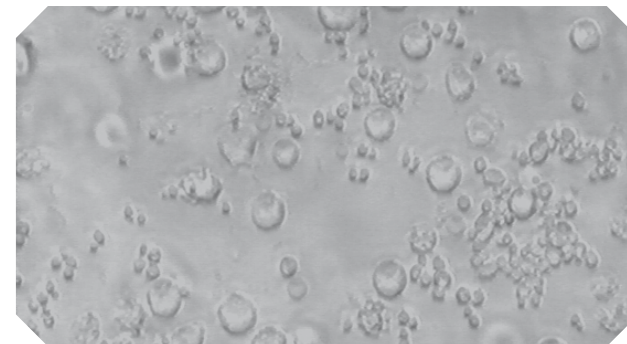
Abstract:

Apical periodontitis is primarily a sequel to microbial infection of the root-canal space in teeth. The clinical management of apical periodontitis involves infection control by root canal treatment, which is the only viable alternative to tooth loss. Epidemiological studies have shown that the prevalence of apical periodontitis in root-filled teeth ranged from 40% to 51%. However, the magnitude of this problem has not been fully appreciated. *E. faecalis* is found to persist in harsh environmental conditions existing in the endodontically treated tooth, and they have been observed to be the most predominant bacteria in the teeth where root canal therapy fails. A multi-disciplinary approach to study the ability of this microorganism to survive the harsh, post-endodontic environmental conditions and their ability to cause persistent infection in the periapical region is crucial in understanding the disease process and to design treatment strategies.

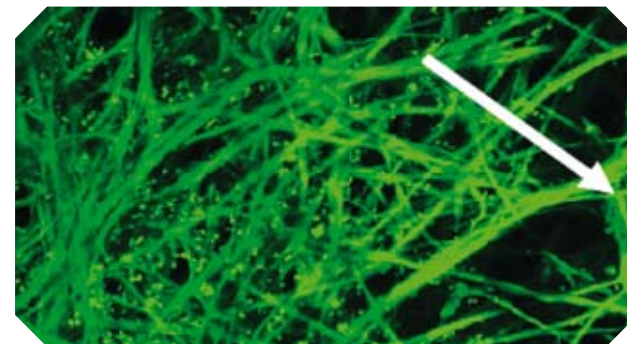
Clinical Relevance:

This study will provide in-depth understanding on persistent endodontic infections.

This study will compliment our on-going project in which we are developing an alternative treatment approach to disinfect root canal systems.



Interaction of Enterococcus faecalis and premonocyte cells



Bacterial adherence to collagen substrate

Development of Antimicrobial Nanoparticulate System to Prevent Biomaterial-centred Infections in Endodontics



Principal Investigator: Dr Anil Kishen
Total Project Value: \$166,895.65

RESEARCH HIGHLIGHTS

Aims:

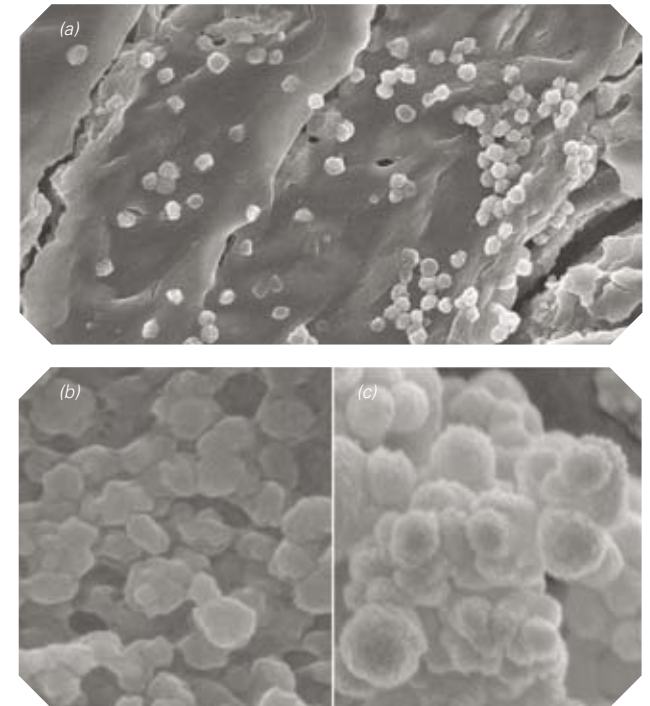
Develop, characterise and test functionalised polymeric microbead and chitosan nanoparticles to impede biomaterial-centered endodontic infections.

Abstract:

Biomaterial-centered infection results when bacterial cells adhere to the surface of a biomaterial and/or tissue and forms a recalcitrant biofilm structure. Biofilms formed on biomaterial surfaces are resistant to antibiotic therapy and can lead to chronic and/or persistent infections, in which the pathogenesis of the tissue damage is dominated by a persistent immune complex mediated inflammation. Apical periodontitis is viewed as a dynamic encounter between microbes and host defences at the interface between an infected tooth and the supporting bone. Epidemiological studies of previously root-filled teeth from different populations have reported persistent apical periodontitis in relatively high proportion (35% to 65%). Persistence of bacteria, adherence of bacteria to substrates and the development of biofilm are all contributing factors to biomaterial centered persistent apical periodontitis.

Clinical Relevance:

To develop biomaterials that prevent bacterial adherence and subsequent biofilm formation.
To develop treatment strategies to prevent biomaterial-centered infections in endodontics.



FE-SEM images of chitosan nanoparticles ((a) and (b)) and quaternized chitosan nanoparticles (c).

Load Fatigue Performance of Implant-Ceramic Abutment Combinations



Principal Investigator: Dr Willy Chang
Total Project Value: \$91,300

Aims:

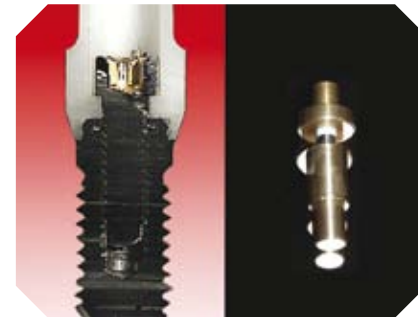
The use of ceramic implant abutments has been gaining popularity as a result of a high demand for anterior aesthetic restorations. The aim of this study is to investigate the load fatigue performance of various implant-ceramic abutment combinations. The influence of variables such as the connection design, the implant diameter and the torque level applied to the abutment screw on fatigue failure will be examined.

Abstract:

The Zirconia abutment/implant combination is a unique interface that involves two entirely different materials. The failure mode of this screw joint has not been studied in detail. A rotational load fatigue testing jig has been developed and used for previous studies completed at the NUS Department of Restorative Dentistry. Rotational fatigue testing is able to simulate the loading conditions of oral function and the use of this methodology should give a more reliable prediction of long-term clinical performance. The previous studies have focused on examining the effect of three variables at the metal to metal implant-abutment interface (different connection designs, different implant diameters, different torque levels applied to the abutment screw) on the number of cycles to failure. This investigation will be an extension of those previous studies, following the same protocol but testing abutments that are ceramic-based.

Clinical Relevance:

The relative performance of various implant-ceramic abutment combinations and the associated failure modes will provide insights into the weaknesses of current ceramic abutments and may lead to patents for new abutment designs.



*Cross-section of
the external hexed
implant-ceramic
abutment joint and
an assembled test
specimen.*



*Cross-section of
the internal connec-
tion implant-ceramic
abutment joint and a
rotational load fatigue
testing jig.*

The Effect of Ferrule Width on the Fracture Resistance of Endodontically treated Maxillary Anterior Teeth



Principal Investigator: Dr Willy Chang
Total Project Value: \$15,794.50

Aims:

Examine the effect of different ferrule widths (0.5 mm and 1.5 mm) on the fracture resistance of endodontically treated maxillary anterior teeth with a optimal ferrule height of 1.5 mm.

Abstract:

In assessing whether a tooth should be restored, the clinician must consider the amount of remaining supragingival tooth substance. A ferrule in connection with a structurally compromised tooth is defined as a 360 degree metal collar of the crown surrounding the parallel walls of the dentine extending coronal to the shoulder margin preparation. The influence of ferrule height on the fracture resistance of endodontically treated anterior teeth have been investigated by various researchers. While it is generally agreed that a ferrule length between 1.5 and 2.0 mm will provide optimal resistance to fracture, the issue of ferrule width has not been addressed in the dental literature to date. Many clinical situations arise in which the width of the coronal dentine that contributes to the ferrule effect is very narrow, as a result of decay or

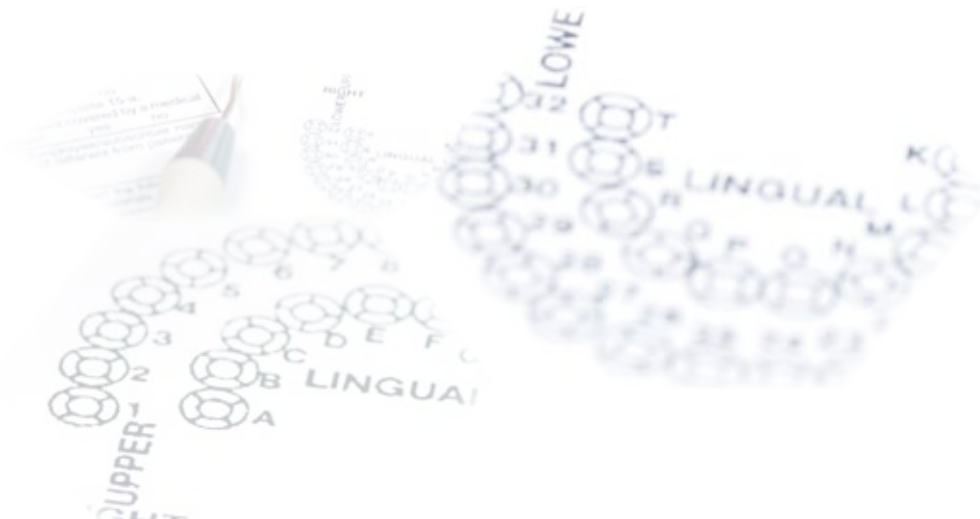
previous endodontic over-instrumentation. The clinician is often left with the question whether such a ferrule would still be effective even when an ideal ferrule height between 1.5 and 2.0 mm is present.

The purpose of this pilot study, therefore, is to examine the effect of ferrule width on the fracture resistance of maxillary anterior teeth restored with cast posts-and-cores and prefabricated posts plus composite resin cores.

For better simulation of clinical conditions, these tooth specimens will be restored additionally with cast crowns before fracture testing by the Instron machine. Stress variation that occurs in each tooth specimen during the period of Instron loading will be monitored by strain gauges cemented below the crown margin on the buccal and lingual aspect of the tooth until failure occurs.

