

RGC Ref.: N_HKU 776/10 NSFC Ref. : 81061160511 (please insert ref. above)

NSFC/RGC Joint Research Scheme
Joint Completion Report

*(Please attach a copy of the completion report submitted to the NSFC
by the Mainland researcher)*

Part A: The Project and Investigator(s)

1. Project Title

Enamel microstructure regeneration in macroscale by molecular mimetic method

2. Investigator(s) and Academic Department/Units Involved

	Hong Kong Team	Mainland Team
Name of Principal Investigator <i>(with title)</i>	Dr. Chu Chun Hung	Dr. Li Quan-Li
Post	Associate Professor	Professor
Unit / Department / Institution	Faculty of Dentistry, University of Hong Kong	College of Stomatology / Key Laboratory of Stomatology of Anhui Province, Anhui Medical University
Co-investigator(s) <i>(with title)</i>	Prof. Lo Chin Man Edward Faculty of Dentistry The University of Hong Kong	Prof. Zhou Jian College of Stomatology, Anhui Medical University Prof. Xu Yan College of Stomatology, Anhui Medical University

3. Project Duration

	Original	Revised	Date of RGC/ Institution Approval <i>(must be quoted)</i>
Project Start date	01/01/2011		
Project Completion date	31/12/2013		
Duration <i>(in month)</i>	36		

Part B: The Completion Report

5. Project Objectives

5.1 Objectives as per original application

1. To engineer and produce oligopeptides that self-assemble into nanospheres.
2. To examine the status of nanospheres and formulate a gel matrix carrier.
3. To test nanosphere-gel matrix activity on enamel defects by generating enamel-like hydroxyapatite nanorods in vitro.
4. To test the extent of in vitro repair of defects in tooth enamel by this biomimetic mineralization method.

5.2 Revised Objectives

Date of approval from the RGC: _____

Reasons for the change: _____

1. _____

2. _____

6. Research Outcome

Major findings and research outcome

(maximum 1 page; please make reference to Part C where necessary)

1) We have developed 2 amelogenin-like oligopeptides which can self-assemble into a supramolecular structure, as a mineralization template to control hydroxyapatite (HA) crystal growth, which are (Gln-Pro-X)₄-Thr-Lys-Arg-Glu-Glu-Val-Asp, and C₁₈H₃₅O-Thr-Lys-Arg-Glu-Glu-Val-Asp.

2) We have found 3 approaches to induce enamel-like tissue regeneration.

a) We have synthesized calcium and phosphate loaded temperature sensitive liposomes by interdigitation-fusion method with 1,2-bis(palmitoyl)-sn-glycerol-3-phosphocholine (DPPC) and 1,2-bis(myristoyl)-sn-glycerol-3-phosphocholine (DMPC) at mass ratio of 9:1. The liposomes were stable at room temperature, but slowly released calcium and phosphate ions if heated to 37 °C. We have integrated the calcium phosphate loaded liposomes and the self-assembly amelogenin-inspired peptide ((Gln-Pro-X)₄-Thr-Lys-Arg-Glu-Glu-Val-Asp) to build a novel biomimetic mineralization strategy for enamel remineralization.

b) We have added the peptide controlling nano amorphous calcium phosphate formation to form “polymer-induced liquid-precursor (PILP)” C₁₈H₃₅O-Thr-Lys-Arg-Glu-Glu-Val-Asp) to induce enamel remineralization in the presence of acid and calcium ions.

c) We have built a hydrogel model of calcium and phosphate ions diffusing in agarose gel to induce enamel remineralization. We constructed a kind of Ca²⁺ and PO₄³⁻ loaded agarose hydrogel mineralization micro-environment to control HA crystals self-assembling into the structure of enamel prisms-like tissue.

3) We have designed an agarose hydrogel model aided by electrophoresis to accelerate the speed of regeneration of the enamel prisms-like tissue. Based on the previous findings of this project, we improved the hydrogel model in which the process of biomimetic mineralization aided by electrophoresis. This

Seven research articles with impact factors have been published based on this project, two manuscripts are under review,

7. The Layman's Summary

(describe in layman's language the nature, significance and value of the research project, in no more than 200 words)

Traditional ways to repair tooth defect has focused primarily on treatment via the excision of diseased tissues and subsequent restoration of defect. Mechanical tooth preparation is a destructive and irreversible method of removing the natural dental tissues, and while dental materials have improved significantly in recent decades, they are artificial. We provided new biomimetic ways for enamel mineralization. The enamel-like tissue generated in our studies has similar microstructural and micromechanical properties as natural enamel. This brings a new possible way to repair the tooth defect such as tooth decay and tooth erosion by using biomineralized methods.

Part C: Research Output**8. Peer-reviewed journal publication(s) arising directly from this research project**

(Please attach a copy of each publication and/or the letter of acceptance if not yet submitted in the previous progress report(s). All listed publications must acknowledge RGC's funding support by quoting the specific grant reference.)

