

Research Report
08/09

Faculty of
Dentistry



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Foreword

Research vibrancy is integral for an institution's sustainable growth and development. While the past two years have witnessed infrastructural consolidation, Academic Year 2008/09 was when effort was focused on emerging areas of research engagement and multi-disciplinary collaboration.

The setting up of a state-of-the-art Fluoride Laboratory as well as the establishment of an Oral Biofilm Analysis facility in collaboration with the University of Otago, under the Craniofacial Clinical Research Unit (CCRU) / Dental Biophotonics & Biomaterials Programme (DBBP) Research Initiatives will facilitate the study of a diverse spectrum of bacteria and yeasts, and promises to bring the Faculty to another intellectual paradigm. The Oral Tissue Repository under the Centre for Craniofacial & Regenerative Biology (CCRB) has supported the maiden steps in the study of ethically less controversial, dental pulp stem cells, which holds up the potential of bridging Dentistry with other life-science related platforms.

The pursuit of academic excellence would only be possible if existing strengths are capitalized upon, coupled with continual recruitment of global research talent. The Faculty has provided an engine ready to be driven, working in concert to create an incubator that would empower us to take on the increasing research challenges that are emerging.

Citing Arthur Schopenhauer "...the greatest amount of knowledge, if not elaborated by our own thoughts, is worth much less than a far smaller volume that has been abundantly and repeatedly thought over.". Excellence is not about capacity, it's about mind power. The Faculty's research enterprise may be small, but if we persevere positively, we can make an impact.

Associate Professor Varawan Sae-Lim
Vice Dean (Research)



Faculty Research Strategy

Faculty Vision

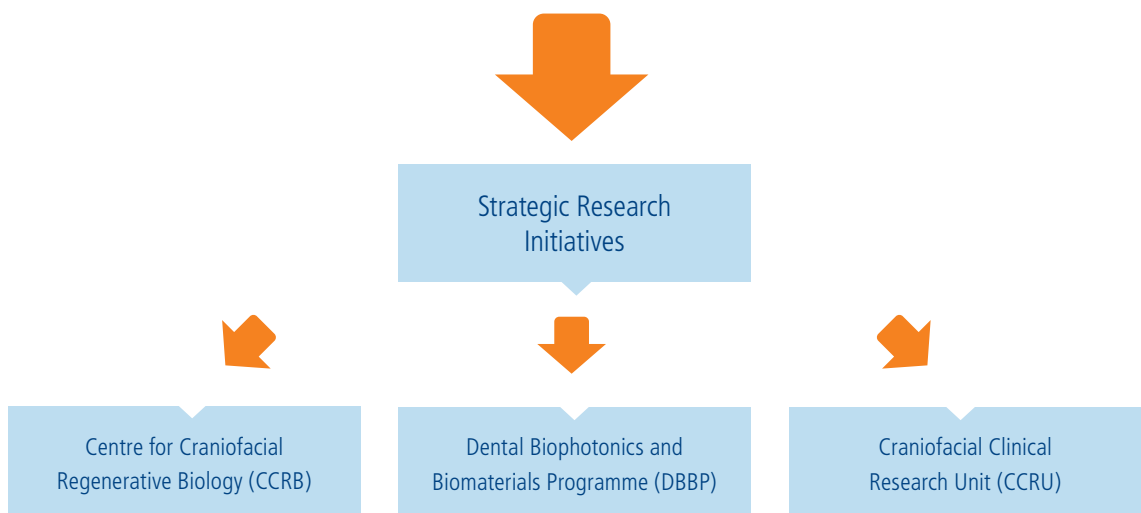
To be a Dental Institution of International Distinction

Faculty Mission

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

Research Mission

To improve Oral, Dental and Craniofacial Health and the
Delivery of Clinical Care



The Centre for Craniofacial and Regenerative Biology (CCRB)

Contributed by Ag. Director Assoc Prof Yeo Jin Fei

Overview:

In the academic session reviewed, besides facilitating established research programmes like embryonic stem cell research and orofacial pain research, CCRB is pleased to report the completion of the set up of key infrastructure and capability, i.e. 'Oral Tissue Depository [OTR]' which is essential to nurture budding research that harness oral tissue-derived adult stem cells. With the acquisition of this capability of dental pulp stem cell, CCRB aims to advance cell-based research exploitable in craniofacial tissue regeneration and other translational medical research entities. The CCRB-OTR will therefore position the FoD in the research forefront of this global research arena.

Progress in FY 2008/09:

The Oral Tissue Repository, which is established as a core research facility following the approval of Institutional Review Board, started its initial operation by setting up all the basic equipments and consumables required for tissue collection and banking. The OTR – Patient Information and Consent form, required for the workflow, was revised and had received approval from IRB. Other OTR forms include:

1. OTR Data Collection Form
2. OTR Laboratory Information Sheet
3. OTR Interim sheet
4. OTR Participant Contact information sheet

A brief workflow for the operations of OTR was introduced starting from taking patient's consent to collection of specimen from the NUH Operation Theatre. A successful trial run was completed for the collection of a few specimens i.e. the first three to be collected. At present, OTR is functioning successfully with a few tooth specimens in store. A pilot study is being implemented on isolation and cryopreservation of dental pulp cells from healthy wisdom teeth. In future, we anticipate collecting and cryopreserving gingival and Periodontal ligament cells along with non-wisdom tooth specimens.

In the year under review, CCRB has secured three Academic Research Fund (AcRF) research and one start-up grant (with a total grant amount of S\$580,560) and another external collaboration grant with SIMTech amounting to S\$88,7859. Dr. Liu Hua in the research team under AP Cao Tong won "The China Scholarship Council Award" with a prize money of US\$5000. AP Cao Tong together with Professor Yu Guang-yan of Peking University PRC secured an International Collaboration grant amount for RMB2,570000 from the Ministry of Science and Technology, PRC. CCRB through its research teams under AP Cao Tong & AP Yeo Jin Fei published four full-length papers in premier journals.

The Dental Biophotonics and Biomaterials Programme (DBBP)

Contributed by Director: Assoc Prof Stephen Hsu

Overview:

Progress in FY 2008/09:

This year the members of DBBP have obtained two Academic Research Fund (AcRF) research, one start-up grant and one external grant (with a total of S\$427,414.47), 13 articles (with nine published in the premier journals) and two regional research awards. The thematic progress is summarized below:

Tooth-biofilm Interaction:

- Dr. Anil's group successfully published two articles in premier journals. The team has leveraged on the high intensity focused ultrasound to deliver antibacterial nanoparticles into dental tubules. One UROP student team utilized the Light Activated Disinfection (LAD), with MB in emulsion (PF4), to generate singlet-oxygen for destruction of biofilm bacteria. The student research team won an award in the 2008 IADR-SEA Manila meeting and published their article in a reputable journal.
- Another undergraduate research team, supervised by A/P Hsu, challenged the "textbook truth" and demonstrated the cariostatic potential of an acidic drink containing sucrose, glucose, and lactobacillus (Yakult™, pH=3.65). This clinical trial, driven by a counter-intuitive hypothesis, won them the Best Paper Award in the 2008 "GC Asia-SEAADE Student Prevention Program Competition". Their results have paved the way to secure a research grant furthering their work to prevent white spot lesions around orthodontic brackets.

Laser-tissue interaction:

- Dr. Anil's team published an article augmenting antibacterial efficacy of Advanced Non-Invasive Light Activated disinfection, in addition to their success in monitoring compositional changes during dentin demineralization employing Electronic Impedance Based Spectroscopy.
- A/P Hsu's team investigated the "masking effects" of saliva on laser/heat-induced physicochemical changes in enamel, which is a critical issue for clinical laser application on caries prevention.

Bio-imaging research:

- A/P Kelvin Foong's team continued building 3-D statistical models to profile tooth and human face using laser imaging modalities, MRI, and cone beam CT. The team published two articles using MRI to conduct quantitative analysis on human masticatory muscles.
- A/P Hsu's team employed the 2nd and 3rd harmonic generation microscopy to characterize the crystalline lattice structures of pathological enamel hydroxyapatite.

The Dental Biophotonics and Biomaterials Programme (DBBP) cont'd

Biomaterial Research:

- A/P Keson Tan's group published three premier journal articles investigating osseointegration and implant stability using finite element analysis and a neural network. He also secured a grant investigating the 3-D accuracy of plastic transfer impression copings for three implant systems.
- Dr. Clarisse Ng launched her start-up grant to study bio-mimetic surface modification.
- A/P Ngo utilized his start-up grant to work on the mechanisms involved in the remineralization of partially demineralized dentine in the presence of glass-ionomer.

Craniofacial Clinical Research Unit (CCRU)

Contributed by Director: Assoc Prof Jennifer Neo

Overview:

In the year of review, two ARF and two start-up grants (totaling S\$534,460) were obtained. Four articles were published, two of which were in premier journals. The progress is summarized below:

Fluoride Studies

The unit also established a state-of-the art fluoride laboratory (Ion Chromatography) which will be used to support projects which include the detection of fluoride in fluoridated salt, fluoridated toothpaste, finger nail samples and baby milk formulae.

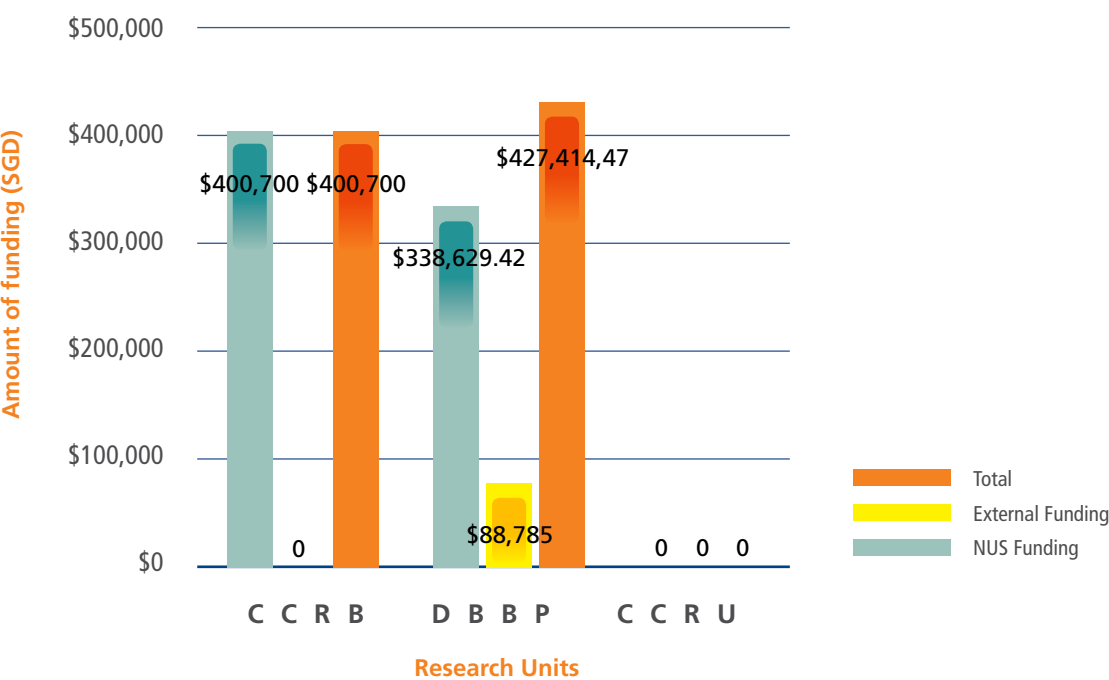
Caries Risk Assessment (CRA)

A/P Stephen Hsu's research team has carried out the first of its kind community-based nation-wide survey to assess the caries risk among preschoolers in Singapore. A total of 1,782 preschoolers were randomly selected for oral examination, salivary tests, and questionnaire survey. The study established biophysiological CRA models which could be useful for early detection of caries in children and early intervention with cost-effective caries prevention program in the community. In the clinic, it can be utilized for evidence-based diagnosis and treatment planning.