Clinical Relevance:

New clinical guidelines can be developed on the basis of this study for a minimal ferrule width commensurate with optimal resistance against fracture.



RESEARCH HIGHLIGHTS

Characterisation of Osteogenesis by Human Embryonic Stem Cell derived Osteogenic Cells

Principal Investigator: Dr Victor Fan
Total Project Value: \$179,850

Aims:

Investigate the efficacy of applying hESCs-derived osteogenic cells for osteogenesis ex/in vivo by comparing with osteogenesis by human somatic osteoblasts.

Abstract:

In the human body, adult stem cells are stimulated and directed to differentiate into osteogenic cells to form bone eventually. To enable bone growth experimentally, there are limitations to the use of adult stem cells. By contrast, embryonic stem (ES) cells may represent an ideal human cell source. The Faculty of Dentistry (FOD) team has recently successfully differentiated osteogenic cells from human embryonic stem cells (hESCs) [Cao et al, 2005]. The Stem Cell Team from our Faculty currently hold several hESCs lines to work in collaboration with US institutes in investigation of various aspects. Four of them are from Harvard University [Cowan et al, 2004], and two from University of Wisconsin Madison [Thomson et al, 1998].

After McWhir's group of Roslin Institute first succeeded in osteogenic differentiation ex vivo of hESCs more than a year ago [Sottile et al 2003], Buttery's group of Imperial College London first reported the mineralised tissue formation in vivo with hESCs-derived osteogenic cells a few months ago [Bielby et al, 2004]. Though we managed to differentiate hESCs into osteogenic cells [Cao et al, 2005] after those two groups, no comparison study has yet been accomplished for osteogenesis between hESCs-derived osteogenic cells and human somatic osteoblasts.

As a result of this project, it is hoped that scientific data and intellectual properties of osteogenesis comparison between hESCs-derived osteogenic cells and human

somatic osteoblasts will be established in FOD/NUS for the first time in the world to be used in various applications in near future. The data and intellectual properties from this project will definitely be of great benefit to investigations in congenital and postnatal bone defect repair and reconstruction and research in bone grafting for dental implantation.

Clinical Relevance:

hESCs-derived osteogenic cells are genetically young and healthy bone forming cells. They can be immediately utilised for many purposes once the function of the cells is evaluated. The major applications are:

- (1) the study of genetic and developmental mechanisms relating to osteogenesis and bone regeneration,
- (2) R&D of gene/protein delivery therapy to treat bone lesions;
- (3) R&D of cell-injection therapy for bone repair;
- (4) R&D of cell transplantation-based bone reconstruction and tissue engineering; and
- (5) R&D of cytotoxicity / genotoxicity screening tests for bone-related biomaterials and drugs.

These research findings will have great impact on clinical applications in congenital and postnatal bone defects repair and reconstruction and for bone grafting in dental implantation.

Role of Brain Lysophospholipids in Pain



Principal Investigator: A/P Yeo Jin Fei
Total Project Value: \$200,000



Set of Von-Frey Hairs used to elicit Nociceptive response from response from the animal model used for this project.

Aims:

- Elucidate the role of lysophospholipids in neurotransmission.
- Study the effect of lysophospholipids in mediating pain transmission in the central nervous system.

Abstract:

Tissue injury and inflammation results in an enhanced response to subsequent noxious stimuli (hyperalgesia). Current work emphasises that this exaggerated response arises in part because of a sensitisation of the peripheral terminal and partly by the initiation of a facilitated state of processing of afferent input in the spinal cord or brainstem. In our recent study, we have shown that intracerebroventricular injections of inhibitors to phospholipases A2 (PLA2) isoforms were effective in modulating pain responses induced by facial injections of a chronic inflammatory agent, carrageenan (Yeo et al. 2004). PLA2 hydrolyzes the sn-2 ester bond in neural membrane phospholipids to generate free fatty acids and lysophospholipids.

The effects of lysophospholipids on pain transmission have been studied in the peripheral nervous system. Lysophosphatidylcholine causes demyelination of axons, which causes increased sodium and potassium channel clustering. Intraplantar injection of lysophosphatidic acid (LPA) at doses of 0.1-100 pmol into the hind limb of mice resulted in dose-dependent nociceptive flexor responses (Renback et al. 1999). This lipid metabolite also triggers calcium signals in cortical astrocytes (Fuentes et al 1999) and calcium plays an important role in the pathogenesis of pain. In addition, demyelination of afferent A-fibers by lysophosphatidylcholine in the saphenous nerve has been shown to induce neuropathic pain (Wallace et al., 2003).

In contrast to the above mentioned peripheral effects of lysophospholipids on nociception, little is known about the

central effects of these compounds on pain transmission. Lysophospholipids may alter the membrane fluidity of the neurons, resulting in changes in ion homeostasis. There is evidence that lysophosphatidylcholine could increase calcium influx in cardiac myocytes (Liu et al., 1991; Magishi et al., 1996), exocytosis in mouse pancreatic beta-cells (Juhl et al., 2003), and vascular smooth muscle cells (Durante et al 1997), but thus far, little is known about whether lysophospholipids could affect ion channels or synaptic vesicle exocytosis in neurons.

The major objective of the present proposal is therefore to study the effect of lysophospholipids on those properties of neural membrane that are related to synaptic plasticity. This would be carried out by:

- 1) elucidating the role of lysophospholipids in neurotransmission. This would be carried out by studying the effects of lysophospholipids in stimulating miniature end plate potentials in cultured neurons, and effects of lysophospholipids in causing exocytosis. The possible intracellular signaling pathways by which lysophospholipids could exert their effects would also be studied, using inhibitors to block these pathways.
- 2) studying the effect of lysophospholipids in mediating pain transmission in the central nervous system. Since enhanced pain transmission may indicate increased neurotransmission at synapses, it is hoped that this research would yield not only insights into the role of lysophospholipids in pain transmission, but also neurotransmission, in general.

Clinical Relevance:

It is hoped that this research would yield not only insights into the role of lysophospholipids in pain transmission, but also potential uses of inhibitors of lysophospholipid receptors in clinical management of pain.

RESEARCH HIGHLIGHTS

To Investigate the Molecular Profiles of Actinobacillus Actinomycetemcomitans, Porphyromonas Gingivalis and Bacteroides Forsythus and to establish a Clinical Correlation between these Pathogens and Aggressive Periodontitis



Principal Investigator: Assoc Prof Grace Ong
Total Project Value: \$95,000

Major Achievements of Projects Completed in Academic Year

Major Achievements:

The association of *A. actinomycetemcomitans* in periodontal diseases among patients was evaluated. The bacteria is found to be predominant in samples from diseased patients using molecular techniques. Of the many potential target genes available, the leukotoxin gene of AA was found to be useful in determining the presence of the pathogenic strains of bacteria. Moreover, transcription of leukotoxin operon was found to occur during the early growth phase of the bacteria, suggesting that leukotoxin is important for the bacteria to establish an initial infection. A significant accomplishment was the discovery of intron splicing in cytolethal toxin gene of AA. This suggests a potentially new pathogenicity mechanism of bacteria.

Our molecular analyses of the bacteria on clinical plaque samples showed that polymerase chain reactions (PCR) could be used to differentiate bacterial strains according to their pathogenicity. The use of different gene targets, for example, virulence factor gene and 16S rDNA gene, could provide information on whether the bacteria are present, and if they are, whether they are pathogenic. The use of real-time PCR to quantitatively detect AA from both healthy and diseased samples was found to have potential utility in monitoring the amount of bacteria present. Real-time PCR is also faster and more sensitive.

Tissue Engineering of an Autogenous Periodontal Transplant for the Regeneration of the Periodontium



Principal Investigator: Assoc Prof Varawan Sae-Lim
Total Project Value: \$140,500

Major Achievements:

Engineering periodontal tissue regeneration entails the establishment of the characterised and optimised primary cell lines in vitro. Both human periodontal ligament fibroblasts (hPDLFs) and human alveolar osteoblasts (hAOs) retain osteogenic potential in vitro, a function of osteo-progenitors or osteoblast-like cells in vivo. While hAOs exhibit higher osteogenic differentiation capability, hPDLFs preserve extracellular matrix (ECM) synthesis ability. On the other hands, scaffolds modification for the development of optimal cell-scaffold constructs is essential for optimal cellular adherence and proliferation facilitating subsequent differentiation for tissue formation. A composite-scaffold of polycaprolactone-tricalcium phosphate (PCL-TCP) (80:20) demonstrating improved hydrophilicity, yield strength and compressive modulus but lower porosity and surface/volume ratio appears to lead to improved hAOs proliferation and earlier expression of the related protein markers. Nevertheless, collagen 1-modified PCL-TCP scaffolds

with the higher initial hAOs attachment do not seem to bring about the significant expected synergistic benefits of differentiation expressions. Alkali-hydrolyzed perforated PCL scaffolds and membranes with the corresponding increased wettability and surface roughness appears to enhance in vitro hAO osteogenic differentiation and hPDLFs attachment and differentiation depositing major ECMs similar to 2-D plastic culture. This project illustrates the potential of hPDLF-hAO double PCL membrane/scaffold preformed constructs upon optimization in facilitating tissue growth in vivo for ultimate clinical application.

This project work received recognition in terms of a few prestigious presentation awards obtained at different conferences. It also received the honour of being highlighted in the NUS Research Annual Report 2003-2004 and was featured in NUS INNOVATION [the magazine of research & technology]: Outstanding Biomedical Research Wins Recognition by Ms Tan Lay Leng, Vol 3(2), 2002 page 66.

Regeneration of Bone using a Bioresorbable 3D Scaffold-Osteoblast Construct



Principal Investigator: Assoc Prof Ho Kee Hai
Total Project Value: \$173,000

Major Achievements:

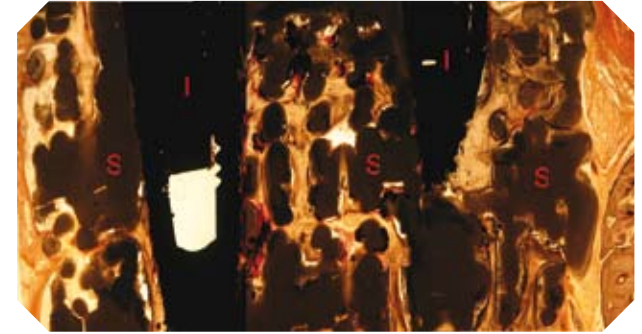
This research has stumbled upon several exciting discoveries. The novel biomaterial was a biodegradable, bioresorbable and bioactive composite scaffold consisting of polycaprolactone (PCL) physically blended with 20% tricalcium phosphate (TCP). It represents the second generation scaffold manufactured specially by the fused deposition modeling technique.