The Latest Status of Publications				Author(s) <i>(bold the authors belonging to the project teams and denote the corresponding author with an asterisk*)</i>	Title and Journal/Book <i>(with the volume, pages and other necessary publishing details specified)</i>	Submitted to RGC <i>(indicate the year ending of the relevant progress report)</i>	Attached to this report <i>(Yes or No)</i>	Acknowledged the support of this Joint Research Scheme <i>(Yes or No)</i>
Year of publication	Year of Acceptance <i>(For paper accepted but not yet published)</i>	Under Review	Under Preparation <i>(optional)</i>					
2011	2011			T. Y. Ning, X.H. Xu, L.F. Zhu, X.P. Zhu, C.H. Chu Liu L.K., Q.L. Li*	Biomimetic mineralization of dentin induced by agarose gel loaded with calcium phosphate <i>J Biomed Mater Res Part B</i> 2012; 100B: 138-144 Impact Factor: 2.308	2012	No	Yes

2012	2012			M. L. Mei Q.L. Li C.H. Chu* C.K.Y. Yiu E. C.M. Lo	The inhibitory effects of silver diamine fluoride at different concentrations on matrix metalloproteinases <i>Dental Materials</i> 2012; 28: 903-908 Impact Factor: 3.773	2012	No	Yes
2012	2012			J. Luo, T. Y. Ning, Y. Cao, X.P. Zhu, X.H. Xu, X.Y. Tang, C.H. Chu* Q.L. Li*	Biomimic Enamel Remineralization by Hybridization Calcium- and Phosphate-Loaded Liposomes with Amelogenin-Inspired Peptide <i>Key Engineering Materials</i> 2012; 512-515: 1727-1730	2012	No	Yes
2012	2012			Y.Z. Zhou, Y. Cao, W. Liu, C.H. Chu*, Q.L. Li*	Polydopamine-induced tooth remineralization. <i>ACS Appl Mater Interfaces</i> . 2012 Dec;4(12):6901-10. Impact Factor: 5.008	2013	Yes	Yes
2013	2013			Y. Cao M. L. Mei J. G. Xu E.C.M. Lo C. H Chu** Q.L. Li*	Biomimetic mineralization of phosphorylated dentine by CPP-ACP. <i>Journal of Dentistry</i> 2013 41:818-825 Impact Factor: 3.200	2013	Yes	Yes
2013	2013			Y. Cao W.Liu T.Ning M.L.Mei C. H Chu,* Q.L. Li* E.C.M. Lo	A novel oligopeptide simulating dentine matrix protein I for biomimetic remineralization of dentine. <i>Clinical Oral Investigation</i> 2013 Aug 4. [Epub ahead of print] Impact Factor: 2.200	2013	Yes	Yes
2013	2013			M.L. Mei L. Ito Y. Cao Q. L. Li C. H Chu,* E.C.M. Lo	The inhibitory effects of silver diamine fluorides on cysteine cathepsins. <i>Journal of Dentistry</i> [In Press, accepted on 4Dec 2013] Impact Factor: 3.200	2013	Yes	Yes

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2013	2013			Y. Cao M. L. Mei Q.L. Li* E.C.M. Lo C. H Chu**	An agarose hydrogel biomimetic mineralisation model for the regeneration of enamel prism-like tissue <i>ACS Applied Materials & Interfaces</i> [In Press, accepted on 18Dec 2013] Impact Factor: 5.008	2013	Yes	Yes
		Yes		Q.L. Li * T.Y. Ning Y. Cao W.B.Zhang M.L.Mei C. H. Chu*	A novel self-assembled oligopeptide amphiphile for biomimetic mineralization of enamel <i>BMC Biotechnology</i> Impact Factor: 2.165			

9. Recognized International conference(s) in which paper(s) related to this research project was/were delivered (Please attach a copy of each delivered paper)

Month/Year/ Place	Title	Conference Name	Submitted to RGC (indicate the year ending of the relevant progress report)	Attached to this report (Yes or No)	Acknowledged the support of this Joint Research Scheme (Yes or No)
June/ 2012/ Iguaçu Falls, Brazil	The inhibitory effects of silver diamine fluoride at different concentrations on matrix metalloproteinases	International Association of Dental Research General Session 2012	2012	Yes	Yes
August/2012/ Hong Kong	Biomimetic mineralization of phosphorylated dentine by CPP-ACP.	100th FDI Annual World Dental Congress	2012	Yes	Yes
November/20 12/Hong Kong	A novel oligopeptide simulating dentine matrix protein I for biomimetic remineralization of dentine.	International Association of Dental Research/DIV/SEA 2012	2012	Yes	Yes
March/2013/ Seattle/USA	Developing a hydrogel micro-environment for biomimetic mineralization of enamel	International Association of Dental Research General Session 2013	2013	Yes	Yes
August/2013/ Bangkok/Tha iland	The inhibitory effects of silver diamine fluorides on cysteine cathepsins.	International Association of Dental Research/DIV/SEA 2013	2013	Yes	Yes

(Revised 07/09)

10. Student(s) trained *(Please attach a copy of the title page of the thesis.)*

Name	Degree registered for	Date of registration	Date of thesis submission/ graduation
Nil			

11. Other impact *(e.g. award of patents or prizes, collaboration with other research institutions, technology transfer, etc.)*

1. FDI Poster Award in the theme of Dental Treatment and Restorative Dentistry. *FDI World Dental Federation*. 2012
2. HKU Outstanding Research Award (Translational Research). 2013