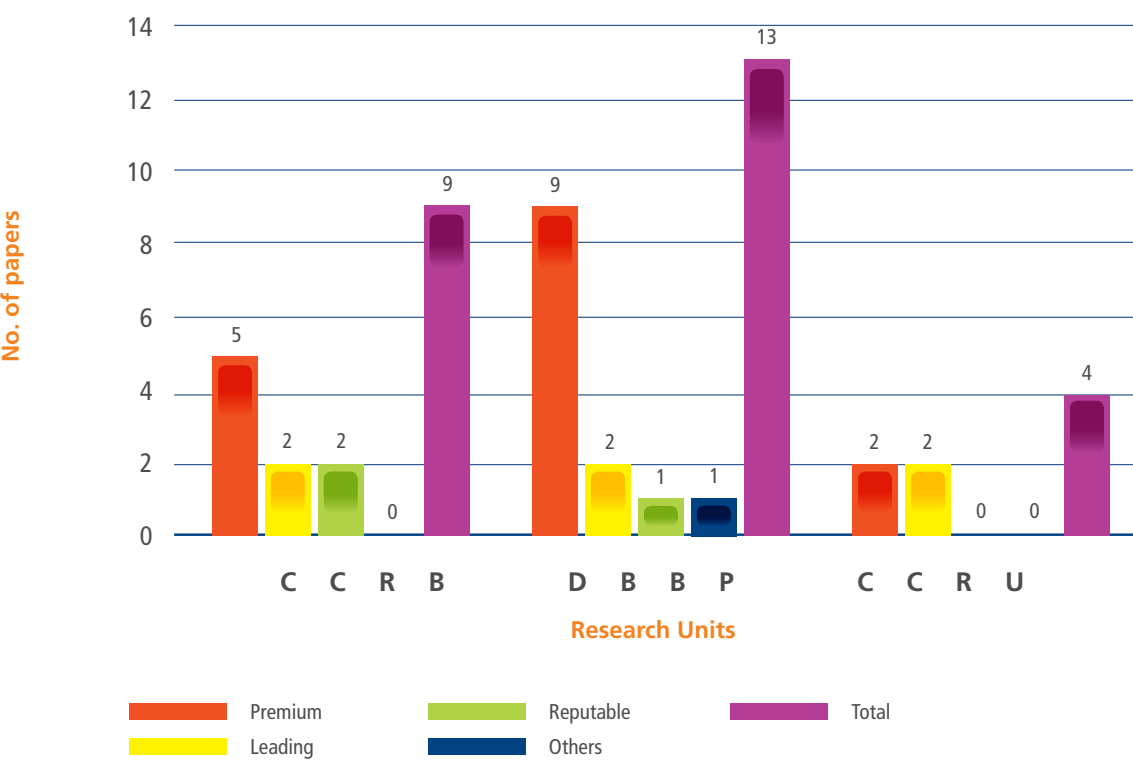
Studies in the pipeline include the following

- The impact of oral health on the daily performance of institutionalized elderly Singaporeans – a pilot study
- Evaluation of caries risk assessment models among individuals undergoing multi-bracket therapy (fixed orthodontic appliance)
- Identifying risk of exacerbation of asymptomatic persistent endodontic lesions (APEL) and building a risk assessment model for evidence-based management
- Real-time computation models for determining the centre of resistance for Orthodontics

Research Funding in FY 2008/09



Research Publication in AY 2008/09



List of Conferred MSc and PhD Students in AY 2008/09

| Name | Main Supervisor | Degree | Nationality | Thesis Title |
|-----------------|-----------------|--------|-------------|---|
| Annie Shrestha | A/P Anil Kishen | M.SC. | Nepal | Chairside Optical Sensor to Monitor Bacterial - Mediated Acidogenic - Profile of Saliva in Children |
| Md Nazrul Islam | Dr. Victor Fan | M.SC. | India | Radiographic assessment of bone regeneration in alveolar sockets with PLGA bioscaffold after teeth extraction |
| Shibi Mathew | A/P Anil Kishen | M.SC. | Indian | Enterococcus Faecalis Biofilm Mediated Inflammatory Potential |
| Khoo Suan Phaik | A/P Adrian Yap | PH.D. | Malaysian | Biopsychosocial characteristics as predictors of treatment outcome of TMD patients with symptoms of pain |

List of Conferred MDS Students in AY 2008/09

| Endodontics | | |
|--|--|---|
| Student Name Lim Siow Hooi Intake AY2006/07 | Main Supervisor/ Co-Sup(s) A/P Varawan Sae-Lim Dr. George Yip CI A/P Chen Nah Nah | Research Title IL-6 Expression Following Delayed Tooth Replantation in a Canine Model |
| Student Name Ng Yuk Ching Intake AY2006/07 | Main Supervisor/ Co-Sup(s) A/P Varawan Sae-Lim Dr. George Yip CI A/P Chen Nah Nah | Research Title IL-8 Expression Following Delayed Tooth Replantation in a Canine Model |
| OMS | | |
| Student Name Poh Hze-Khoong, Eugene Intake AY2006/07 | Main Supervisor/ Co-Sup(s) Dr. Khoo See Meng Adj A/P Adrian Yap Dr. Chan Yiong Huak A/P Yeo Jin Fei | Research Title A Clinical Prediction Rule for Obstruction Sleep Apnea |
| Student Name Wee Tze Haur Intake AY2006/07 | Main Supervisor/ Co-Sup(s) Dr. Poon Choy Yoke A/P Yeo Jin Fei Dr. Andrew Tay | Research Title Neurosensory Disturbance Following Mandibular Setback Surgery Using Bilateral Sagittal Split Osteotomy: A Pilot Study of 10 Patients |
| Student Name Norhisham Bin Mohamed Intake AY2006/07 | Main Supervisor/ Co-Sup(s) A/P Yeo Jin Fei Dr. Aidan Yeo Dr. Chan Yiong Huak | Research Title Surgical Complications Following Mandibular Third Molar Removal: A Comparative Retrospective study between the Young and Matured Population |
| Orthodontics | | |
| Student Name Chan Feng Yi Intake AY2006/07 | Main Supervisor/ Co-Sup(s) Dr. Soh Jen Dr. Chew Ming Tak Dr. Chan Yiong Huak A/Prof Kelvin Foong | Research Title Orthodontics and Quality of Health: A Patient-Centered Evaluation |
| Student Name Chong Canon Intake AY2006/07 | Main Supervisor/ Co-Sup(s) A/P Kelvin Foong Dr. Goh Poh Sun A/P Ho Yew Kee A/P Ong Sim Heng Dr. Chan Yiong Huak | Research Title Computed Tomographic Scanning of Plaster Models – A Study of Validity and Cost Benefit |
| Student Name Low Hwee Hiang Intake AY2006/07 | Main Supervisor/ Co-Sup(s) Prof Murray Meikle A/P Cao Tong A/P Kelvin Foong | Research Title The development of a new in vitro model to study the effects of comprehensive mechanical strain on human periodontal ligament cells |
| Student Name Koh Poh Leong, Kelvin Intake AY2006/07 | Main Supervisor/ Co-Sup(s) Dr. Soh Jen Dr. Chan Yiong Huak A/P Kelvin Foong | Research Title A Patient-Centred Perspective of Facial Profile Aesthetics |

List of Conferred MDS Students in AY 2008/09 (cont'd)

| Orthodontics | | |
|--|---|---|
| Student Name Tan Ching Ching Intake AY2006/07 | Main Supervisor/ Co-Sup(s) A/P Kelvin Foong Prof Toshio Deguchi Dr. Chew Ming Tak A/Prof Ong Sim Heng Dr. Chan Yiong Huak | Research Title Three-Dimensional Smile Arc Analysis in Orthodontically Treated Class III Malocclusion Patients |
| Student Name Wong Liping, Florence Intake AY2006/07 | Main Supervisor/ Co-Sup(s) A/P Kelvin Foong Prof Toshio Deguchi Dr. Arthur Lim Dr. Chan Yiong Huak | Research Title Reliability of the 3dMDface Stereophotogrammetric System: Towards Developing an Industry Standard for Reliability Testing of Surface Imaging Devices |

| Periodontology | | |
|--|--|---|
| Student Name Ng Cher Hui, Mervyn Intake AY2006/07 | Main Supervisor/ Co-Sup(s) Dr. Marianne Ong A/P Lim Lum Peng Dr. Koh Chu Guan Dr. Chan Yiong Huak | Research Title Tooth Loss & Patient Compliance in Periodontally Treated Patients: A Retrospective Analysis 7 Years or More After Active Periodontal Treatment |
| Student Name Yap Kin Wai Intake AY2006/07 | Main Supervisor/ Co-Sup(s) A/P Lim Lum Peng Dr. Madeliene Gunaratnam Dr. Chan Yiong Huak | Research Title Self Reported Periodontal Disease and Periodontal Health Status in Adults in a Hospital and Private Practise Setting |

| Prosthodontics | | |
|---|--|--|
| Student Name Chan Wee Kiong Intake AY2006/07 | Main Supervisor/ Co-Sup(s) A/P Keson Tan Dr. Ansgar Cheng Dr. Wong Keng Mun | Research Title Interface Fit Accuracy of 3 Implant-Conical Abutment Systems |
| Student Name Lim Sze Kheng Intake AY2006/07 | Main Supervisor/ Co-Sup(s) A/P Hien Chi Ngo A/P Keson Tan Dr. Anil Kishen | Research Title Anti-Bacterial Property of An Electroplated Dental Casting Alloys |
| Student Name See Toh Young Liang Intake AY2006/07 | Main Supervisor/ Co-Sup(s) A/P Keson Tan CI A/P Chua Ee Kiam Dr. Quek Heng Chuan | Research Title Load Fatigue Performance Conical Implant Abutment Combinations |
| Student Name Sng Hong Cheong, Jeffrey Intake AY2006/07 | Main Supervisor/ Co-Sup(s) Prof Chew Chong Lin CI A/P Chua Ee Kiam Dr. Teoh Khim Hean A/P Keson Tan | Research Title Bond Strength of Repaired Zirconium Ceramic Crowns |

Undergraduate Research Opportunities Programme (UROP)

| Group No. : 07-01 | Group No. : 07-02 |
|--|--|
| <p>Pain Reduction Following Third Molar Surgery with 830nm GaAlAs Low Level Laser Therapy of Energy Densities 50 & 100 J/cm²</p> <p>Group members Zhou Shicai, Chua Chew Kiat Simon Jude Chan Pei Yuan Song Yi Lin Luo Wenyuan</p> <p>Supervisors Prof Loh Hong Sai A/P Yeo Jin Fei</p> | <p>3D Digitisation of Plaster models Using Computed Tomography- A Pilot Work on the Accuracy and Validation of the Approach</p> <p>Group members Melvin Liew Kang Ming Ng Jing Hao Hoo Swee Tiang Tan Jiunn Ming Gary Ode Wataru See-Toh Kai Mun</p> <p>Supervisors A/P Kelvin Foong A/P Keng Siong Beng</p> |
| Group No. : 07-03 | Group No. : 07-04 |
| <p>Advanced Non-invasive Light Activated Disinfection (ANILAD) : An alternative to caries removal by hand instrumentation for deep occlusal caries?</p> <p>Group members Tan Hui Xian Melissa Cai Xingni Esther Ogawa Chong May May Gomes Mario Regino Wenliang</p> <p>Supervisors A/P Anil Kishen A/P Jennifer Neo</p> | <p>A 3D Interactive and Visualisation Educational Platform in Oral Histopathology</p> <p>Group members Zhuang Ronglin Lim Min Min Low Minhui Lu Zhiyin Yim Shao'en Joey Emilia Balasubramanian Suraj</p> <p>Supervisors A/P Yeo Jin Fei A/P Kelvin Foong A/P Keng Siong Beng</p> |
| Group No. : 07-05 | Group No. : 07-06 |
| <p>Cytotoxicity Testing of Hemostatic Agents, Bonewax and Surgicel, on CRL-1486 Cells</p> <p>Group members Leonardo Saigo Chew Qin'An Amelia Kwan Yi Alexia Chan Wai Seng Ong Guo An Sia Kia Suan Priscilla</p> <p>Supervisors A/P Cao Tong A/P Yeo Jin Fei</p> | <p>Fibre Post : Does Fit or Different Post Space Cleaning Methods Affect Retention ?</p> <p>Group members Tan Jun Da Joanne Ou Jiazhen Tang Hui Yun Marian Elizabeth Ho Swee Ferng Cindy Tan Wye Lynn Tan Hui Lu Shella</p> <p>Supervisor Dr. Lim Kian Chong</p> |

Faculty Research Day 2008

The purpose of the Undergraduate Research Opportunities Programme (UROP) was to promote and develop research interest in every undergraduate student within the Faculty. It also enabled students and faculty members to interact so as to foster ties in performing the research work and providing the opportunity to acquire skills for the intellectual process of inquiry. Students worked in groups under the supervision and guidance of a research mentor to explore research ideas and test hypotheses.

The programme commenced in Year 2 Term 3 and lasted for about 2 years. A final research report has to be submitted at the end of the programme and selected groups will then present their research findings during the Faculty Research Day. Faculty Research Day 2008 was held on 7 Nov 2008 and a total of six groups presented their findings to a panel of judges comprising Prof Toshio Deguchi, Prof Murray Clyde Meikle and Assoc Prof Stephen Hsu.

The results of the competition were as follows:



Winning Group - Group 2 (07-02)

Project Title
3D Digitisation of Plaster models
Using Computed Tomography-A Pilot
Work on the Accuracy and Validation
of the Approach

Starting from Left: Mr Tok Wee Wah, A/P Keng Siong Beng, See-Toh Kai Mun, Hoo Swee Tiang, Tan Jiunn Ming Gary, Ode Wataru, Ng Jing Hao, Melvin Liew Kang Ming and A/P Kelvin Foong



1st Runner Up - Group 3 (07-03)

Project Title
Advanced Non-invasive Light
Activated Disinfection (ANILAD) : An
alternative to caries removal by hand
instrumentation for deep occlusal
caries?

*Starting from Left: A/P Jennifer Neo, Cai Xingni, Chong May May, Esther Ogawa, Tan Hui Xian Melissa and A/P Anil Kishen
(Not in photo: Gomes Mario Regino Wenliang)*



2nd Runner Up - Group 6 (07-06)

Project Title
Fibre Post : Does Fit or Different
Post Space Cleaning Methods Affect
Retention ?

Starting from Left: Tan Jun Da, Joanne Ou Jiazhen, Tang Hui Yun Marian Elizabeth, Tan Hui Lu Shella, Ho Swee Ferng Cindy, Tan Wye Lynn and Dr. Lim Kian Chong

MSc Project

Chairside Optical Sensor to Monitor Bacterial-Mediated Acidogenic-Profile of Saliva in Children

Student: Dr. Annie Shrestha

Supervisor: Assoc Prof Anil Kishen

Summary

Despite many advances in dentistry today, a reliable, cost effective and simple chairside method to monitor caries activity in an individual is still lacking. The multifactorial etiology of dental caries is considered to be the main obstacle in this development. The cardinal step in caries process is the formation of acid following carbohydrate intake, which lowers the pH below the critical level, resulting in the dissolution and disintegration of dental hard tissues. Further, certain salivary proteins are known to facilitate bacterial adherence and colonization to the tooth surface. The levels of salivary total-protein have been associated with both caries activity and periodontal disease conditions.