- It is crucial to prove for any potential biomaterial with medical-related applications that the material facilitates the attachment of host cells, followed by their proliferation and then differentiation into new tissue. In no instance in this process should the scaffold material or its degradation by-products cause the apoptosis or necrosis of the cells. PCL-TCP scaffolds loaded with osteoblasts sustained excellent osteogenic expression in vitro. The osteoblasts readily colonised the surfaces, rods and pores of the scaffolds while maintaining their osteogenic phenotype for four weeks. The addition

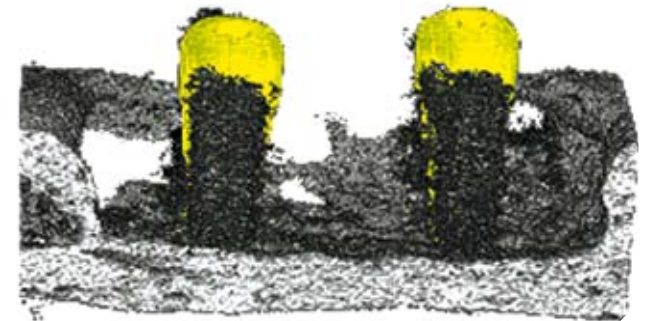
of recombinant human bone morphogenetic protein-2 (rhBMP-2) enhanced the differentiated function of these osteoblasts that resulted in accelerated mineralisation, followed by their death as they underwent terminal differentiation. Hence, the scaffolds were (1) capable of facilitating the process from cellular attachment to differentiation to mineral, (2) not toxic to the cells and (3) its 3D-architecture and porosity allowed for the infiltration of cells and loading of proteins.

- The application of our bone regenerative strategy to a canine model and for a longer-term period was investigated. The research showed that Platelet-rich plasma (PRP) loaded PCL-TCP scaffolds could facilitate the placement of dental implants, shorten wound healing time and stimulate mandibular bone regeneration simultaneously in mongrels. PRP-treated defects had 98.3 and 58.3% higher bone volume than controls at 6 and 9 months respectively. New bone trabeculae were observed in close apposition to the dental implants and had penetrated the defect site. The scaffolds experienced 33% degradation from 6 to 9 months, finally occupying only 46.9% of the cross-sectional area.

In conclusion, the research work showed that three-dimensional, bioactive polycaprolactone scaffolds can serve effectively as graft material for bone regeneration and has potential for clinical applications.



Histological section of platelet-rich plasma (PRP)-treated PCL-TCP scaffolds at 6 months implanted in the mandible of a dog. The two dental implants and scaffold remnants appeared black and dark brown respectively. The section was stained with Von Kossa, which stains calcium salts brown and non-mineralized tissue pink. It showed significant bone formation within the scaffolds. Implant = I, Scaffold = S. (Original magnification: (A) x 20, (B and C) x 40).



Micro-CT of the PCL-TCP scaffold with PRP implanted in the mandible of a dog (9mths) with the two dental implants showing bone formation as a result of the effect of PRP and the scaffold bioactivity and architecture.

Development of a Fiber Reinforced Polymer Orthodontic Wire and Arch Wire



Principal Investigator: Prof Chew Chong Lin
Total Project Value: \$464,700

Major Achievements:

This research project has successfully developed a fiber-reinforced polymer orthodontic wire and archwire. Aesthetic orthodontic wires having good translucency and mechanical properties were developed with braided glass fibers using the pultrusion method. Similarly, orthodontic archwires that possess the desired aesthetic appeal and good mechanical properties were developed with unidirectional glass fibers using flexible shrinkage tubes. US patents have been filed for both techniques.

The fabrication technique of the wires has been published by the US Patent Application Publication on 13 January 2005 under publication no. 2005/0008984. Likewise, the novel fabrication technique of archwires has also been published by the US Patent Application Publication on 24 March 2005 under publication no. 2005.0064170, and recently entered the national phase with a Singapore and a European Patent Application. Furthermore, this archwire fabrication technique was awarded a Tan Kah Kee Young Inventors' Award in 2003.

On top of that, a NUS start-up company will be exploiting these two patent-pending fabrication techniques to manufacture and market translucent orthodontic braces. Consequently, fiber-reinforced polymer orthodontic wires and archwires could potentially be available in the market within the next few years.



BioMers wire (upper jaw) compared to metal wire (lower jaw)



RESEARCH HIGHLIGHTS

Tooth/Pulp Culture for Dental Biomaterials Cytotoxicity Testing



Principal Investigator: Dr Cao Tong
Total Project Value: \$99,000

Major Achievements:

The project has produced one international award, three full papers and two short papers in peer reviewed international journals, one full paper in a CD-ROM publication, four international, and local conference papers. It has led to further successful grant application of ARC, MOE, at S\$671,000.

The project stimulated further work in the genotoxicity testing for dental materials and other biomaterials; and in the cytotoxicity testing for PLGA scaffold and other dental materials and biomaterials, which is related to the new project of in-vitro and in vivo testing of Bio-scaffold for Bone Re-construction and Implants (R-221-000-010-29, The Enterprise Challenge, Prime Minister Office, S\$ 700,000). the project has also trained manpower of 16 persons through one MSc project and five UROP projects.

A full time MSc Research Scholar, Ms Judy Saw, was trained and graduated through the project. She finished her MSc project, passed her MSc thesis exam and was awarded a MSc degree. After MSc graduation, she joined IMCB, A*STAR as a Research Assistant. Five UROP projects have been resulted from the project. Two Faculty of Science UROP and ten Faculty of Dentistry UROP students have been trained.

Currently four FOD UROP students are being trained. All students are keen and highly motivated to do related research.

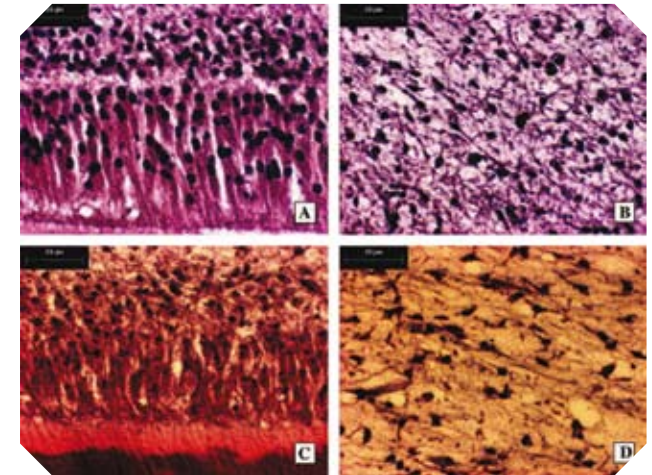


Fig. 1.
(A & B) Normal intact OD and PF using the first culture model at Day 7. Cells still maintain their normal morphology.
(C & D) Reduction in cell densities of OD and PF with significant morphology changes by Day 14 in culture (Magnification, 40 H & E staining).

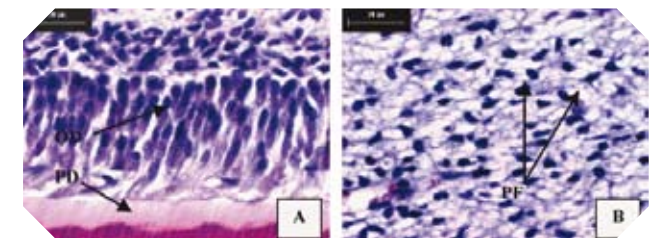


Fig. 2. Day 0 control tooth slice
(A) Healthy morphology of long columnar odontoblasts (OD) with basal nuclei, attached to the predentine (PD) and
(B) Pulp fibroblasts (PF) within the pulp chamber (Magnification, 40 H & E staining).

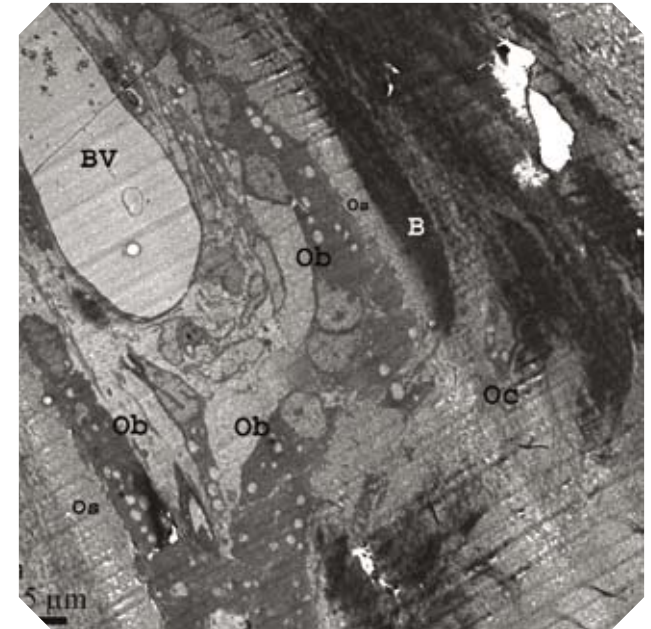
**Vascular Endothelial
Growth Factor, VEGF:
Therapeutic Angiogenesis
and Osteogenesis for Bone
Regeneration**



Principal Investigator: Dr Cao Tong
Total Project Value: \$78,213

Major Achievements:

The project has produced one full paper and one short paper in peer reviewed international journals, one full paper in submission to a peer reviewed international journal, four international, and local conference papers. One work from the project has been shortlisted for an international award and the other has been shortlisted for a local award. We have quantified the amount of new bone formation and the rate of new bone formation, identified blood vessels and osteogenic cells involved in the healing of the defects and examined the interaction of blood vessels and osteogenic cells within the PCL scaffold. Two MDS Residents, Dr Janee Lim and Dr Lo Tong Soon, were trained and graduated through the project. Both of them have attended three modules/ courses and received all necessary training of animal surgery, histology, SEM, TEM, etc. They finished their research project, passed their MDS thesis exam and been awarded a MDS degree. After MDS graduation, both of them joined the National Dental Centre as Registered Dentists.



TEM of VEGF/Fibrin/PCL group near host bone. Active osteoblasts (Ob) covering the osteoid (Os) as a sheath of closely fitted cells. Mineralized bone (B) is seen just beneath the osteoid layer. An osteocyte (Oc) is seen trapped within the new bone area. Blood vessel (BV) is situated near to the site of new bone formation.