Optical spectroscopy is a highly sensitive technique that can determine biochemical parameters from saliva both quantitatively and qualitatively. This study aimed to apply the principles of optical spectroscopy to monitor bacterial-mediated acidogenic-profile and total-protein concentration of saliva. Experiments were conducted using optical spectroscopic

sensor (OSS) to monitor the bacterial-mediated acidogenic-profile of saliva mixed with sucrose from 70 children of age group 6-12 years. Bromophenol blue, a pH sensitive photoindicator, was used to monitor the rate of acid production by salivary bacteria following the addition of sucrose. The findings from the OSS were compared with the past caries experience (caries scores: dmfs index), caries activity determined using mutans streptococci counts (Dentocult SM) and Lactobacilli counts (Dentocult LB) and pH shifts (pH-meter). The OSS showed a decrease in the absorption intensity at 595nm wavelength of saliva-sucrose sample with decrease in the pH. The half-life decay value determined from the OSS differed significantly between the caries-active (CA), caries-inactive (CI) and caries-free (CF) groups ($P < 0.05$). Children in CF group (90%) showed low MS and LB counts. However, this correlation was weak in cases of the CA and CI groups. The OS was able to distinguish children showing different caries activity.

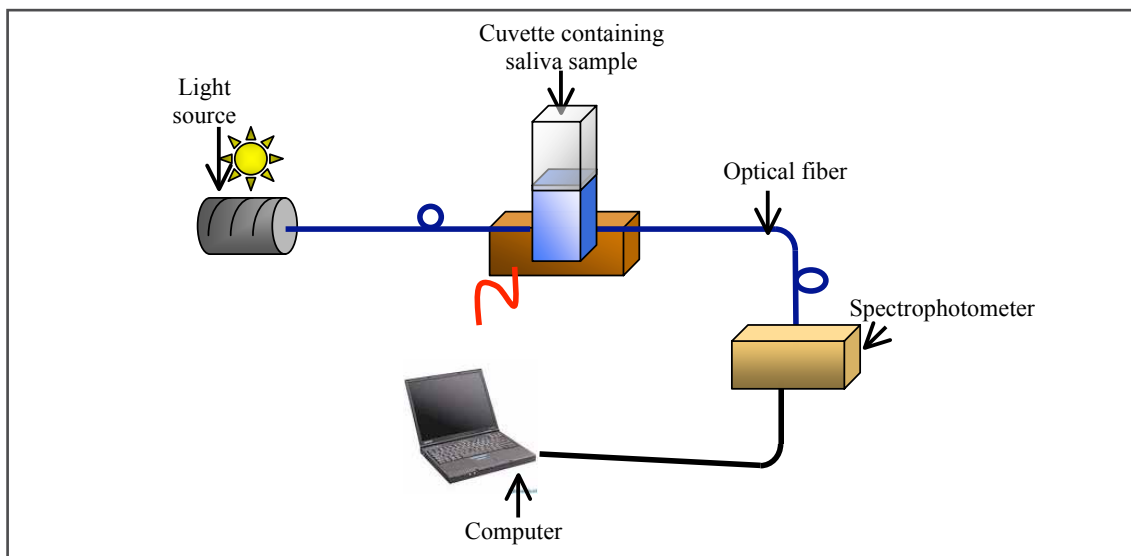


Figure 1: Schematic diagram of the experimental setup of the OSS used in the study.

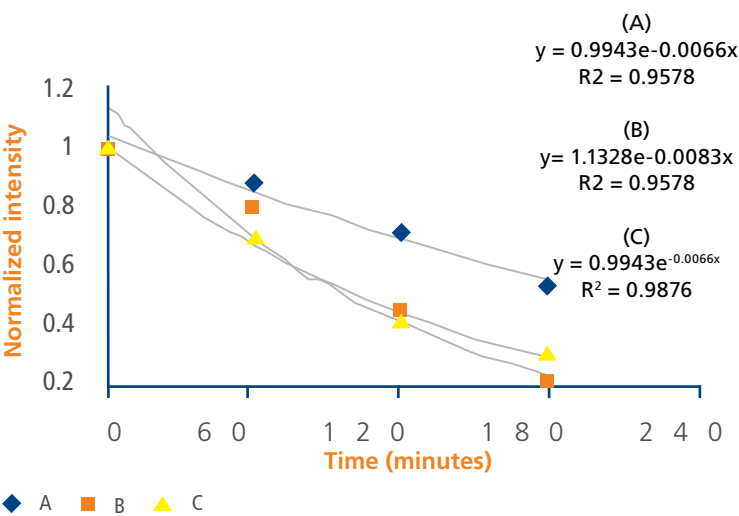


Figure 2: Graphs showing decrease in the absorption intensity (595nm) of saliva due to pH change as detected by the OSS; (A) caries-active (CA); (B) caries-inactive (CI) and (C) caries-free (CF) groups.

| | Caries-Active (CA) | Caries-Inactive (CI) | Caries-Free (CF) | Caries-Active (CA) | | |
|--|--------------------|----------------------|------------------|--------------------|-----------|-----------|
| dmfs/ ds | ≥1/ ≥1 | ≥1/ 0 | 0/ 0 | CA vs. CF | CA vs. CI | CI vs. CF |
| pH (T ₀ -T ₁₈₀) | 1.91±0.47 | 1.73±0.46 | 1.64±0.56 | 0.10 | 0.237 | 0.46 |
| I ₀ -I ₁₈₀ | 0.66±0.15 | 0.64±0.19 | 0.58±0.09 | 0.02* | 0.77 | 0.40 |
| Half life (t _{1/2}) | 94.92±57.49 | 66.88±62.53 | 136.72±46.30 | 0.005** | 0.20 | 0.005** |

Table 1: Different parameters measured from children of the three caries status groups. Where, I₀- optical intensity at time 0; I₁₈₀- optical intensity at time 180 min and t_{1/2}- half-life decay of the bacterial mediated exponential reaction.

Experiments were also conducted to quantify the total-protein concentration of saliva using OSS. Absorption Intensities for various protein concentrations were characterized using a protein sensitive indicator coomassie brilliant blue (CBB). Finally, considering the ability of the OSS to detect multiple parameters, a fiber optic based sensor incorporating two sensing regions for pH (methyl red as the photosensitizer) and protein (CBB as the photosensitizer) was fabricated using the principles of fiber optic evanescent wave spectroscopy (FOEWS) and sol-gel technology. This experiment demonstrated the ability of FOEWS to quantify total-protein concentrations and monitor the acidogenic-profile of saliva using a single sensor.

This study highlighted the ability of OSS to determine bacterial-mediated acidogenic-profile of saliva, which can be used as a caries activity indicator. The FOEWS developed was able to monitor the acidogenic-profile as well as quantify the total-protein content of saliva. The OSS can be a significant application for the chairside measurement of clinically important parameters from saliva.

PhD Project

Biopsychosocial Characteristics as Predictors of Treatment Outcome of Temporomandibular Disorders (TMD) Patients with Symptoms of Pain

Student: Prof Khoo Suan Phaik

Supervisor: Assoc Prof. Adrian Yap & Dr. Chan Yiong Huak

Introduction:

Temporomandibular Disorders (TMD) encompasses a collection of medical and dental problems that involve the muscles of mastication, the Temporomandibular joint as well as associated structures. Pain is the common reason why patients with TMD seek treatment. The biopsychosocial factors associated with pain symptoms (WIPS) in TMD patients and their role in the prediction of TMD treatment response are still largely unknown.

Aims:

The aims of this project were to (a) develop a cross-culturally adapted RDC/TMD (Research Diagnostic Criteria for TMD) for use in Malaysia, (b) compare the biopsychosocial characteristics of TMD patients with WIPS and without pain symptoms (WOPS) in a multi-racial urban population and (c) construct a predictive model for identification of non-responders to conservative TMD treatment.

Methods:

The RDC/TMD was cross-culturally adapted using standard procedures and was used to collect data on the biopsychosocial characteristics of 314 TMD patients aged between 18 to 74 years from an urban Malaysian setting. A cross-sectional study comparing the biopsychosocial characteristics of TMD patient WIPS and WOPS was carried out in order to determine factors that were likely to be associated WIPS. Selection criteria for patients WIPS was the presence of pain as the main symptom. Patients WIPS (n=100) were given conservative TMD treatment without occlusal splints. Patients' progress was documented at 6 weeks and at 6 months. Outcome measures included improvement in CPI (Characteristic Pain Intensity) and maximal width of pain-free mouth opening. Data were subjected to univariate followed by multivariate analysis with SPSS.

Findings:

The cross-culturally adapted RDC/TMD was found to be valid, reliable and suitable for use in Malaysia. Differences in sociodemography, physical and self-reported characteristics and psychological status

were observed between TMD patients WIPS and WOPS. Of these, factors associated with pain symptoms were limited width of pain-free mouth opening ($p=0.011$), self-report of nocturnal tooth grinding/jaw clenching ($p=0.036$), presence of a myofascial pain diagnosis ($p=0.001$) and larger LRMF (limitation related to mandibular functioning) scores ($p=0.003$).

Of the 100 TMD patients WIPS who received conservative TMD treatment, 69 responded positively while 31 did not. The significant factors predictive of non-response to conservative TMD management were the female sex ($p=0.013$), limited excursive-protrusive jaw movement ($p=0.014$), higher muscle palpation scores ($p=0.047$), lower depression scores ($p=0.044$) and self-reports of uncomfortable/usual bite ($p=0.014$).

A model was developed for the prediction of non-response to conservative TMD treatment. This was found to have a sensitivity of 80.6%, specificity of 95.7%, negative predictive value of 91.7% and positive predictive value of 89.3%. Responders had greater improvement in psychological distress scores over time when compared to non-responders to conservative TMD treatment.

Conclusions:

The findings of this study validate the importance of biopsychosocial factors in TMD. The four significant factors that were associated with pain symptoms in TMD patients were reflective of the patients' self-reported and physical characteristics whilst the five significant predictive factors of non-response to conservative TMD treatment were reflective of patients' sociodemographic, psychological status, physical and self-reported characteristics. Potential non-responders to conservative TMD management can be identified by these biopsychosocial predictors so that a more tailored treatment can be planned from the outset. Conservative TMD treatment appeared to have beneficial effects on TMD patients with high depression scores.

MDS Project

Tooth Loss & Patient Compliance in Periodontally Treated Patients: A Retrospective Analysis 7 Years or More After Active Periodontal Treatment

Student: Dr. Ng Cher Hui, Mervyn

Main Supervisor: Dr. Marianne Ong

Co-Supervisors: Assoc Prof Lim Lum Peng, Dr. Koh Chu Guan & Dr. Chan Yiong Huak

Introduction:

It has been well-established that supportive periodontal therapy (SPT) is important in the maintenance of oral health. There has been increasing emphasis on the use of “true” endpoints (e.g. tooth loss) rather than “surrogate” endpoints for the evaluation of effectiveness of periodontal therapy.

Objectives:

The aims of this study were to investigate the incidence and reasons for tooth loss during active periodontal therapy (APT) and supportive periodontal therapy (SPT) in a cohort of patients treated in an institutional practice (National Dental Centre Singapore, NDCS). Comparison was made with a sub-set of patients who failed to attend SPT following APT. Prognostic factors associated with tooth loss during the SPT were also identified.

Subjects and Methods:

This research comprised of two parts – a longitudinal retrospective cohort study (SPT group) and a clinical recall cross-sectional study (non-compliance group). The longitudinal retrospective cohort comprised of patients with chronic periodontitis treated and maintained for at least 7 years by periodontists at the Department of Restorative Dentistry, National Dental Centre Singapore (NDCS). Patients were identified from an electronic patient database and their record folders were retrieved and reviewed. The number of teeth present was determined at three time points: Initial examination and consultation, end of APT and the most recent SPT appointment visit. Reasons and clinical/periodontal parameters for tooth loss were documented. Total number of folders drawn was 478 and upon review, 273 patients met the inclusion criteria.

The cross-sectional cohort comprised of patients who dropped out after completion of APT (non-compliers). They were identified from the database and invited to participate in this part of the study.

The patients were recalled and assessed on the existing number of teeth present. After reviewing 1,318 folders, 207 patients met the criteria but only 39 patients returned for clinical assessment.

Relevant information was collected and entered into an Excel spreadsheet. Descriptive statistics were done using SPSS. The differences in the tooth loss between the 2 groups were analyzed using 2 sample t-test if normality (assessed using Komolgorov Smirnov) and homogeneity assumptions were satisfied otherwise the non-parametric equivalent Mann Whitney U test was applied. A multivariate linear regression was performed to adjust for relevant covariates. Significance was set at $p < 0.05$.

Results:

For the subjects in the SPT group, a total of 360 teeth were extracted (1.3 teeth/patient) during APT, with multi-rooted teeth having two-fold odds compared with single-rooted teeth. During SPT (mean of 10.7 years), a total of 253 teeth were extracted (0.9 teeth/patient). The annual tooth loss due to periodontitis was 0.03 teeth/patient/year. Logistic regression analysis found that age of >60 was a highly significant predictor of tooth loss during SPT ($p = 0.015$), with adjusted odds ratio of 2.1 (95% CI: 1.14–3.40).

For non-compliers (subjects who failed to attend SPT), a total of 41 teeth were extracted (1.1 teeth/patient) during APT, which was not significantly different from those on SPT. During discontinuation of SPT for 9.6 years, a total of 107 teeth were lost (2.7 teeth/patient), a 3-fold increase compared with those on SPT. The annual tooth loss due to periodontitis in the non-compliers was 0.22 teeth/patient/year, which was 7-fold higher odds than those in the SPT group ($p < 0.05$). Logistic regression analysis failed to identify the age, gender, diabetes, initial periodontal diagnosis as predictors for tooth loss during discontinuation.

Conclusions:

Within the limitations of the current study, provision of SPT led to minimal tooth loss, especially due to periodontitis, for a period of 10 years after APT. SPT is beneficial regardless of compliance. However, completion of APT without SPT will predispose patients to lose significantly more teeth compared to patients who do undergo SPT.



An Assessment of Malocclusion Status in Hospital Based Orthodontic Patients

Principal Investigator: Assoc Prof Kelvin Foong

Total Project Value: S\$66,705

Summary/Achievements

New Direction 1

Aim:

To develop a rapid and accurate solution to convert stored orthodontic plaster model for digital storage using conventional high-resolution computed tomography as a viable solution to the common and expensive problem of storage for physical plaster models.

Method:

A pilot study was conducted on one maxillary arch of a Frasaco model of artificial human teeth. The model was scanned once with the Minolta 900 VIVID surface laser scanner and the 64-slice Siemens Somatom CT scanner. Mesio-distal width and buccal cuspal-gingival height measurements are made on both virtual images. The accuracy is validated against identical parameters taken with a Coordinate Measuring Machine (CMM). In the precision experiment, the virtual models of the CT and laser scanner from the accuracy experiment are used. The inter-canine distance is measured 10 times each on both virtual models. The measurements are repeated 3 days later.

Results:

CT scanning of the plaster model is accurate to 0.39mm and 0.80mm for buccal cuspal-gingival and mesio-distal distances, respectively. The precision error is within 0.2mm for the inner-canine distance.

Conclusion:

The conclusion from the pilot study indicated that physical plaster models could be rapidly and accurately converted to digital proxies using CT scanning.

After the pilot study, an in depth study has since started with the undergraduate UROP and MDS Orthodontic research programmes to (i) identify the optimal CT scanning protocol that gives the

most accurate visual display of the virtual model, and (ii) to determine the cost- effectiveness of CT scanning in comparison with physical storage. An additional step to determine accuracy of multi-slice CT scanned plaster models had been undertaken using conventional CAD-CAM technology in generating a rapid-prototyped (RP) model of the CT scanned plaster model. This RP model has been compared with the original physical model using CMM, and will undergo surface scanning for comparison of surface contours. Data from the in depth accuracy/ precision and cost-effectiveness studies will be represented at the UROP research presentation in November 2008 and via MDS thesis in Jan 2009.

New Direction 2

In developing the rapid and accurate solution to the common and expensive problem of storage for physical plaster models, the second direction is to develop a 3D digital method of assessing the Index of Orthodontic Treatment Need (IOTN) and Peer Assessment Rating (PAR) index status malocclusions from untreated and treated cases using digital plaster models. The outcome of this approach was highly predictable as the current research work of the PI has developed the ability to digitally separate the individual crowns of each tooth from the plaster model base and gingival, and move the separated teeth. The team was also able to digitally occlude the digital plaster models in maximum intercuspation without the aid of reference bases. With digitally occluded models, the digital assessment of the severity of the malocclusions via the Peer Assessment Rating index and the IOTN can be semi-automated. The second direction (started in January 2008) was still work in progress under a Faculty of Engineering Final Year Project to develop the measurement system and Graphical User Interface (GUI) for the virtual plaster models in occlusion.



The Effects of Low Level Laser Therapy on the Rat's Sciatic Nerve, Following Lysolecithin – Induced Focal Demyelination

Principal Investigator: Assoc Prof Yeo Jin Fei

Total Project Value: S\$45,150

Summary/Achievements

Demyelination of the peripheral nerve involves changes in the Ultrastructures of myelin and affects sodium and potassium channels at the nodes of Ranvier. Low Level Laser Therapy (LLLT) has been previously reported to promote myelination. This study used chemical demyelination achieved by lysolecithin application on the exposed sciatic nerves. LLLT was given to the experimental animals. The rate and completion of remyelination is noted together with the return of normal features of sodium and potassium channels. In the control

animals, demyelination was allowed to take its course and the rate & completion of remyelination were assessed. A comparison of the results of the two groups of rats demonstrated a significant effects of the LLLT on remyelination. The results were communicated to the international medical laser community. The impact would be seen in the clinical management of current demyelination associated neuropathic pain conditions like Trigeminal neuralgia.



Prospective Study of Periodontal Disease Risk Markers and Treatment Outcome of a Periodontal Programme for Adult Diabetics in Singapore

Principal Investigator: Assoc Prof Lim Lum Peng

Total Project Value: S\$114,125

Aims

- i) To find out the periodontal health of a cohort of adult diabetes in Singapore
- ii) To evaluate longitudinally the effects of a periodontal health programme on periodontal health status and metabolic control as well as some inflammatory markers in adult diabetics

The subjects were divided into three periodontal treatment modality: Scaling + oral hygiene, scaling and a control. All subjects were examined at baseline, 3 months and 9 months. At 9 months all groups received scaling + oral hygiene. Clinical examinations were carried out using standard periodontal parameters and blood tests were also taken to evaluate the metabolic control.

Results

Patients with good glycaemic control presented with less severe periodontal disease in terms of

% bleeding, % calculus, and sites with increased probing depths.

There was a significant improvement of the plaque and bleeding scores and probing depths of all patients. Improvement was most marked in the scaling + Oral hygiene group. Improvement was comparable in patients with acceptable and unacceptable glycaemic control.

Improvement in periodontal health did not have significant impact on glycaemic and metabolic serum markers.

Conclusion

The study highlighted the relevance of periodontal therapy in improving periodontal health of patients with diabetes.



Biomimetic Remineralization of Demineralized Hard Tissue

Principal Investigator: Assoc Prof Anil Kishen

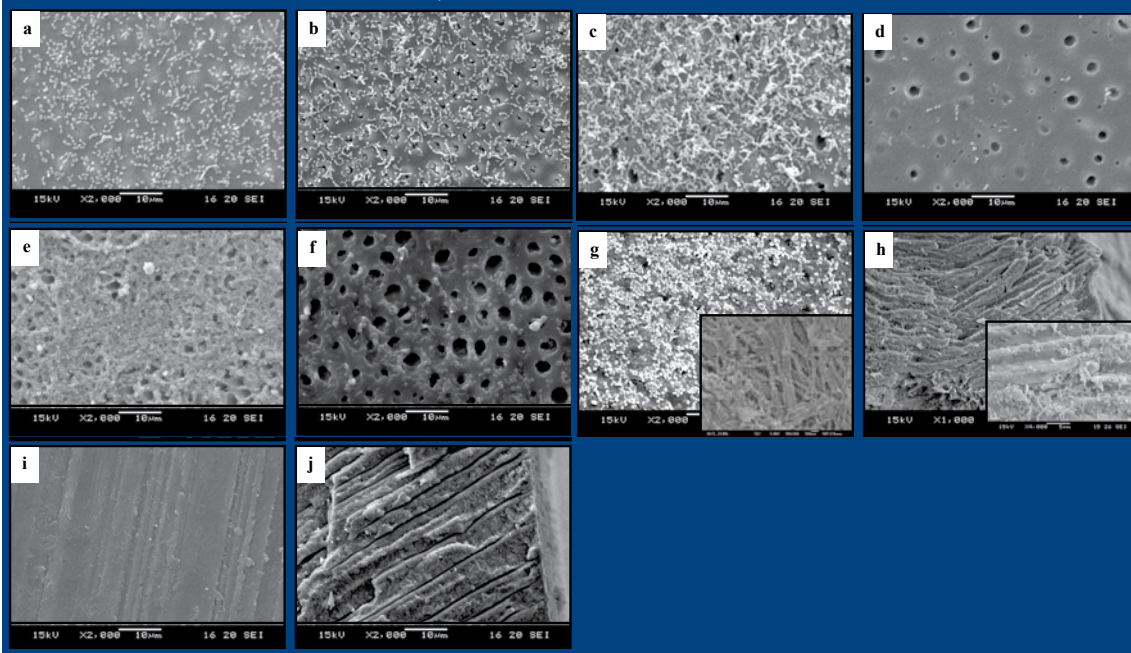
Total Project Value: S\$46,500

Summary/Achievements

Demineralization and resorption of hard tissues are common signs of disease process which often are mediated by bacteria. Bacteria possess the ability to survive harsh environmental and growth conditions by growing as a biofilm and bacterial biofilm has been associated with many chronic infections diseases in human beings. When bacteria grow as biofilms on hard tissue surfaces such as enamel and dentine, under favorable conditions, they increase the acidity at the vicinity of the biofilm/hard-tissue interface. This localized increase in acidity may lead to hard-tissue demineralization and subsequent disintegration (resorption). Understanding this mechanism of biofilm formation would

facilitate us to develop non-invasive strategies (a) to remineralize, the demineralized-hard-tissues and (b) to prevent subsequent bacteria-induced-demineralization of remineralized-hard-tissues. Previous studies had highlighted that collagen fibrils undergo chemical modification during biofilm formation and demineralization. In this study, in vitro demineralization and re-mineralization experiments was conducted on enamel and dentine models using both pH-cycle Model and Bacterial Model. The role of different approaches to functionalize collagen in demineralized substrates (dentine), such as deprotonation, chelation, phosphorylation, etc, were evaluated.

Figure SEM micrographs of cross-section and longitudinal dentine specimens after different periods of demineralization: (a), 2day; (b), 4day; (c) and (d), 6day; (e) and (f), 10day; (g) and (h), 14day; (i) and (j) control. The specimens in (d) and (f) underwent sonication treatment to remove the biofilm. The insert in (g) is a FSEM micrograph showing network of collagen fibrils (arrow) on the surface of intertubular dentine. The insert in (h) is a magnified image of the left of this SEM micrograph showing the bacterial cells (arrow) penetrating into dentinal tubules. ODT: orifice of dentinal tubule DT: dentinal tubule; ID: intertubular dentine; PD: peritubular dentine.





Characterization of osteogenesis by human embryonic stem cell derived osteogenic cells

Principal Investigator: Dr. Victor Fan

Co-Principal Investigator: A/P Tong Cao

Total Project Value: S\$179,850

Summary/Achievements

The aim of this study was to compare ex vivo osteogenesis of hESCs-derived osteogenic cells with that of human somatic osteoblasts; to compare in vivo osteogenesis of hESCs-derived osteogenic cells with that of human somatic osteoblasts.

The conducted study was to compare the osteogenic potential of human embryonic stem cells (hESCs) within two- and three-dimensional (2D and 3D) culture systems. hESCs of the H1 line (Wicell Inc., Madison, Wisc., USA) were induced to form embryoid bodies (EBs) through 5 days of suspension culture within non-adherent culture dishes. Following enzymatic dissociation, the EB-derived single cells were seeded on either novel 3D porous PLGA scaffolds or 2D culture dishes with the same total cell number. Osteogenic differentiation was induced through culture media supplemented with dexamethasone, L-ascorbic acid and β -glycerophosphate. After 3 weeks of in vitro culture, quantitative and qualitative assays of osteogenic differentiation were conducted. Osteocalcin secretion and alkaline phosphatase (AP) activities were detected at significantly higher levels within 3D culture compared with the 2D system. Subsequently, the cell-scaffold constructs were implanted in iliac crest defects of immunosuppressed rabbits. After 4 weeks, the constructs were subsequently explanted and characterized by histology and X-ray analysis.

Formation of new bone was detected within and around the implanted scaffolds. The results demonstrate that the osteogenic differentiation of human embryonic stem cells is enhanced in a 3D culture system compared to a 2D culture environment. Upon implantation in situ, the differentiating human embryonic stem cells can contribute positively to the repair and regeneration of bone defects.

This study also evaluated PLGA scaffolds for bone regeneration within a rabbit model. The scaffolds were implanted at two sites on the same animal, within the periosteum and within bi-cortical bone defects on the iliac crest. Subsequently, the efficacy of bone regeneration within the implanted scaffolds was evaluated at 4, 12 and 24 weeks post-surgery through histological analysis. In both the intra-periosteum and iliac bone defect models, the implanted scaffolds facilitated new bone tissue formation and maturation over the time course of 24 weeks, even though there was initially observed to be little tissue ingrowth within the scaffolds at 4 weeks post-surgery. Hence, the 3D printed porous PLGA scaffolds investigated in this study displayed good biocompatibility and are osteoconductive in both the intra-periosteum and iliac bone defect models.

The project has generated three published papers in peer-reviewed international journals.



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

Principal Investigator: Assoc Prof Jennifer Neo

Total Project Value: S\$51,150

Summary/Achievements

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.

The aim of this study was to evaluate the load fatigue performance of teeth restored with posts and cores, with varying tooth heights, and to compare them with similar groups having no posts and cores. The secondary aim was to determine whether a critical tooth height existed at which the placement of a foundation restoration resulted in no significant difference in the load fatigue performance. Three test groups with prepared tooth heights of 2, 3 and 4 mm were tested. These were compared with another three groups with similar tooth heights, this time restored with prefabricated titanium posts and core heights of 4, 3 and 2 mm, respectively. Cast complete crowns were then fabricated and cemented with zinc phosphate. A fatigue load of 58.8 N was applied at an angle of 135 degrees to the long axis of each crown-tooth specimen. The number of cycles to preliminary failure was determined. The results showed that for all 3 tooth heights, groups with foundation restorations had significantly higher number of cycles to preliminary failure than those without foundation restorations.

This in-vitro study suggests that placement of foundation restorations on teeth with short ferrule heights improve the clinical performance of the final restorations.