RESEARCH HIGHLIGHTS

Occurrence of Gutta Percha-Centered Infection in Endodontically Treated Teeth



From left: Tang Kok Siew, Yap Li Chen, Rachel, Dr Anil Kishen, Zhang Ruping, Serene, Foo Chia Wei, Tabitha

Undergraduate Research Opportunities Programme (UROP) Project

This is the winning project of the 2005 Faculty Research Day. The team represented Faculty at the Dentsply Student Table Clinician Programme at the South East Asia Association for the Dental Education Meeting in Jarkata from 13 to 16 September 2006.

Abstract:

The biofilm forming capacity of *Enterococcus faecalis* on gutta percha (GP) points was examined under the influence of different growth conditions (nutrient-rich and nutrient-deprived conditions), environmental conditions (aerobic and anaerobic conditions), and conditioning fluids (saliva and serum). GP points coated with root canal sealers (Sealapex and Roth) and without sealers were tested in this study.

The specimens were conditioned for periods of 2 weeks, 4 weeks and 12 weeks in saliva and serum and the biofilm forming capacity of *E. faecalis* on different specimens were evaluated under nutrient rich and nutrient deprived (aerobic and anaerobic) conditions.

During the experiments, GP points were cultured in phosphate buffered saline (PBS) and all culture (AC)

medium to simulate nutrient-deprived and nutrient-rich conditions respectively. All samples were incubated under aerobic and anaerobic conditions for a period of 2 weeks. Following this, the evaluation of the biofilm-forming capacity of *E. faecalis* was carried out by (1) the viable cell assay and (2) scanning electron microscopy.

These experiments highlighted that the *E. faecalis* cells adhered with GP points under all tested conditions (nutrient rich (aerobic and anaerobic) and nutrient deprived (aerobic and anaerobic) conditions) after conditioning with saliva and serum. Adherence of *E. faecalis* to GP points without sealers was observed under all environmental conditions. Under nutrient deprived conditions, longer conditioning time in saliva and serum was required for bacterial adherence. SEM reflected that the biofilm formed under nutrient rich conditions were regular and multilayered, while the biofilm formed under nutrient deprived conditions were irregular and mono-layered in appearance. These findings suggest the possibilities of gutta-percha centred infection as a potential cause of persistent endodontic infection.

Outcome of Research Day held on 28 October 2005

Winner	First Runner-up	Second Runner-up
<p>Project Title : Occurrence of Gutta Percha Centered Infection in Endodontically Treated Teeth</p> <p>Group members :</p> <ol style="list-style-type: none"> 1) Foo Chia Wei 2) Tang Kok Siew 3) Yap Li Chen, Rachel 4) Zhang Ruping, Serene <p>Supervisor: Dr Anil Kishen</p>	<p>Project Title : Cytotoxicity Study of The Interaction between Stainless Steel Brackets and Beta Titanium/ Nickel Titanium Wires</p> <p>Group members :</p> <ol style="list-style-type: none"> 1) Goh Enhui , Charlene 2) Leong Jack Min , Daylene 3) Li Shanshan , Angela 4) Phang Hui Jing 5) Poh Shuxian , Sharon <p>Supervisors: Dr Cao Tong A/P Kelvin Foong Weng Chiong</p>	<p>Project Title : Effect of occlusal splints on masticatory muscle EMG during clenching</p> <p>Group members :</p> <ol style="list-style-type: none"> 1) Jee Shizhuan 2) Lai Wen Pui Bien 3) Lee Weizhi, Alvin 4) Loke Weiqiang <p>Supervisor : A/P Adrian Yap U-Jin</p>

Simulations and Modulations of Chondrogenic Differentiation from Human Embryonic Stem Cells



Student: Toh Wei Seong

Abstract:

In our study, BMP2 was able to induce chondrogenic differentiation and hypertrophy in both 2-D EB monolayer and 3-D high-density micromass (HDMM) systems, of which a distinct temporal pattern of chondrogenic activation and hypertrophic development were observed. BMP2 induced an earlier activation of Collagen II (Col 2), and a robust activation of Collagen X (Col 10) in HDMM system, when compared to the monolayer system (Fig. 1). This demonstrated the importance of cell-to-cell contact, which made the HDMM system a more appropriate system to study chondrogenesis.

Further analysis suggested that BMP2 probably exerts a bipotent effect in inducing both chondrogenic and osteogenic differentiation, while TGF-beta 1 plays a stirring effect in driving chondrogenesis predominantly. Both factors revealed little synergistic cooperation in enhancing chondrogenic differentiation, as compared to TGF-beta 1 alone. When these hEB-derived chondrogenic cells were implanted in an ectopic site of SCID mice, TGF-beta 1-pretreated cells demonstrated maximum cartilage formation (Fig. 2). These implied that TGF-beta 1 is critical in driving hEB chondrogenesis and phenotype stability of the differentiated chondrocytes for eventual purification of these cells for cartilage repair.

A Master of Science (MSc) Project

Clinical Relevance:

Cartilage cells from human embryonic stem cells (hESCs) serve as an ideal unlimited source of human chondrocytes for

- the study of sequential events of chondrogenesis during embryogenesis,
- the study of developmental and genetic disorders of cartilage, as well as
- cell-based therapy for cartilage regeneration. In order to optimise the use of hESCs for cell-based tissue repair, fundamental issues such as lineage commitment and phenotype stability of differentiated cells need to be addressed. Understanding and defining the cellular and molecular mechanism of differentiation are critical.

This study emphasised the importance of the microenvironment and exogenous growth factor stimulation in modulating the chondrogenic differentiation and maturation of hEB-derived chondrogenic cells and provided an experimental system for study of their physiological development and maturation in a controlled context both in vitro and in vivo. This study therefore paved the way for further optimisation of hESC chondrogenic differentiation and purification of putative chondrocytes for developing an efficient cell-based therapy for cartilage regeneration.

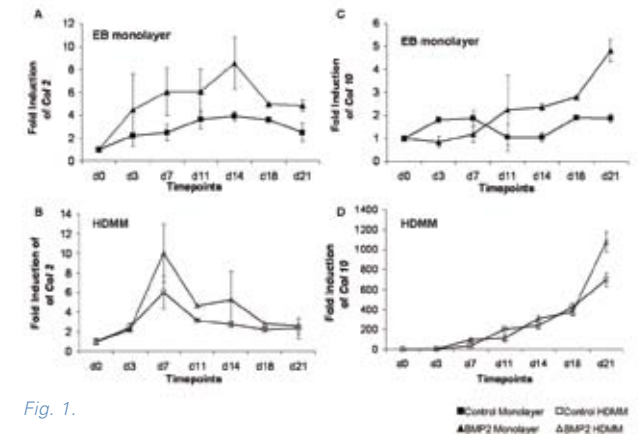


Fig. 1.

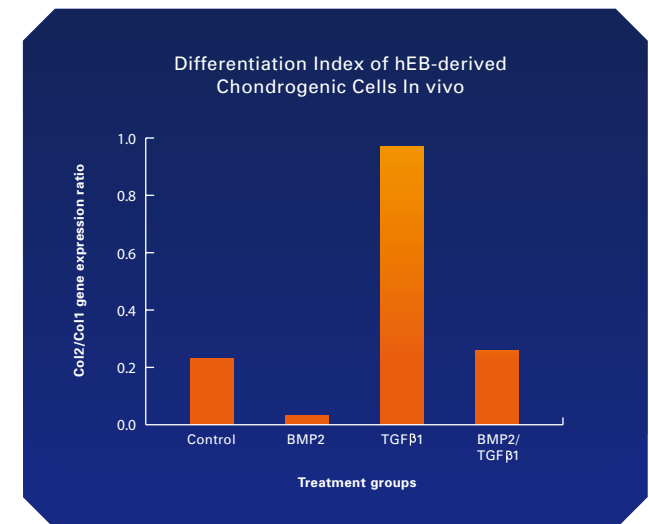


Fig. 2.

Proteoglycans and Palatal Wound Healing



Student: Dr Zou Xiao Hui

Abstract:

Congenital cleft palate is one of the most common birth defects, having an incidence of 1.5 to 2 per 1000 births. Timely surgical correction is the mainstay of treatment. Critical events for wound healing after surgical closure of cleft palate are palatal fibroblast proliferation, adhesion, and migration. Chondroitin sulfate (CS) is a glycosaminoglycan, which can be found within intracellular organelles, on the cell surface, and in the extracellular matrix. However, the regulating role of CS during palatal wound healing is not well-understood.

Five experiments were designed:

- The roles of CS and its sulfate group in human palatal fibroblast (HEPM) adhesion, proliferation, and migration were studied.
- The expression of chondroitin sulfate proteoglycans (CSPGs), chondroitin sulfate synthases (CHSYs) and chondroitin sulfate sulfotransferases (CHSTs) on HPF were evaluated in an in vitro wound model.
- The importance of CS was evaluated through blocking down the expression of CHSY1 by RNA interference (RNAi) in HEPM.
- The efficiency of extraneous CS on collagen-fibroblast-gel contraction was studied.

RESEARCH HIGHLIGHTS

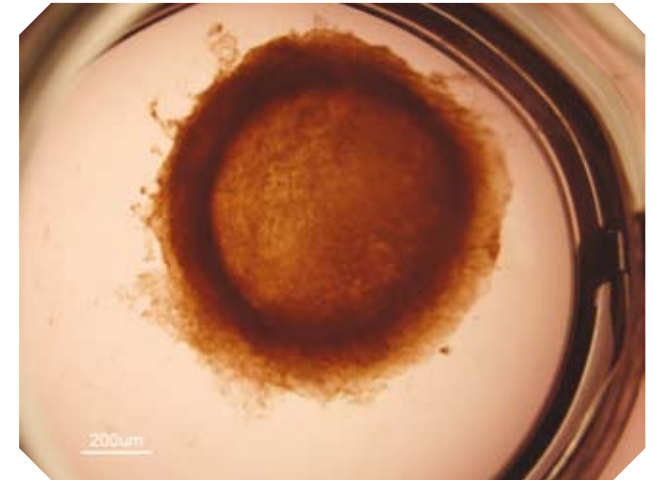
A Doctor of Philosophy (PhD) Project

- The expression of CS was investigated in an in vivo rabbit palatal wound model by immunohistochemical method.