Intra-radicular Causes of Persistent Endodontic Infection

Principal Investigator: Assoc Prof Anil Kishen

Total Project Value: S\$166,895

Summary/Achievements

This project was conducted in two parts. The first part of the study was carried out to obtain better insight into the causes of persistence of *Enterococcus faecalis* in root canal treatment failed teeth. This investigation was carried out to examine *E. faecalis* biofilm mediated inflammatory response. Three strains of *E. faecalis* (ATCC29212, OG1RF and FA2-2), grown as planktonic and biofilm were tested for (1) their hydrophobicity and surface charge (2) intracellular survival (3) ability to induce inflammatory mediators (TNF- α , IL-6 and NO) production by monocytes, and (4) ability to co-aggregate with *Actinomyces israelii* to stimulate inflammatory responses in monocytes. In the first phase of the study monospecies biofilm/planktonic bacteria (*E. faecalis*) were tested for their interaction with THP1 cells (monocyte) and *in-vitro* differentiated macrophages. In the second phase of the study, a dual species biofilm/coaggregation (*E. faecalis* strains with *A. israelii*) was similarly tested. Findings from this study showed that nutrient-deprivation could significantly increase the hydrophobicity and surface charge of biofilm cells. In addition, nutrient deprivation significantly increased ($p \leq 0.05$) the intracellular viability of *E. faecalis*

cells internalized by monocytes and *in-vitro* differentiated macrophages. Among the three *E. faecalis* strains tested, OG1RF and ATCC29212 strains exhibited longer duration of survival than FA2-2 strain. *In-vitro* differentiated monocytes when co-cultured with planktonic *E. faecalis* cells exhibited a significantly higher ($p \leq 0.05$) production of TNF- α , IL-6 and nitric oxide than with biofilm cells from nutrient-rich and nutrient-deprived conditions. Planktonic monocultures of *A. israelii* cells were able to induce a significantly higher ($p \leq 0.05$) TNF- α , IL-6 and nitric oxide production by the monocytes compared to *A. israelii* biofilm cells. However, the secretion of TNF- α , IL-6 and nitric oxide decreased when monocytes were co-cultured with *A. israelii*-*E. faecalis* coaggregates or as co-adhered biofilm. This study shows that bacterial biofilms, a mode of growth in harsh environments similar to post-treatment endodontic environment, could potentiate *E. faecalis* cells to survive within the host immune cells and stimulate an inflammatory response. In addition, coaggregation of *E. faecalis* with *A. israelii*, another endodontic pathogen, could attenuate the inflammatory response and facilitate the intracellular survival of bacteria.

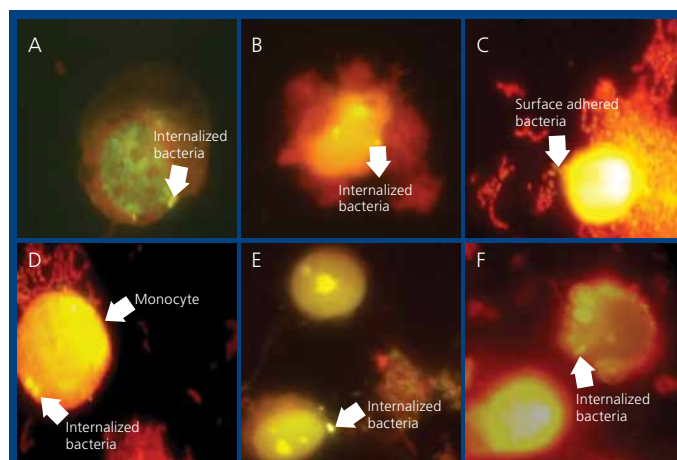


Figure: THP1 cells infected with *E. faecalis* (ATCC29212) planktonic and biofilm bacteria. A&B THP1 cells infected with planktonic bacteria. Arrow in figure A shows the internalized bacteria (green fluorescent). C&D shows green fluorescing nutrient rich biofilm bacteria within THP1 cells and surface adhered bacteria appear red. Arrow indicates surface bound bacteria (red fluorescent). E&F show nutrient-deprived biofilm cells within the THP1 cells. Data is representative of three independent experiments.



Removal of Bacterial Biofilms Using Focused Ultrasound for Endodontic Disinfection

Principal Investigator: Assoc Prof Anil Kishen

Total Project Value: S\$46,500

Aims

High-intensity focused ultrasound (HIFU) produces collapsing cavitation bubbles. This study aims to investigate the efficacy of collapsing cavitation bubbles to deliver antibacterial nanoparticles into dentinal tubules to improve root canal disinfection.

Methods

In stage 1, experiments were performed to characterize the efficacy of collapsing cavitation bubbles to deliver the miniature plaster beads into a tubular channel model. In stage 2, experiments were conducted on root-dentin blocks to test the efficacy of HIFU applied at 27 kHz for 2 minutes to deliver antibacterial nanoparticles into dentinal tubules. After the stage 2 experiment, the samples were sectioned and analyzed using field emission scanning electron microscopy and energy dispersive X-ray analysis.

Results

The stage 1 experiment showed that collapsing cavitation bubbles using HIFU delivered plaster beads along the entire length of the tubular channel. It was observed from the stage 2 experiments that the diffusion of fluids alone was not able to deliver antibacterial nanoparticles into dentinal tubules. The collapsing cavitation bubbles treatment using HIFU resulted in significant penetration up to 1,000 μm of antibacterial nanoparticles into the dentinal tubules. The statistical analysis showed a highly significant difference in the depth of penetration of antibacterial nanoparticles between the two groups ($p < 0.005$).

Conclusion

The cavitation bubbles produced using HIFU can be used as a potential method to deliver antibacterial nanoparticles into the dentinal tubules to enhance root canal disinfection. (Journal of Endod 2009;35:1028–1033)

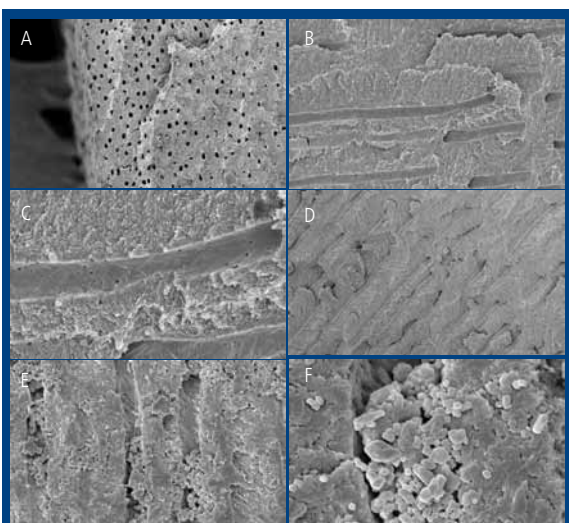


Figure. Field Emission Scanning Electron Micrographs of dentine sample from control group without HIFU treatment (A-C). The dentinal tubules opening towards the root canal wall is devoid of any antibacterial-nanoparticles attached to the surface (A). The cross-section of the dentine samples with exposed dentinal tubules does not show antibacterial-nanoparticles within the lumen (B, C magnified inlet from B). Field Emission Scanning Electron Micrographs of dentinal tubules from the HIFU treatment group sample (D-F). Lower magnification view of dentinal tubules (D). The inlet in (D) is magnified in (E) showing antibacterial-nanoparticles penetrating into the dentinal tubules. The distribution of antibacterial-nanoparticles was found to be non-uniform along the lumen of the dentinal tubules (black arrow) and the nanoparticles showed a tendency to form aggregates (white arrow). A single dentinal tubule with antibacterial-nanoparticles within its lumen (F) showing aggregation of antibacterial-nanoparticles of $100 \pm 20 \mu\text{m}$ sizes.



Caries Risk Assessment for Children in Singapore

Principal Investigator: Assoc Prof Stephen Hsu

Total Project Value: S\$144,925

Summary/Achievements

Despite the advances in oral health promotion, dental caries remains a main health problem threatening children's health worldwide. In Singapore, although periodic oral health surveys were conducted among schoolchildren, the caries prevalence among preschoolers has not been documented. Caries risk assessment (CRA) is considered an essential component for cost-effective caries control and evidence-based treatment planning. Nevertheless, the application of caries risk assessment in the community and clinical settings is hampered by the lack of a practical caries risk assessment tool with sufficient simplicity and accuracy. The main objectives of this study were to profile the caries status of preschoolers in Singapore and to establish and validate an epidemiologically and clinically practical tool for caries risk assessment for cost-effective caries control.

With ethical approval and parents' written consents, 1,782 children aged 3-5 years were recruited from 13 randomly selected kindergartens. The baseline data were obtained in 2005 through a parent-administered questionnaire, an oral examination, and salivary tests. After 12 months, the caries status of 1,576 (88%) children was followed up. The plaque pH values of 1,207 children were measured through a micro-touch method. The caries prevalence and oral health knowledge attitudes and practice were described and compared among ethnic and socioeconomic groups. Both traditional statistical methods (multiple regressions) and artificial neural networks (ANN) were employed for constructing and validating caries risk assessment models.

This study revealed that dental caries is a severe oral health problem affecting 40% children aged 3-5 years in Singapore. The caries distribution was highly skewed. Prominent oral health disparity existed among ethnic and socioeconomic groups and was partly explained by a multilevel behavioral pathway substantiated by Structural Equation Modeling. Multiple biopsychosocial caries risk factors/indicators were identified. Various caries risk assessment models were constructed and validated. With the sensitivity/specificity of 82%/73% and 90%/90%, the screening and full-blown models reached a higher accuracy in caries prediction, as compared with Cariogram. These models, catering to various needs at the community and clinical settings, are promising tools for cost-effective caries control and evidence-based treatment planning.

The results of this study has elucidated the current caries profile among the preschoolers in Singapore and confirmed the resurgence of caries. The high accuracy of the CRA models achieved in this study have won an international research award conferred by the International Association for Dental Research (IADR). The results have also drawn the attention of governmental agents and have been reviewed for the related healthcare policy planning.



The Bio-molecular Responses of Rat-derived Osteoblasts to Mechanical Strain in vitro

Principal Investigator: Dr. Li Xiaobing

Total Project Value: S\$128,500

Summary

Mechanical stress is an important determinant of bone mass and architecture. Increases in bone strains above a certain threshold have a positive effect on bone mass, whereas reductions in strain magnitude lead to bone loss and osteopenia. The aim of this study is to test the hypothesis that mechanical strain is a key determinant of osteoblast differentiation and function, and can act on cells of the osteoblast lineage in a dose-dependent manner. In other words, whether the osteoblastic response results in an osteogenic or resorptive stimulus in bone is dependent upon the biomechanical environment of the cells.

Specifically, mechanically-induced strain will be applied to rat calvarial osteoblasts in vitro in a Flexercell apparatus designed to deliver tension or compression of variable duration to cultured cells under controlled experimental conditions. Total RNA will be extracted from the cells, assessed for degradation status and then assayed for the differential expression of genes involved in (1) osteoblast differentiation and bone formation, (2) cell-cell and cell-matrix interactions, and (3) apoptosis (programmed cell death). For genes showing significant differential expression, the culture supernatants will be assayed for the corresponding protein by enzyme-linked immunosorbent assays (ELISAs), and their biological activity tested using in vitro bone resorptive assays.

The research includes:

1. osteoblast primary culture: getting osteoblasts from neonate SD rat's calvarial bone and characterizing the osteoblasts;

2. tests of osteoblasts' functions under mechanical tension:

(a) *vitality of osteoblasts under the mechanical tensions:*

(b) *apoptosis of osteoblasts under the tension;*

(c) *biomolecular reactions of osteoblasts to mechanical tension: RNA extraction; RT-PCR microarrays; ELISAs analysis, etc;*

3. results/statistical analysis;

Osteoblast primary culture and characterization:

1: primary culture: 16/02/2009 ---- 25/03/2009.

10 neonatal SD rats used: calvarial bones cut, digested, and plate out, and cells passaged to Passage five (fig. 1).



(fig. 1): primary calvarial derived osteoblasts: P5;



Biomimetic Surface Modification of Dental Implants for Enhanced Osseointegration

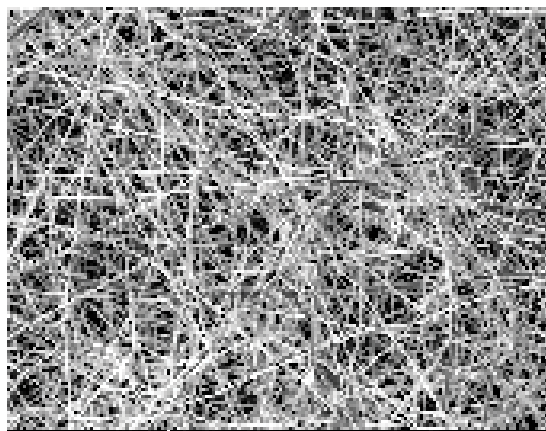
Principal Investigator: Dr. Clarisse Ng

Total Project Value: S\$165,829.42

Summary

Dental implants require a period of limited or no loading in order for bone ingrowth and osseointegration to progress sufficiently for the implant to bear load. Premature or inadvertent loading during the period after implantation may result in loss of fixation with the formation of fibrous tissue at the implant bone junction. Current practice is to limit early load bearing activities, however, this may not be desirable from a functional or rehabilitative perspective. Therefore, it is highly desirable to enhance and accelerate bone ingrowth and osseointegration immediately after surgery. This study uses electrospun nanofibers and biomineralization to modify the titanium surface to enhance osseointegration. Our hypothesis is that the modified surface will improve stem cell capture and therefore increase the number of osteoprogenitor cells at the implant site. Ti6Al4V discs were pretreated and PLGA, collagen blended PLGA, nano-hydroxyapatite/PLGA, and nano-hydroxyapatite/collagen-blended PLGA nanofibers were fabricated using a standard electrospinning process. Human bone marrow derived mesenchymal stem cells were then seeded onto the test samples with untreated titanium disc as the control. The samples were incubated for 10, 20, 30 and 60 minutes, after which the attachment efficiency of each sample was evaluated. At 10 minutes, cells started to adhere to all the modified surfaces. There

was 50% or more cell adhesion on the nano-hydroxyapatite/PLGA, and nano-hydroxyapatite/collagen-blended PLGA nanofibers at 30 minutes. At 60 minutes, cell adherence was 75% in the nano-hydroxyapatite/collagen blended PLGA, 64% in the nano-hydroxyapatite/PLGA, 52% in the collagen blended PLGA and 38% in the PLGA nanofibers. No cell adhesion was seen on the untreated titanium plates at 60 minutes. This suggests that the surface modifications enhance early cell capture when compared to untreated titanium. A nano-hydroxyapatite/collagen blended PLGA coated titanium surface in particular improves initial cell attachment which may prove to be beneficial for enhancing osseointegration.