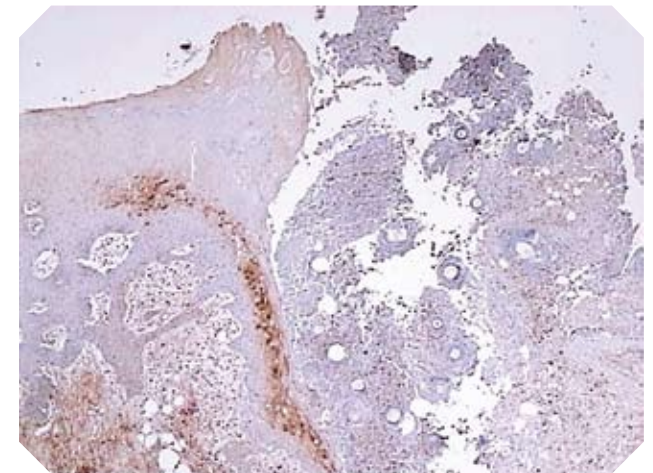
The results showed that:

- Inhibition of CS sulfation slowed the wound-closure process in vitro.
- CSPGs, CHSYs and CHSTs had a burst expression at an early time after wounding in the in vitro wound model.
- Blocking down of CS expression by RNAi resulted in the inhibition of palatal fibroblast proliferation, adhesion and migration. Also more cells were arrested in G2/M phase.
- Extraneous CS efficiently inhibited contraction of collagen-fibroblast-gels.
- The expression of CS56 around wound bed increased in the early healing stage.

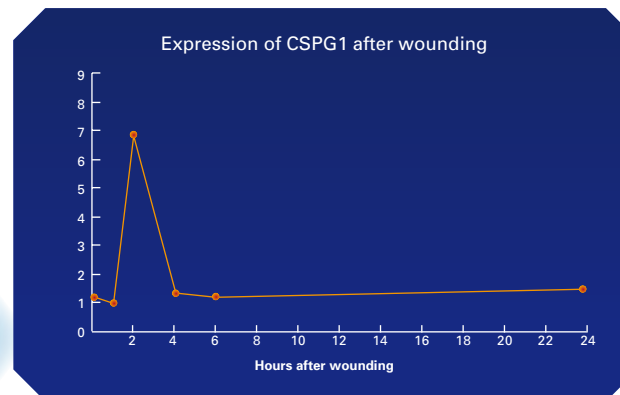
In all, these experiments proved that CS are involved in the palatal wound healing by affecting palatal fibroblast adhesion, proliferation, migration and the cell cycle; and extraneous CS inhibited contraction of collagen-fibroblast-gels. These findings provide a biological basis for future application of CS for palatal wound healing.



Cell - gel contraction



The expression of CS-56 on a 5-day- post-surgery wound model



Effects of Non-Surgical Periodontal Therapy on Periodontal Health, Metabolic Control and Cardiovascular Risks in Diabetics

Student: Dr Chee Hoe Kiat
Other Contributors: A/P Lim Lum Peng, Dr Wah Ching, Dr Khurram Ataullah, Dr Tan Ching Ching, Dr Hla Myint Htoon, A/P Thai Ai Chuan, A/P Sum Chee Fang and Dr Fidelia Tay.



From left : Drs Chee Hoe Kit, Tan Ching Ching, Lim Lum Peng, Fidelia Tay, Khurram Ataullah

RESEARCH HIGHLIGHTS

A Master of Dental Surgery (Periodontology) Project

Abstract:

Diabetes is an established risk factor for periodontal disease. Poor metabolic control of diabetes has been associated with an increased risk for coronary heart disease (CHD) which is identified as one of the main causes of mortality and morbidity in diabetes. Bi-directional association between periodontitis and metabolic control has been implicated although findings to date have not been consistent. In view of the high prevalence of diabetes and periodontal disease in the adult population in Singapore, there is a need to investigate the various risk factors that may be associated with periodontal disease in diabetic patients in the local context.

Aim:

A series of studies have been conducted by the Research group to determine the effects of non-surgical periodontal treatment on the impact of metabolic control and cardiovascular risks on periodontal health in a cohort of patients with diabetes.

Materials & Methods:

A single blind randomised controlled trial was carried out on 161 adult diabetics, randomly divided into three different groups of periodontal intervention: Group 1 – Scaling & Oral hygiene group which received oral hygiene education and scaling; Group 2 - Oral hygiene group which receive oral hygiene education as the sole modality of therapy and Group 3 - a Control group which did not receive any treatment. The clinical examination consisted of full mouth periodontal assessment and serum lipid panel, HbA1c and HsCRP at baseline, 3 months and 9 months.

Results:

A significant and sustained improvement in periodontal parameters was found in Group 1 and Group 2 during the review visits. Some improvement in plaque score was also shown in the control group. Group 1 showed the best overall improvement in all parameters. While some improvement in HDL, LDL, HsCRP levels were also observed, the differences however did not reach statistical significance.

Conclusion:

Periodontal therapy resulted in significant improvement in periodontal health irrespective of glycaemic control and metabolic control. Within the confines of the study, the improvement in periodontal health is attributed mainly to the modality of treatment rendered; metabolic control did not appear to have a significant impact on treatment responses. The findings highlight the need for an in-depth study in a larger sample group and a more holistic approach in the overall management of oral health problems in diabetes.

One of the papers, "Effects of Non-Surgical Periodontal Therapy on Lipid levels in diabetics", presented by Dr Chee Hoe Kit was awarded the best poster award for the Officer / Registrar category SGH Annual Scientific Meeting in April 2006.

RESEARCH ACHIEVEMENTS

7th Dental Students' Scientific Conference

The 7th Dental Students' Scientific Conference was held at University of Malaya in Kuala Lumpur, Malaysia from 9 to 10 December 2005. Organised by the Faculty of Dentistry of University of Malaya, the competition featured two categories namely oral presentations and poster presentations.

The NUS team was led by Loke Weiqiang, and his team members Alvin Lee, Terence Jee and Bien Lai took part in the Oral & Poster Presentation competition (International Students category). Their research supervised by A/Prof Adrian Yap was entitled: 'Effect of Occlusal Splints on Masticatory Muscle EMG during Clenching'.

The NUS team emerged as Champions out of a total of 14 participants from five participating universities and was awarded the Champions trophy and the coveted Hashim Yaacob Award and Challenge Trophy. The four other participating universities were Prince Songkla University, University of Indonesia, Universiti Sains Malaysia and University of North Sumatera.



(from Left) The NUS team : Alvin Lee, Bien Lai, Loke Weiqiang and Terence Jee

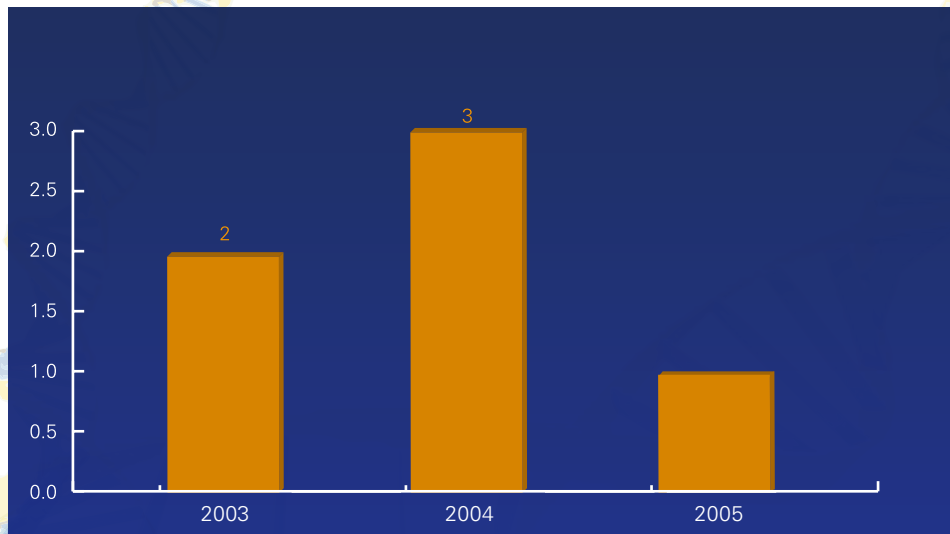


The winning team together with local participants.



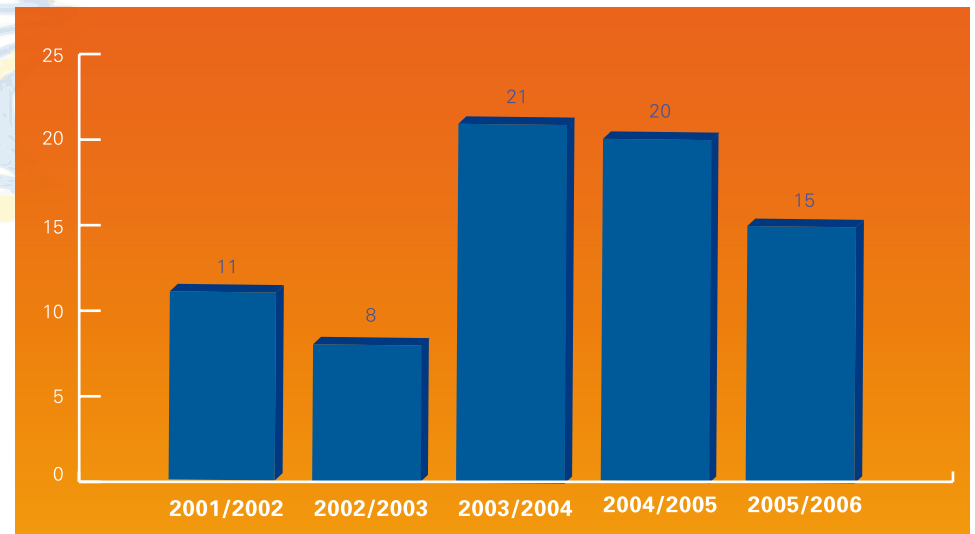
RESEARCH ACHIEVEMENTS

PATENTS



FINANCIAL YEAR

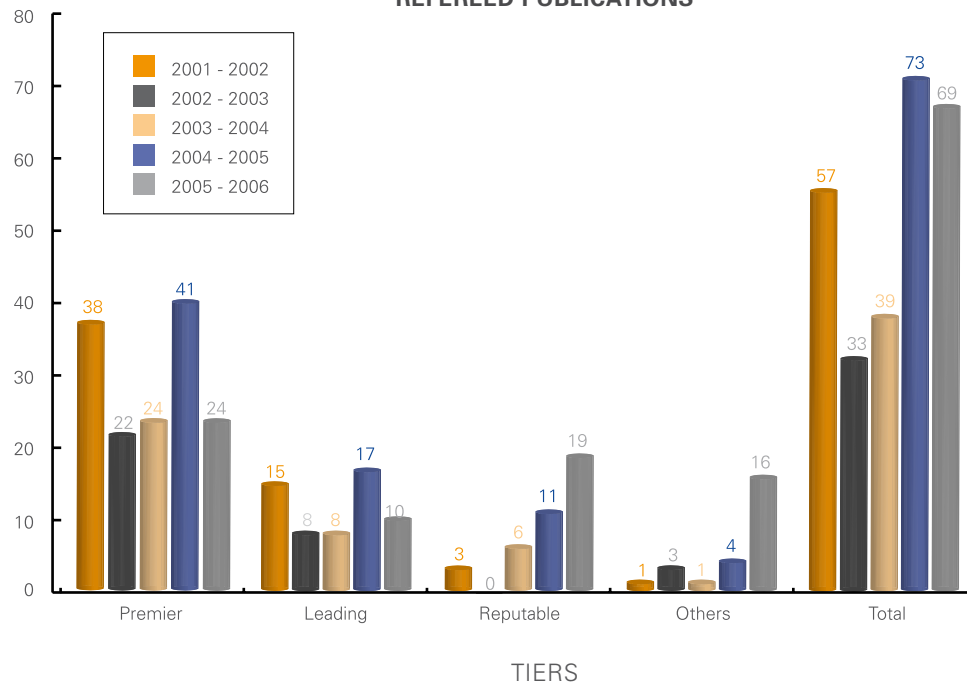
EDITORIAL MEMBERSHIPS



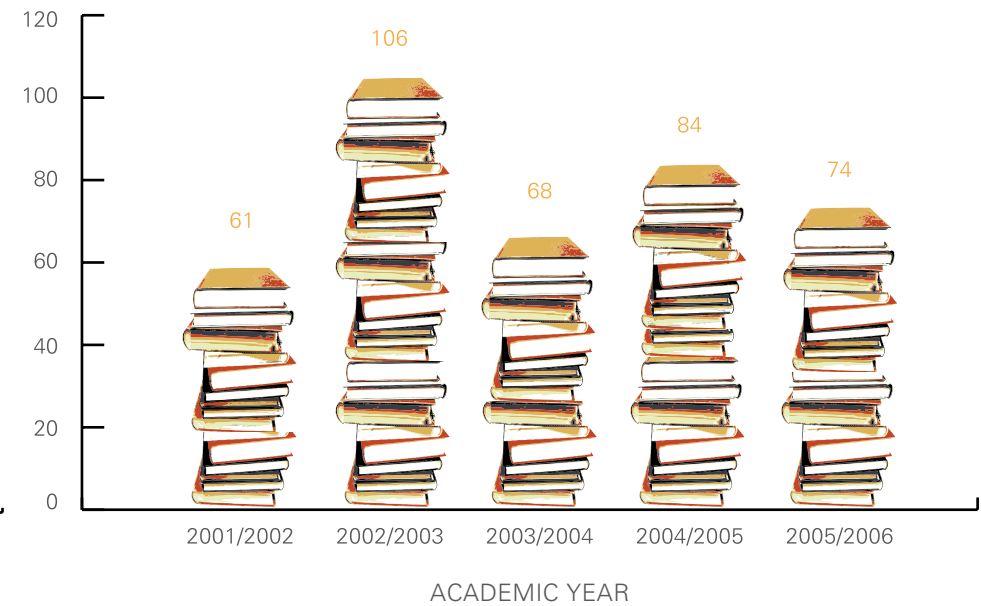
ACADEMIC YEAR

RESEARCH ACHIEVEMENTS

REFEREED PUBLICATIONS

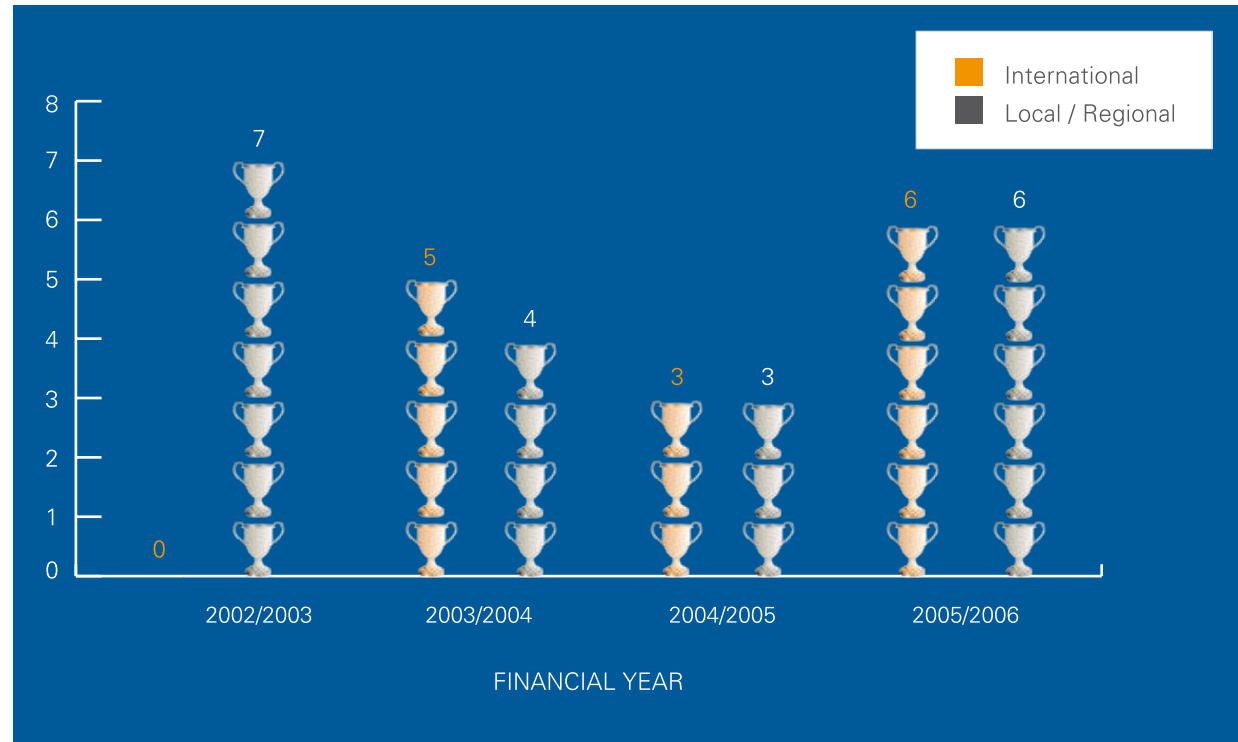


CONFERENCE PAPERS



RESEARCH ACHIEVEMENTS

PRIZES & AWARDS



RESEARCH ACHIEVEMENTS

BioMers Scaling Heights

BioMers Pte Ltd (www.biomersbraces.com) is a medical device company with an initial focus on the orthodontic treatment market. The company's first products are translucent orthodontic wires that are almost invisible but still strong enough to straighten teeth effectively. The wires are an ideal solution for people who want to straighten their teeth, but are embarrassed by unsightly metallic wires.

The company's products have been well received as an attractive new invention. To date, they have won the 6th Start-Up@Singapore national business plan competition beating 200 teams, the Asian Idea to ProductTM competition beating invited teams from all over Asia and the Best Elevator Pitch at the University of Oxford international Business Plan Competition where 106 teams competed. The company was also awarded the special prize for Best Technology Impact at the Intel - UC Berkeley Technology Entrepreneurship Challenge.

The company's products have also been well received by the market. A market survey done by the company on orthodontists in four countries (US, UK, Singapore and Canada) revealed strong interest in adopting the braces. The company is currently preparing to conduct a clinical study on their products at the University of Washington. The clinical study will serve to prove the treatment efficacy of their products as well as provide the basis to obtain Food and Drug Administration A approval for sales in the US. The company will begin sales once regulatory approval is obtained.



Mervyn Fathianathan and George Aliphtiras of BioMers receiving the Special Prize for Best Technology Impact at the Intel – UC Berkeley Technology Entrepreneurship Challenge.

Developing a plastic wire is relatively easy but the challenge is to design one which has similar properties to the metal wires used for moving teeth.

Prof Chew Chong Lin,
Director of BioMers Pte Ltd



Novel Scaffold to Support and Guide Bone Regrowth

Dedication to alleviating suffering of oral cancer patients has led Dr Victor Fan to an arduous search for the ideal scaffold that forms a matrix congenial to the regrowth of bones, a process crucial in reconstructive surgery for patients with facial deformities after cancer surgery or facial injuries.

RESEARCH ACHIEVEMENTS

Resorbable Bioscaffold Trial Wins Award



NOVEL BIOSCAFFOLD: Dr Cao Tong (left) and Dr Victor Fan with a model of their bioscaffold and Award.

In-Vitro, In Vivo and Clinical trial for Bioscaffold for Bone Reconstruction and Implants won The Enterprise Challenge (TEC) 2005's Enterprising Agency Award and Innovator Award presented by the Prime Minister's Office.

The Award provides the funding needed to translate the research into clinical trials and gives due recognition to the ingenuity of Dr Victor Fan, Assistant Professor with the Department of Oral and Maxillofacial Surgery and Dr Cao Tong, Assistant Professor, Department of Dentistry.

The project, the brainchild of Dr Fan, focused on searching for a scaffold that forms a matrix congenial to the regrowth of bones, which is a critical process in reconstructive surgery for patients with facial deformities after cancer surgery or facial injuries.

The team, in collaboration with Rapid Tech Pte Ltd, used a polymer which is able to biodegrade in the body

within six months leaving no toxic side effects and yet retaining the crucial strength and shape to allow the regrowth of bones in the first few months of implantation.

With further development in tissue regeneration, not only bone growth can be achieved. Other tissues like cartilage and skin tissues can also be directed to grow into these bioscaffolds.

"There will be broad applications in facial plastic surgery, maxillofacial trauma and reconstructive surgery as well. These bioscaffolds can also be used for preserving or augmenting bone for dental implants in patients who need their teeth removed," Dr Fan was quoted as saying.

For a scaffold to be clinically applicable, the manufacturing process has to be novel enough to be able to vary the pore size to promote bony in-growth and yet retain the necessary configuration and shape and strength for clinical use.