Electrospun nanofibers



3-D Accuracy of Plastic Transfer Impression Copings for 3 Implant Systems

Principal Investigator: Assoc Prof Keson Tan

Total Project Value: S\$50,880

Summary

The aim of this study was to measure the 3-D accuracy of plastic transfer impression copings of 3 implant systems, as a function of implant angulations. The newer plastic transfer impression copings had not been tested for their accuracy in transfer of implant position to a master model. Errors during this stage of fabrication of prosthesis had been shown to lead to stress build-up in the implant components and/or prosthesis. Non-parallel or angulated implants could lead potentially to increased dimensional inaccuracy. The use of a Coordinate Measuring Machine (CMM) allowed the 3 dimensionally detection of these errors. This study was intended to compare components from three implant systems, viz Tissue Level Implant System

(Institut Strauman AG), Osseotite Certain System (Implant Innovations Inc) and Branemark Implant System (Nobel Biocare). Master models using two adjacent implants with differing angulations will be fabricated. A standardized impression and model fabrication technique would be used to create working casts. The difference in position of the implants between the master models and the working casts shall be measured using CMM. Quantification of these transfer inaccuracies in terms of the θ_x , θ_y and θ_z rotational displacements as well as x,y and z linear displacements (6 degrees of freedom) would provide clinicians with relevant information in assessing the clinical suitability of the components and techniques studied.

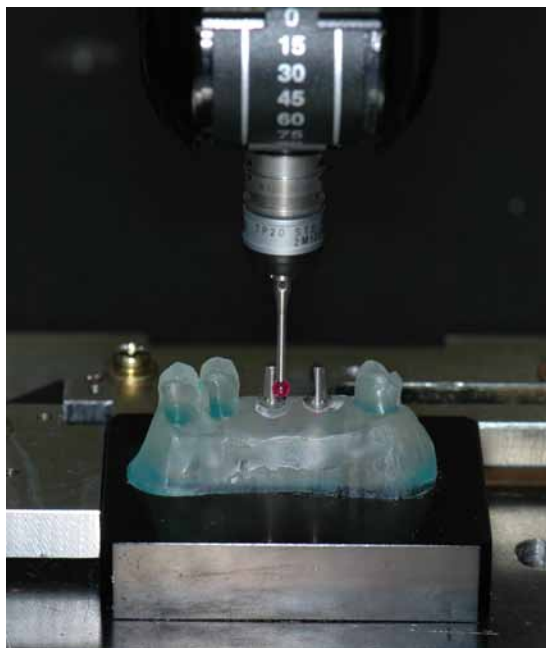


Fig 1 Implant Master Model with Plastic Pick-up Impression Coping



Fig 2. CMM probe measurement to define 3-D position of Implant abutments



Global Gene Expression Analysis in the Mouse Brainstem after Hyperalgesia Induced by Facial Carrageenan Injection

Principal Investigator: Assoc Prof Yeo Jin Fei
Total Project Value: S\$146,400

Summary

Present study was carried out to examine global gene expression in the brainstem, in a mouse model of orofacial pain. Mice that received facial carrageenan injection showed increased mechanical allodynia, which peaked at 3-4 days after facial carrageenan injection, demonstrated by increased responses to von Frey hair stimulation of the face (Fig. 1.). The mice brainstem were harvested at 3 days post-injection, and analyzed by Affymetrix Mouse Genome microarrays. Common genes that are changed in the respective sides of the brainstem were identified and classified using the Gene Ontology (GO) term enrichment analysis from the DAVID resource website (<http://david.abcc.ncifcrf.gov/>). The top category showed

“leukocytes adhesion” and the 2 genes involved in this category are P-selectin and Icam-1. P-selectin and Icam-1 expression were further validated using real-time RT PCR and western blot (Fig. 2 & 3). We postulate that increased P-selectin and Icam-1 expression could contribute to pro- rather than anti-nociception, probably through the enhancement of macrophage / monocyte entry into the brain. An attempt to reverse facial carrageenan induced hyperalgesia using inhibitors to the differentially expressed genes will be carried out. These could pave the way for identification of novel drug targets for the clinical treatment of human orofacial pain.

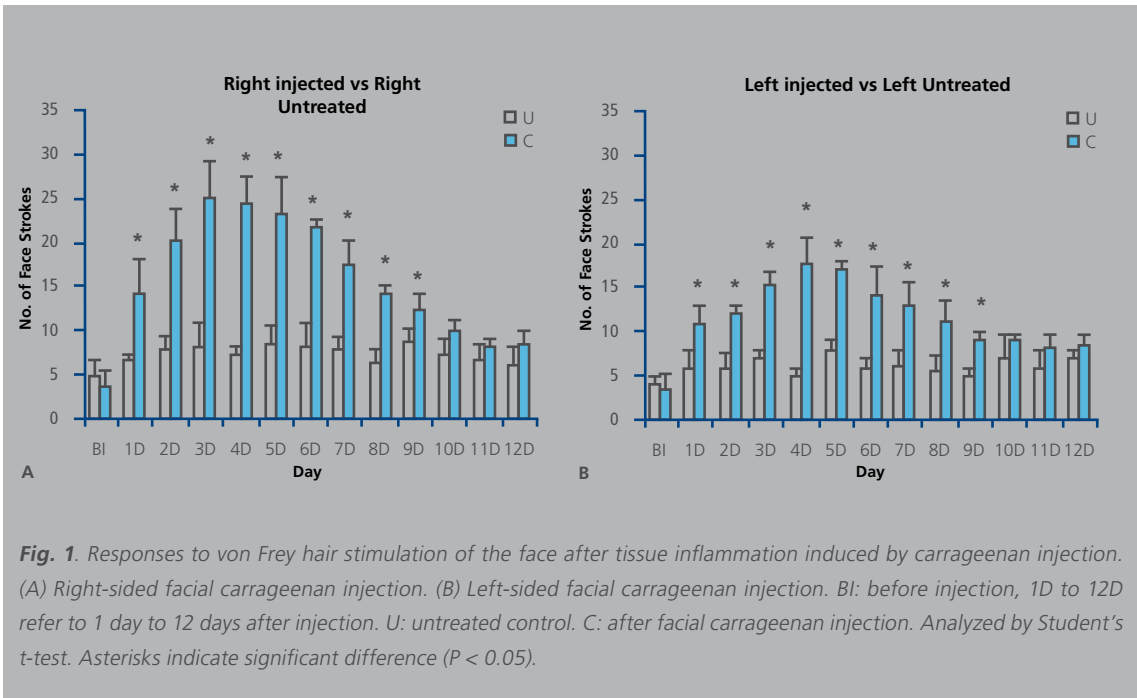


Fig. 1. Responses to von Frey hair stimulation of the face after tissue inflammation induced by carrageenan injection. (A) Right-sided facial carrageenan injection. (B) Left-sided facial carrageenan injection. BI: before injection, 1D to 12D refer to 1 day to 12 days after injection. U: untreated control. C: after facial carrageenan injection. Analyzed by Student's t-test. Asterisks indicate significant difference ($P < 0.05$).

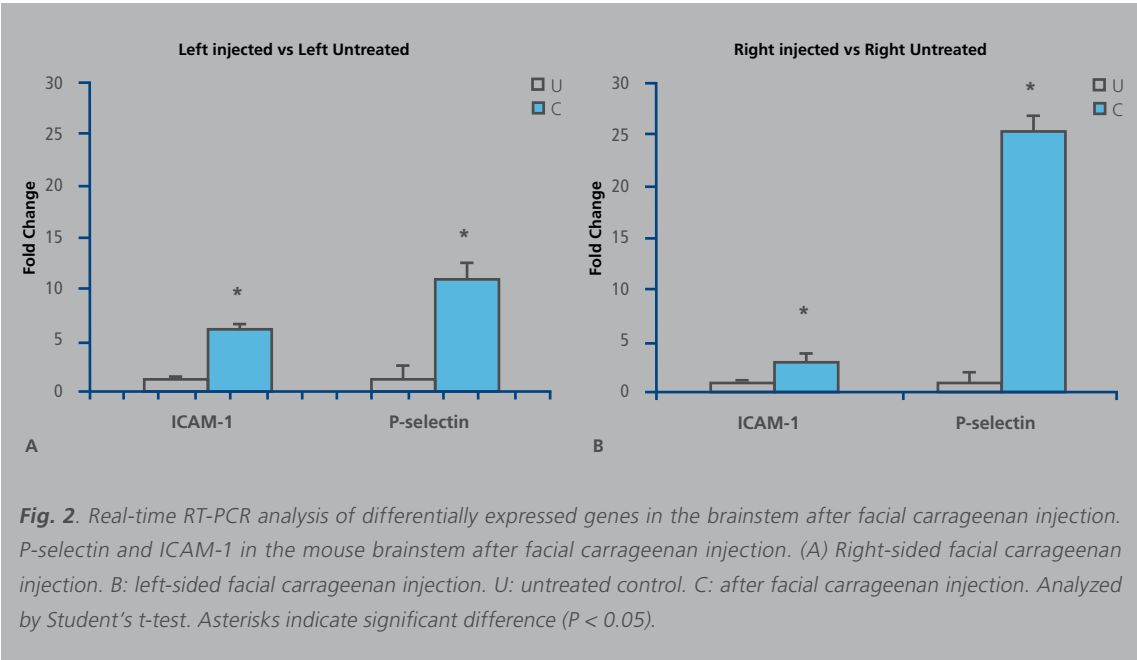


Fig. 2. Real-time RT-PCR analysis of differentially expressed genes in the brainstem after facial carrageenan injection. P-selectin and ICAM-1 in the mouse brainstem after facial carrageenan injection. (A) Right-sided facial carrageenan injection. B: left-sided facial carrageenan injection. U: untreated control. C: after facial carrageenan injection. Analyzed by Student's t-test. Asterisks indicate significant difference ($P < 0.05$).

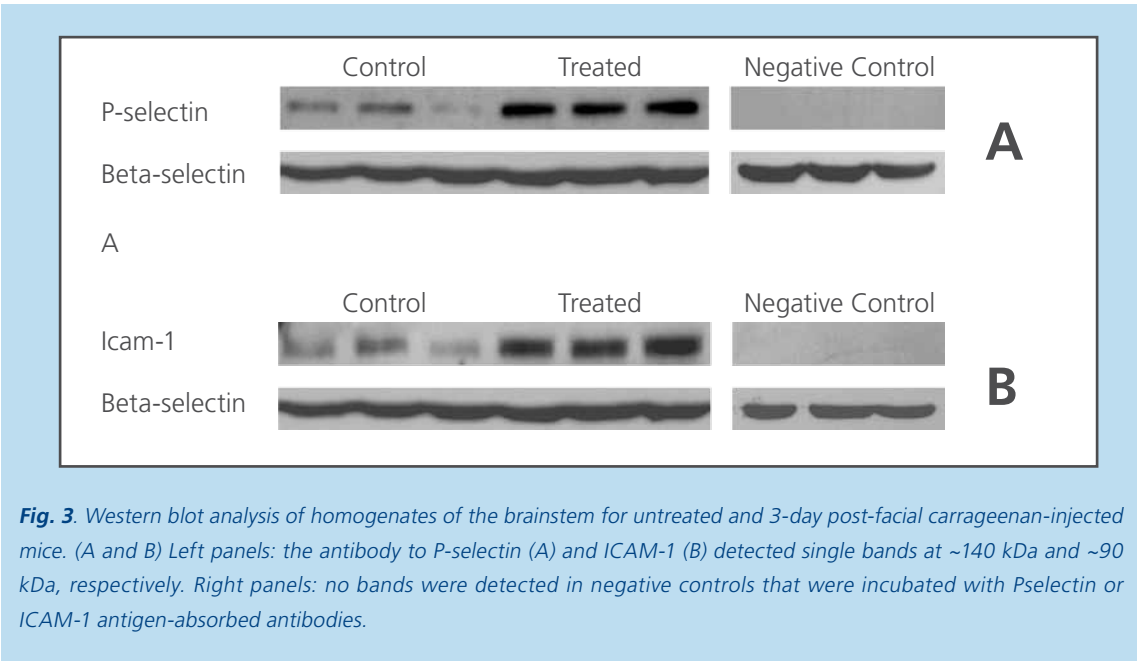


Fig. 3. Western blot analysis of homogenates of the brainstem for untreated and 3-day post-facial carrageenan-injected mice. (A and B) Left panels: the antibody to P-selectin (A) and ICAM-1 (B) detected single bands at ~140 kDa and ~90 kDa, respectively. Right panels: no bands were detected in negative controls that were incubated with Pselectin or ICAM-1 antigen-absorbed antibodies.