Dr Victor Fan,
Assistant Prof of Department
of Oral and Maxillofacial Surgery

RESEARCH COLLABORATIONS

Research Collaborations in Financial Year 2005

Collaborating Organisations	Year	Department	Region
Universities			
Saratov State University, Russia	2004 - 2007	Restorative Dentistry	International
Nanyang Technological University	2004 - 2006	Restorative Dentistry	Local
Nanyang Technological University	2005 - 2006	Restorative Dentistry	Local
National Taiwan University	2004 - 2006	Preventive Dentistry	International
Sichung University	2004 - 2005	Preventive Dentistry	International
Eastman Dental Institute	2003 - 2005	Oral and Maxillofacial Surgery	International
Georgia Tech Research Institute	2005	Oral and Maxillofacial Surgery	International
Center of Oral Biology, Karolinska Institute	2004 - 2006	Dean's Office	International
University of Wisconsin Madison	2004 - 2006	Dean's Office	International
Harvard University	2004 - 2006	Dean's Office	International
University Medical Center Groningen	2005 - 2006	Dean's Office	International
Industries			
3M Singapore Pte Ltd	2002 - 2006	Restorative Dentistry	International
Rapid Tech Pte Ltd	2004 - 2006	Oral and Maxillofacial Surgery & Dean's Office	Local
Research Institutions			
Genomic Institute of Singapore, A*STAR	2004 - 2006	Dean's Office	Local
SIMTech Pte Ltd, A*STAR	2004 - 2006	Dean's Office & Oral and	Local

RESEARCH ACTIVITIES

Peking University and NUS seek research collaboration



Professor Xu Tianmin, who holds the position of Chairman, Department of Orthodontics at the Peking University School of Stomatology visited the Faculty of Dentistry from 2 to 6 March 2006 under the Overseas Attachment (Fellow – Inbound) Programme. The visit saw him having discussions and visiting research labs in a bid to develop a sustainable research co-operation in the area of 3D imaging and visualisation of the craniofacial region

through complementary strengths in the image processing and modeling (NUS) and the availability of clinical data (Peking University).

He was also one of the key speakers at the 2nd Singapore-China Clinical Symposium on "Reconstructive and Cosmestic Oral and Maxillofacial Surgery" held on 4 March 2006.

Forging closer ties with UMCG

Dr Cao Tong visited the University Medical Center Groningen (UMCG), Groningen, Netherlands from 10 to 17 October 2005 under the Overseas Attachment Programme (Fellow – Outbound) Programme. The objective of the trip was to seek research collaboration on stem cell and tissue regeneration to which Dr Cao received a positive response from UMCG. Keen to forge a closer working relationship, UMCG agreed to a reciprocal visit to NUS led by Dean Prof Dr Sibrand Poppema in March 2006 who signed a letter of intent

on research co-operation. UMCG also offered spare human IVF embryos (<14 days) from IRB-approved donors in UMCG for joint research on new human embryonic stem cell lines development.



Dr Cao Tong visited the UMCG.

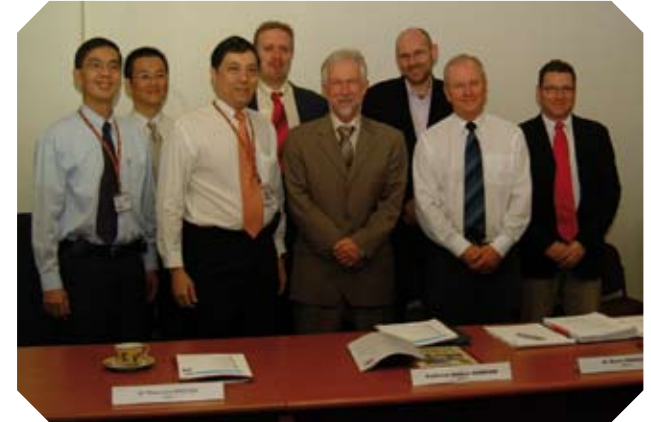
RESEARCH ACTIVITIES

UMCG Signs Letter of Intent

The visit was the result of Dr Cao's fruitful trip to University of Groningen in October 2005 to seek collaboration on stem cell research. The UMGC delegation consisted of Prof Dr Sibrand Poppema (Dean, UMCG) Prof Dr Andrew Sandham (Head, Orthodontics Department), Dr Marco Harmsen (Head, Laboratory of Molecular Biology, Department of Medical Biology), Dr Theo van Kooten (Head Section Biocompatibility and Biomaterials, Department of Biomedical Engineering) and Dr Eugenius G.J.M. Arts (Head Laboratory/Clinical Embryologist, Laboratory for Reproductive Medicine, Department of Obstetrics and Gynaecology).

The visit aimed to establish strategic research collaboration in the areas of lineage differentiation of adult & embryonic stem cells and tissue regeneration between the University Medical Centre Groningen (UMCG) and the Faculty of Dentistry (FOD), NUS. To this purpose a Letter of Intent was signed between A/P Keson Tan, Dean of FOD and Prof Dr Sibrand Poppema, Dean, UMCG.

Additionally, a talk on stem cells was conducted by Dr Marco Harmsen and on Tissue Engineering by Dr Theo van Kooten.



Group photo of UMCG Delegation



RESEARCH ACTIVITIES

Research Interns at Faculty of Dentistry.

Names of Research Interns		
<ul style="list-style-type: none"> • Kumar Neeraj Bachelor of Technology (Electrical) Year II • Pandey Gaurav Bachelor of Technology (Mechanical) Year II From Indian Institute of Technology 	<ul style="list-style-type: none"> • Tuchina Elena Dept of Microbiology Year IV student • Dr Surmenko Elena PhD (Physic and Maths) in Laser Physics, From Saravtov State University, Russia 	<ul style="list-style-type: none"> • Ms Patrina Maryann D/O Adakalaisamy • Ms Adelina Tan Yi Ping From Temasek Polytechnic, Singapore
Supervisor (s)		
<ul style="list-style-type: none"> • A/P Kelvin Foong Weng Chiong, Dept of Preventive Dentistry, Faculty of Dentistry • A/P Ong Sim Heng Dept of Electrical and Computer Engineering, Faculty of Engineering. 	<ul style="list-style-type: none"> • Dr Anil Kishen Dept of Restorative Dentistry, Faculty of Dentistry • A/P Jennifer Neo Chiew Lian Dept of Restorative Dentistry, Faculty of Dentistry 	<ul style="list-style-type: none"> • A/P Yeo Jin Fei Dept of Oral and Maxillofacial Surgery, Faculty of Dentistry • A/P Ong Wei Yi Dept of Anatomy Yong Loo Lin School of Medicine
Period		
20 May 2005 - 20 July 2005	13 October 2005 – 12 December 2005	14 September 2005 – 10 February 2006
Research Project		
<p>Research Project: 3D Modelling of Craniofacial Images for Computer Visualisation.</p> <p>They are trained to document and critically assess the current published protocols for experimental validation for the accuracy of image processing and integration of 3-dimensional images of the oral and craniofacial anatomical regions.</p> <p>They develop new and utilise existing image processing capabilities to achieve anatomical accuracy of the 3-dimensional shape of the human face and structures of the human facial skeleton derived from various 3D imaging modalities such as surface scanning and computer tomographic scanning.</p>	<p>Research Project: Infra-Red Spectroscopy and X Ray diffraction Analysis on Normal and Pathological Dental Hard Tissues.</p> <p>The two interns spent their one and a half months doing the Fourier Transform Infrared and X-ray diffraction analysis of normal and carious enamel & dentine tissues and remineralised enamel & dentine.</p>	<p>Research Project on: Role of Nitric Oxide and Lipid Mediators in Orofacial Pain.</p> <p>They were trained in animal handling, immunohistochemistry, biochemical analyses, and observation of allodynia behavior in an animal model of orofacial pain.</p>

RESEARCH ACTIVITIES

Kyushu University Offers Scholarship and Attachment Opportunities

Professor Kunio Ishikawa, Vice Dean, Chairman, Department of Biomaterials, Faculty of Dental Science, Kyushu University, visited on 10 March 2006 with the aim of promoting PhD programme and research attachment opportunities.

Candidates who are deemed to have a promising future in the home country University or college graduate 35 years old or younger can apply for the PhD programme scholarships. The benefits include 180,300 Yen per month allowance, waived tuition fee, 25,000 Yen of settling in allowance, 80% of medical fee assistance and a round trip airfare.

As for the research attachment, the Japanese Society for the Promotion of Science (JSPS) provides Post-Doctoral Fellowships for foreign researchers. Applications are to be made through Japanese researchers. The duration ranges from 12 to 24 months and the terms of the award are a round trip air ticket, 392,000 Yen University allowance, 200,000 Yen settling in allowance and annual tour.

20th IADR (SEA Division) and 16th SAADE Annual Meeting



(from left) Some of the participants from Faculty: A/P Kelvin Foong, A/P Stephen Hsu, Ms Soh Mui Siang, A/P Keson Tan and A/P Keng Siong Beng

Held in Malacca, Malaysia from 1 to 4 September 2005, The meeting were attended by Dean A/P Keson Tan and eight other Academic Staff members from the Faculty of Dentistry. A total of 17 research papers from the Faculty of Dentistry were presented. A/P Kelvin Foong has been elected the Treasurer of IADR (SEA Division) for 2005-2006.

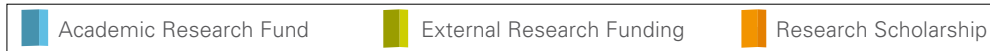
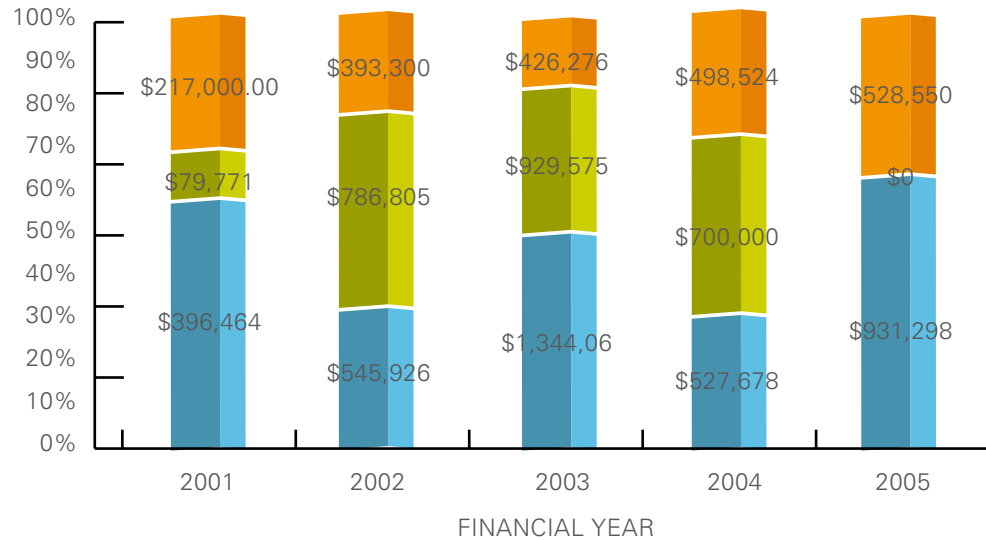
Research Mentorship for Junior College Students

Ms Goh Sher Li, Ms Chia Po Ying, and Ms Long Ying Ying from Victoria Junior College enrolled in the research mentoring programme under Dr Anil Kishen at the Biophotonics Laboratory. The main purpose of this mentorship programme was to foster an interest towards research careers among junior college students. The objective of this project was to evaluate the role of visible light to detect incipient enamel caries. The findings of this laboratory-based-study indicate that visible light can be used to monitor pathological demineralisation and physiological remineralisation of enamel at a very early stage. Keeping in mind the potential benefits of visible-light based fiber-optic diagnostic sensors, this pilot study is anticipated to have significant applications in clinical dentistry.