Keratinocyte Differentiation of hESCs for Potential Dental, Medical and Wide Biotech Needs

Principal Investigator: Assoc Prof Cao Tong

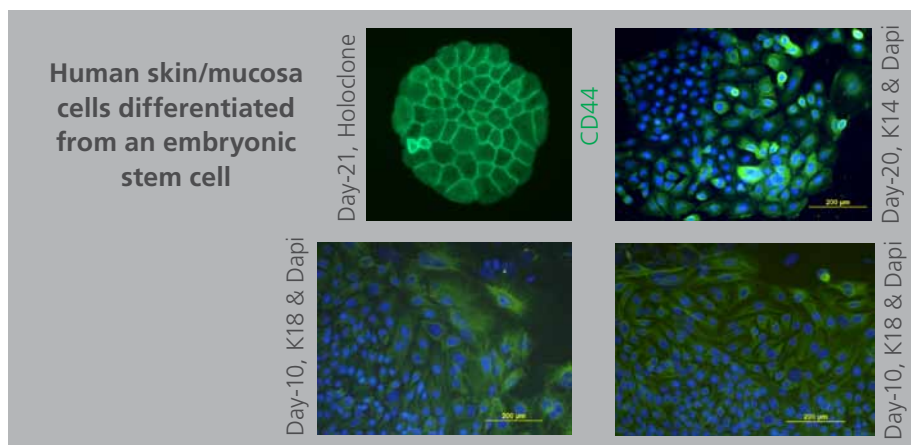
Total Project Value: S\$125,800

Summary

Tissue regenerated oral skin and mucosa equivalents have been suggested to be the ideal substitutes to replace various autologous skin or mucosal grafts for the treatment of defects, usually because of surgical excisions, injuries, and congenital diseases in the oral maxillofacial region. For tissue regeneration of oral skin or mucosal grafts, it could be possible to utilize either ES cells derived from the inner cell mass of blastocyst-stage embryos [Trounson, 2002], or adult stem cells of non-epidermal origin, such as that derived from the bone marrow [Kataoka et al, 2003] and peripheral blood circulation [Korbling M, et al, 2002], which have also been shown to be capable of trans-differentiation into the keratinocyte lineage. Nevertheless, there were a number of factors that would not favor the use of adult stem cells [NIH, 2008a; Coraux, et al, 2003; Green, et al, 2003] over embryonic stem cells. Among them, the mortality and limited renewal capacity of adult stem cells was most ambiguous and the subject of much controversy. By contrast, the immortality and self-renewal capacity of human embryonic stem cells (hESCs) was unquestionable. Besides, hESCs are genetically younger and healthier.

The research was to stimulate and direct the hESC differentiation towards the keratinocyte

lineages. hESCs-derived keratinocytes are the best source to generate human oral skin and mucosa, which could be utilized for many purposes. The major applications are potentially in the dental, medical and biotech areas of: (1) the study of genetic and developmental mechanisms relating to skin or mucosa regeneration, (2) the study of gene/protein delivery therapy to cure skin or oral mucosa lesions; (3) the study of cell-injection therapy for skin or mucosa repair; (4) the study of cell transplantation-based skin or mucosa reconstruction and regeneration; (5) the disease study and drug discovery (NIH, 2001) for skin and mucosa; (6) the development of novel toxicity screening tests for epithelium-related biomaterials and drugs; and (7) the development and validation of hESC epithelial models for wide biosafety-health evaluation of food products and supplements, cosmetics, personal care products, house and office products, living and working environment, water, soil, air and natural environment. The keratinocyte lineages derived from hESCs would be established in Singapore, as a result of this project. Moreover, the scientific data and intellectual properties of hESC keratinocyte differentiation would be set up in FOD/NUS, pioneering in global dentistry, for various applications in the near future.





Effects of Yakult and laser therapy on preventing enamel demineralization around orthodontic brackets in a biofilm model

Principal Investigator: Assoc Prof Stephen Hsu

Total Project Value: S\$121,920

Introduction

The formation of white spot lesions (WSL) around orthodontic brackets is one of the major risks of fixed orthodontic treatment and presents as an aesthetic issue for orthodontists and up to 48% of patients. Several studies have reported the increase in resistance to demineralization in enamel after laser irradiation. However, the laser effects have been characterized in chemical models but not in a biofilm model mimicking intra-oral conditions. Yakult is a popular soft drink for children and teenagers and has demonstrated a cariostatic effect in our previous pilot clinical trial. The combined effect of laser and Yakult has not been investigated in the literature.

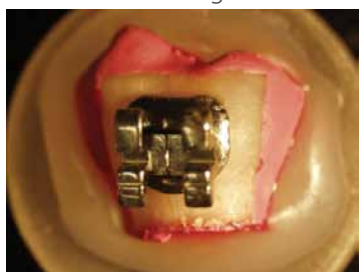
Objective

1) To characterize in a biofilm model the effects of carbon dioxide laser therapy on prevention of enamel demineralization around orthodontic brackets; 2) to evaluate the effects of Yakult on lased enamel around the orthodontic brackets in the same biofilm model.

Methods

For Phase-I: Freshly extracted premolar or molar teeth without decay will be selected and orthodontic brackets will be placed on these teeth with a conventional composite resin. Four defined window area next to the brackets will be irradiated with 3 sets of laser parameters with the remaining non-irradiated area selected

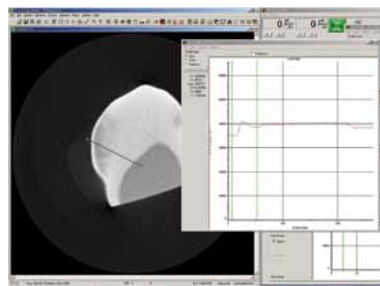
as the control. A biofilm reactor developed by the Center for Disease Control (CDC, USA) will be used to develop a dental biofilm, simulating intraoral condition and demineralization. Before and after 4-week incubation with oral bacteria and pooled human saliva, the mineral content of the experimental and control sites will be quantified by a Micro-computed Tomography (μ CT) scanner. The factorial ANOVA will be employed to statistically evaluate the preventive effects of laser therapies and the site-specificity of laser effect. For Phase-II: The same laser parameter employed in the phase-I study will be used to prevent WSL around orthodontic brackets in a biofilm system supplied with daily Yakult rinse for 2 weeks. The same mineral profiling method (using μ CT) will be conducted before and after the lesion development in the same biofilm system plus a daily 1-min flush of one-bottle Yakult for two weeks. The samples will be retrieved from the system for enumeration of plaque pH at the end of 2-week and 4-week periods. The factorial ANOVA will be employed to statistically evaluate the preventive effects of laser therapies, Yakult, and the site-specificity on plaque pH and mineral loss. The results of this study may deepen our knowledge of preventive laser effect on enamel demineralization in a microbiological system and pave the way for the clinical application of laser and/or probiotic therapies in preventing white spot lesions of orthodontic patients.



Investigating the biofilm around the orthodontic bracket and laser-induced caries prevention



The CDC biofilm reactor, developed by the Centers for Disease Control and Prevention (CDC) in 2002



Mineral profiling using Micro-CT to quantify the caries-preventive effect on enamel

Research Collaborations in AY 08/09

| Collaborating Organizations | Year | Department | Region |
|---|-------------|--------------------------------|---------------|
| Universities | | | |
| Massachusetts General Hospital, Harvard University, USA | 2007 - 2009 | Restorative Department | International |
| University of Texas Health Science Center at San Antonio, USA | 2007 - 2009 | Restorative Department | International |
| University of Wisconsin Madison | 2003 - 2009 | Oral and Maxillofacial Surgery | International |
| Harvard University | 2004 - 2009 | Oral and Maxillofacial Surgery | International |
| Peking University | 2007 - 2009 | Oral and Maxillofacial Surgery | International |
| Tsinghua University | 2006 - 2009 | Oral and Maxillofacial Surgery | International |
| Zhejiang University | 2005 - 2009 | Oral and Maxillofacial Surgery | International |
| University of Otaga | 2009 | Restorative Department | International |
| Jiaotong University | 2006 - 2009 | Oral and Maxillofacial Surgery | International |
| Industries | | | |
| Bio-Scaffold | 2004 - 2008 | Oral and Maxillofacial Surgery | Local |
| Research Institutes | | | |
| SIMTech Pte Ltd, A*STAR | 2007 - 2009 | Oral and Maxillofacial Surgery | Local |
| Tissue Modulation Laboratory | 2007 - 2009 | Preventive Dentistry | Local |

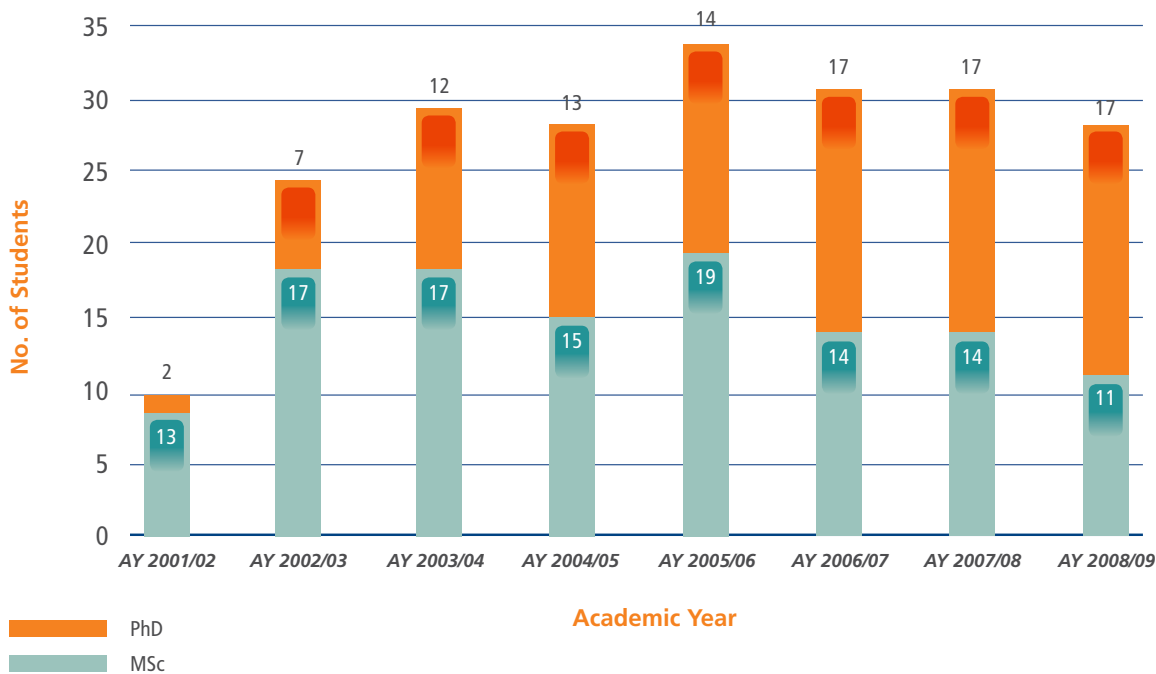
Research Awards & Prizes Awarded in AY 2008/09

| Awardee(s) | Name of Award | International or Local/Regional | Awarding Agency | Title of Article/Project |
|--|--|---------------------------------|---|--|
| A/P Cao Tong | International Collaboration Grant, Ministry of Science and Technology, PRC | International | Ministry of Science and Technology, PRC | Development of hESC models for toxicity evaluation |
| Dr. Liu Hua A/P Cao Tong (Supervisor) | The China Scholarship Council Award 2008 | International | China Scholarship Council | NA |

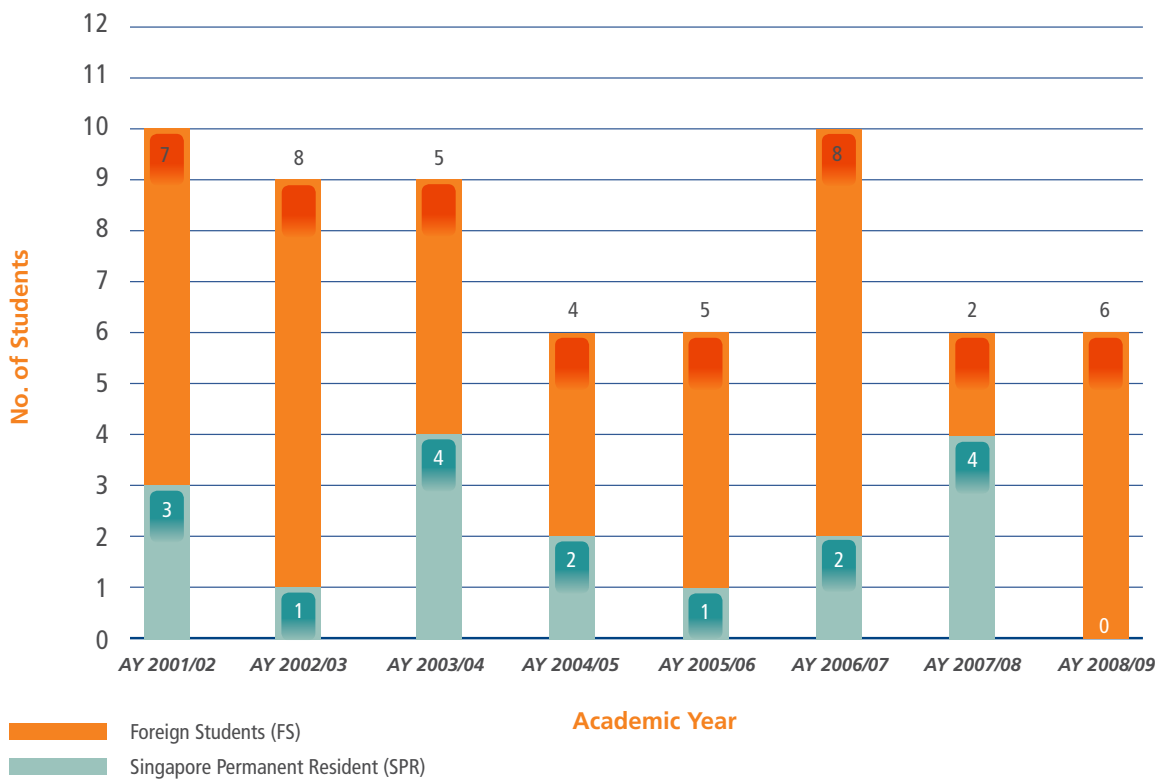
List of Editorial Board Memberships in AY 2008/09