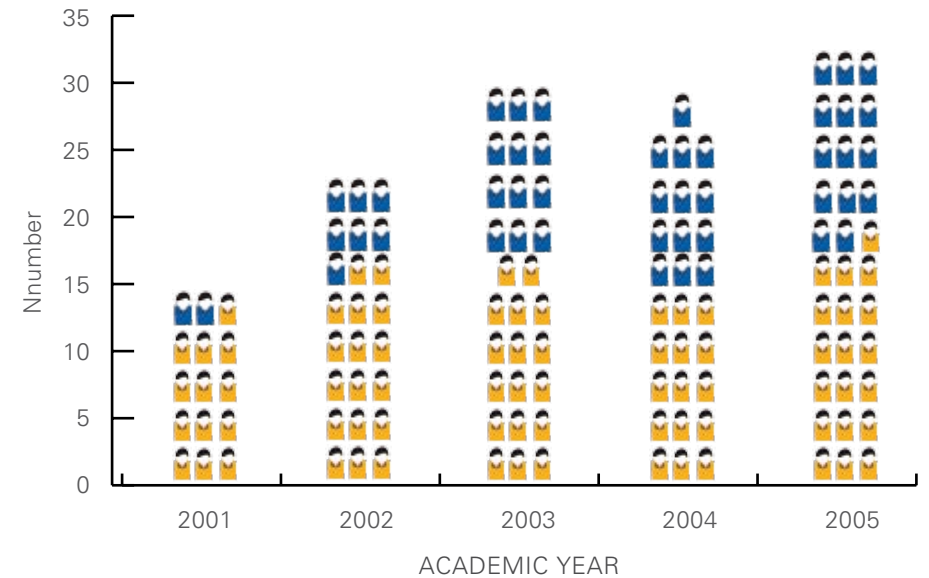
The Singapore Science and Engineering Fair (SSEF) is a national competition organised by the Ministry of Education (MOE), A*STAR, and the Singapore Science Centre (SSC). The judging criteria consisted of "Creative Ability, Scientific Thought, Thoroughness, Skill, Clarity and Teamwork". The above research project, entitled "Investigation into utilising visible light for the diagnosis of incipient enamel caries" was selected for the bronze award in the SSEF 2006 competition.

RESEARCH STATISTICS

RESEARCH FUNDINGS

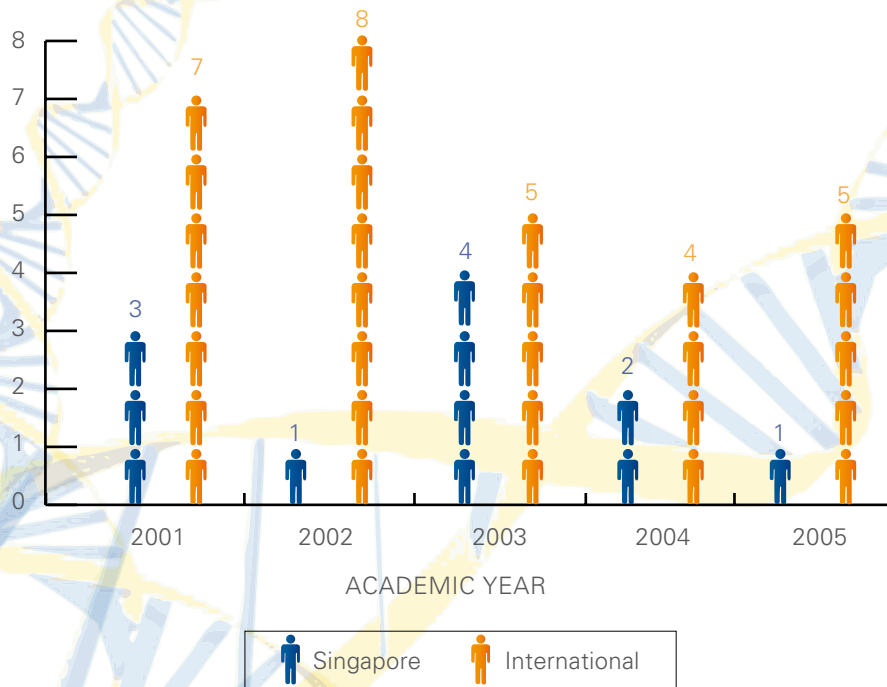


ENROLMENT OF RESEARCH STUDENTS

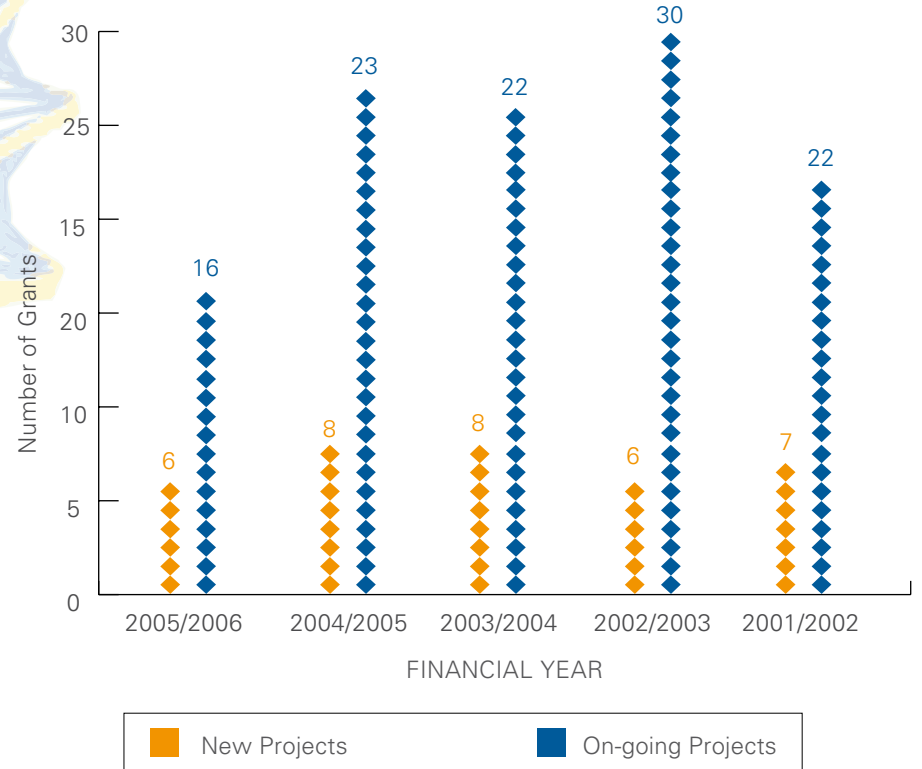


RESEARCH STATISTICS

RESEARCH STUDENTS BY NATIONALITY



NEW AND ON-GOING RESEARCH PROJECTS



The Faculty of Dentistry has engaged the national challenge of making Singapore a hub for biomedical science research and contributes to this end with a mission driven research enterprise to improve oral and craniofacial health and the delivery of clinical care.

The scope of this research enterprise consists of

1. Understanding disease and pain transmission mechanisms;
2. Developing cost-effective strategies to prevent and manage tooth decay, root canal infection, chronic periodontitis and chronic facial pain;
3. Regenerating bone – congenitally missing, lost through disease, trauma, and regenerating periodontal ligament;
4. Replacing lost teeth or tooth structures by creating better and compatible biomaterials, and understanding the biomechanics of artificial oral implants for improved mastication; and
5. Developing 3D virtual models for clinical visualisation and simulation of the dental and craniofacial structures.

Why the three initiatives?

The Faculty embraced three new research initiatives in July 2005 to harness new opportunities and funding appearing in the national research landscape to develop life sciences research in oral and craniofacial health. The three new research initiatives are to focus the Faculty's key research strengths in addressing questions with direct application for the improvement of oral health and the delivery of clinical care.

What they are

The creation of the Center for Craniofacial and Regenerative Biology (CCRB), the Dental Biophotonics

and Biomaterials Programme (DBBP), and the Clinical Craniofacial Research Unit (CCRU) is most timely. These research initiatives serve as incubators for the development of major research programmes leading the Faculty's research thrust in the life sciences.

Functions

The incubators are to provide an environment for programmatic and PI-led intra-faculty and external collaborative research, so as to secure higher amounts of funding from NUS and non-NUS funding streams, and train more research graduate students at the PhD level. Each of the three research initiatives will be governed by defined objectives and performance criteria.

1) Center for Craniofacial and Regenerative Biology

This centre aims to nurture research in (i) understanding the molecular mechanisms regulating chronic facial pain, and in (ii) understanding the mechanisms of healing and regeneration of oral hard and soft tissues such as bone, cartilage, oral mucosa (with no scar formation) and periodontal ligament. The CCRB also aims to (iii) develop novel techniques for such regeneration through the use of human embryonic and adult stem cells and scaffold technologies for improved cellular differentiation, survivability and growth.

2) The Dental Biophotonics and Biomaterials Programme (DBBP)

The Dental Biophotonics (DB) Programme addresses scientific questions related to dental hard tissue diseases and microbial infection by leveraging on the platform technology of biophotonics to understand and

regulate the mechanisms of demineralisation of dental tissues and oral infection.

The Biomaterials (B) Programme focuses on the development and characterisation of biomimetic materials for restorative oral therapy, and includes biomechanics research on oral implants.

3) The Craniofacial Clinical Research Unit

The Craniofacial Clinical Research Unit will coordinate and consolidate clinical research, and facilitate the interaction between clinicians and basic scientists. This Unit will also provide a well controlled setting for translational research and engage industry partners for collaborative research.

Each of the current five key research programmes (table below) and PI-led research projects will be engaged in at least one of the three research initiatives to further build core expertise, generate knowledge and develop peaks of research excellence identifiable with improvement in oral health and clinical care.

	CCRB	DBBP	CCRU
Regenerative biology	✓	✓	✓
Oro-facial pain mechanisms	✓		✓
Biomaterials and Biomechanics	✓	✓	✓
Cariology and microbial infection		✓	✓
Craniofacial imaging and simulation			✓

FACULTY OF DENTISTRY
National University of Singapore

5 Lower Kent Ridge Road,
Singapore 119074

Telephone :
(65) 6772 4987

Facsimile :
(65) 6778 5742

<http://www.dentistry.nus.edu.sg>