| Name of Staff | Name of Journal/ Book Series | Journal Tier | Position Held |
|------------------------------|---|--------------|--|
| Prof Loh Hong Sai | Singapore Dental Journal | Reputable | Section Editor |
| Prof Murray Clyde Meikle | Royal College of Surgeons, Edinburgh. Journal | Reputable | Editorial Board Member |
| A/P Anil Kishen | Singapore Dental Journal | Reputable | Section Editor |
| | Optics and Lasers In Engineering | Leading | Editorial Board Member |
| | Journal of Applied Oral Science | Others | Editorial Board Member |
| | Open Dentistry Journal | Others | Editorial Board Member |
| A/P Keng Siong Beng | Singapore Dental Journal | Reputable | Editorial Reviewer |
| A/P Lim Lum Peng | Singapore Dental Journal | Reputable | Editorial Reviewer |
| | Oral Health & Preventive Dentistry | Others | Editorial Board Member |
| | Hong Kong Dental Journal | Others | Editorial Adviser |
| A/P Neo Chiew Lian, Jennifer | Journal of Dentistry | Premium | Editorial Board Member |
| | Operative Dentistry | Others | Editorial Board Member |
| A/P Ong Hui Lian, Grace | European Journal of Dental Education | Leading | Board member |
| A/P Sae-Lim, Varawan | Journal of Endodontics | Premium | Scientific Advisory Panel of Editorial Board |
| | Journal of Periodontology | Premium | Reviewer |
| | Dental Traumatology | Premium | Editorial Board Member |
| | Journal Of Dental Research | Premium | Reviewer |
| | Acta Biomaterialia | Others | Reviewer |
| | Singapore Dental Journal | Reputable | Reviewer |
| A/P Tan Beng Choon, Keson | Journal Of Oral Rehabilitation | Leading | Editorial Board Member |
| | Singapore Dental Journal | Reputable | Editorial Reviewer |
| A/P Yeo Jin Fei | Singapore Dental Journal | Reputable | Editorial Reviewer |
| Dr. Clarisse Ng Chai Hoon | Journal of Prosthodontics | Leading | Editorial Board Member |
| Dr. Uy Joanne Ngo | Singapore Dental Journal | Reputable | Editorial Review Board Member |
| | Singapore Dental Journal | Reputable | Editorial Reviewer |

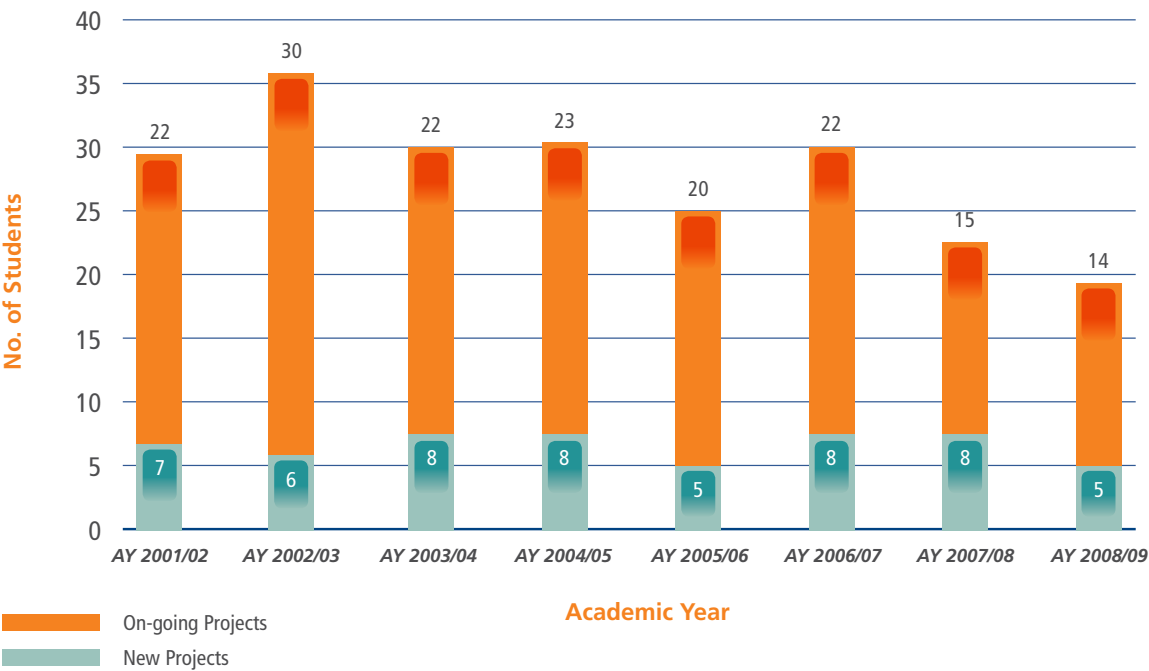
Enrolment of Research Students



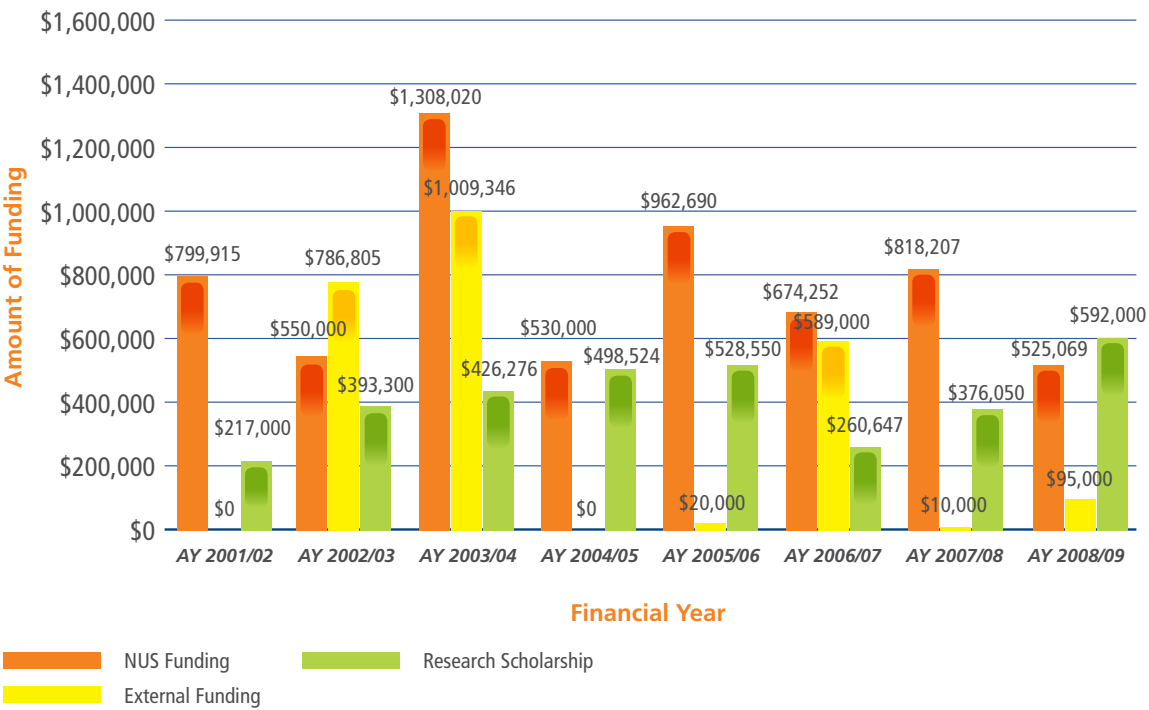
New Research Students by Nationality



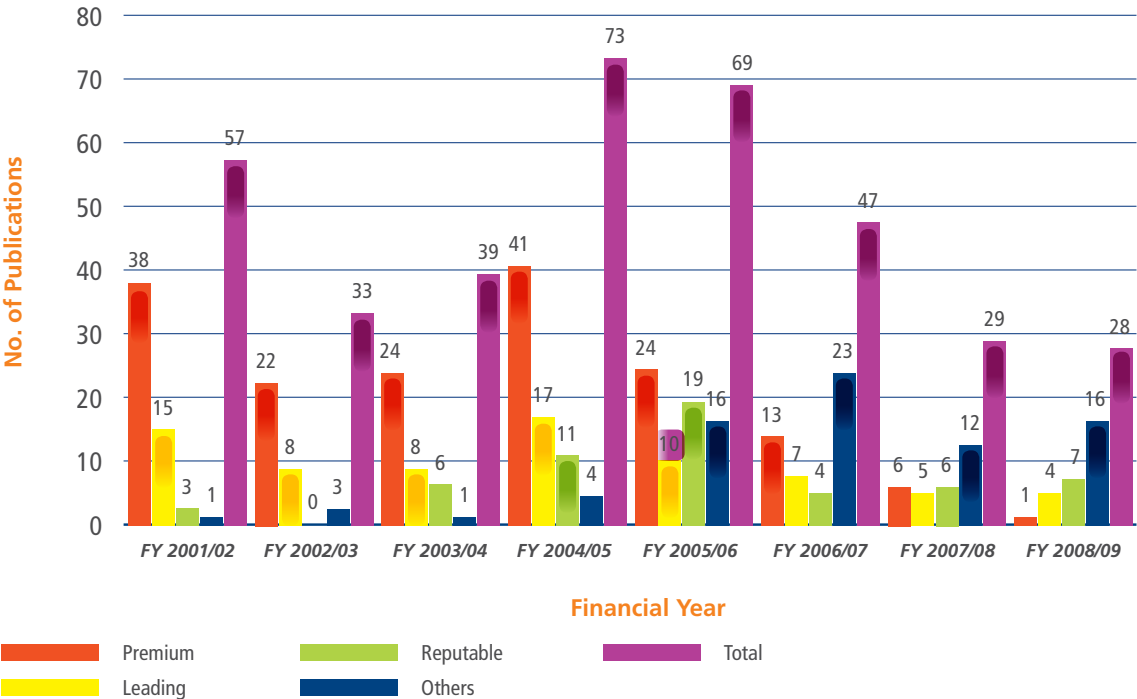
New and On-going Research Projects



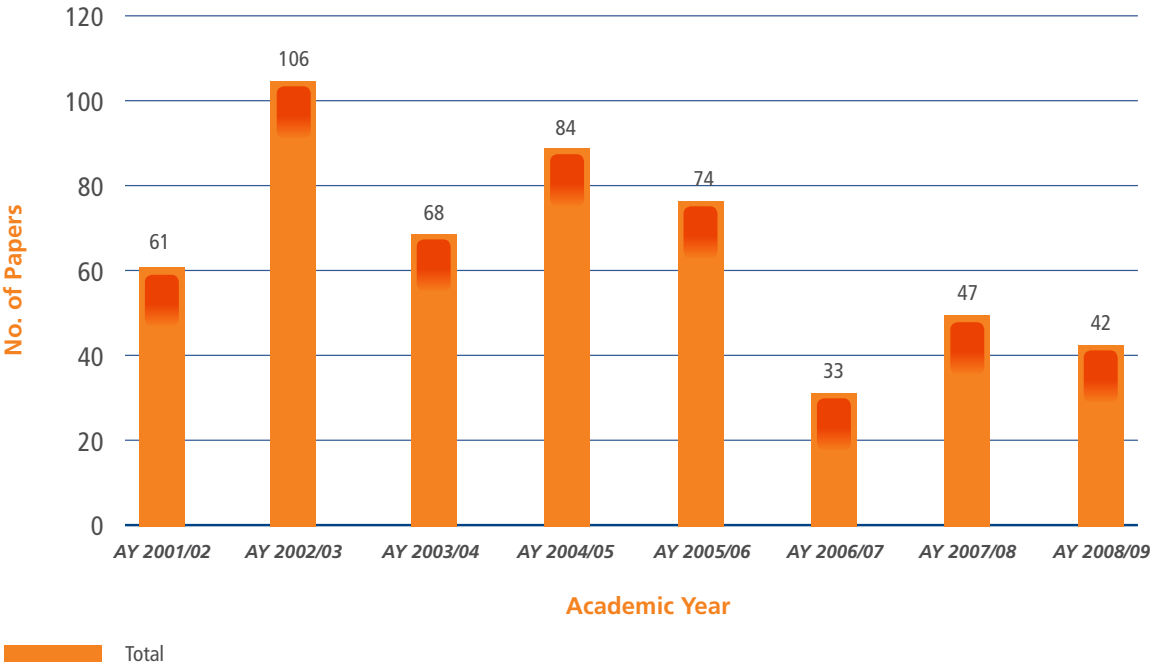
Research Fundings



Research Publications



Conference Papers



Research Internships

The Faculty of Dentistry has received numerous students from various schools, both locally and internationally as research interns. These schools include Junior Colleges, Polytechnics, and overseas Universities. The duration of the internship varies from a few months to about a year. The internship can either be full-time or part-time.

These students receive guidance from the academic staff members from the Faculty, by learning and working under the specific research projects of the staff members.



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