CRF 8G (Revised Sep 15)

RGC Reference **CUHK8/CRF/11R**
please insert ref. above

The Research Grants Council of Hong Kong
Collaborative Research Fund Group Research Projects
Completion Report

(*for completed projects only*)

Part A: The Project and Investigator(s)

1. Project Title

Centre for MicroRNA Study - Basic Research and Clinical Potentials in Cancer

2. Investigator(s) and Academic Department/Units Involved *(please highlight approved changes in the composition of the project team and quote the date when RGC granted approval of such changes)*

Research Team	Name/Post	Unit/Department/Institution	Average no. of hours per week spent on this project in the current reporting period
Project Coordinator	Nathalie WONG/ Professor	Anatomical & Cellular Pathology, The Chinese University of Hong Kong	10h
Co-investigators	Ka Fai TO/ Professor	Anatomical & Cellular Pathology, The Chinese University of Hong Kong	8h
	Kwok Wai LO/ Professor	Anatomical & Cellular Pathology, The Chinese University of Hong Kong	8h
	King-Lau CHOW/ Professor	Division of Life Science, The Hong Kong University of Science and Technology	2h
	Alice S. WONG/ Associate Professor	School of Biological Sciences, The University of Hong Kong	4h
	Terence C. POON/ Associate Professor	Pilot Laboratory and Proteomics Core, Faculty of Health Sciences, University of Macau	2h
	Alfred S. CHENG/ Associate Professor	School of Biomedical Sciences, The Chinese University of Hong Kong	4h
	Stephanie MA/ Assistant Professor	Anatomy, The University of Hong Kong	2h
	Kevin Y. YIP / Assistant Professor	Computer Science & Engineering, The Chinese University of Hong Kong	2h
Collaborators			

3. Project Duration

	Original	Revised	Date of RGC Approval *(must be quoted*)
Project Start Date	1-June-2012		
Project Completion Date	31-May-2015		
Duration (*in month*)	36 months		
Deadline for Submission of Completion Report	31-May-2016		

Part B: The Final Report

5. Project Objectives

5.1 Objectives as per original application

1. To characterize cancer secreted exosomes for the transferred functional miRNAs in cell-cell interactions, and thereof influence on tumor microenvironment
2. To elucidate characteristic EBV miRNA biogenesis in nasopharyngeal carcinoma (NPC) and functional implications of sequence variations in disease pathogenesis
3. To define the role(s) of differential transcribed miRNAs in the stem cell-like properties of NPC and hepatocellular carcinoma (HCC)
4. To investigate regulatory elements that underlie differential expressed miRNA, in particular the repressive histone modifications and DNA methylation

5.2 Revised objectives

Date of approval from the RGC: 13-Feb-2012

Reasons for the change: Due a budget cut of ~50%, some aspects of the work programme under objectives #2 and #4 have been adjusted to accommodate for the change in budget. These revisions were also made according to reviewers' comments.

Objective 2. To characterize sequence variants of miR-BARTs and their functional implications in NPC pathogenesis.

Objective 4. To investigate regulatory elements that underline differential expressed miRNA, specifically the repressive histone modifiers (H3K27me3 and H3K4me3) and DNA methylation modulators (EZH2 and DNMT).

6. Research Outcome

6.1 Major findings and research outcome

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

Cancer-secreted exosomes can promote motility of normal cells through transfer of oncogenic proteins and RNAs

Exosomes are increasingly recognized as important mediators of cell–cell communication in cancer progression through the horizontal transfer of RNAs and proteins to neighboring or distant cells. HCC is a highly malignant cancer, whose metastasis is largely influenced by the tumor microenvironment. In our study of HCC-secreted exosomes, we comprehensively characterized the transcriptome and proteome of exosomes derived from HCC cell lines by Ion Torrent sequencing and mass spectrometry, respectively. Remarkably, we found exosomes from highly metastatic HCC cell lines could markedly induce migratory and invasive behaviors of non-motile hepatocytes. The internalization of exosomes could activate PI3K/AKT and MAPK signaling pathway, and increased secretion of MMP-2 and MMP-9 that favored cell invasion. This phenomenon may have inference on a novel interplay between HCC tumor cells and liver parenchyma cells, where cancer-derived exosomes might alter the liver milieu in support of tumor metastasis. (***Mian H et al, Carcinogenesis 2015***. ***Our published article was also recommended as the Editor's Choice of the published issue***)

Regulatory role of miR-142-3p on the functional hepatic cancer stem cell marker CD133

Tumor relapse after therapy typifies HCC and is believed to be attributable to residual cancer stem cells (CSCs) that survive treatment. We have previously identified a CSC population derived from HCC that is characterized by CD133. Despite our growing knowledge of the importance of this subset of cells in driving HCC, the regulatory mechanism of CD133 is not known. Epigenetic changes are believed to be essential in the control of cancer and stem cells. Here, we report the epigenetic regulation of CD133 by miR-142-3p. The interaction between CD133 and miR-142-3p was identified by in silico prediction and substantiated by luciferase reporter analysis. Expression of CD133 was found to be inversely correlated with miR-142-3p in HCC clinical samples as well as in cell lines. Importantly, lower miR-142-3p expression in HCC was significantly associated with worst survival. Functional studies with miR-142-3p stably transduced in HCC cells demonstrated a diminished ability to self-renew, initiate tumor growth, invade, migrate, induce angiogenesis and resist chemotherapy. Rescue experiments whereby CD133 and miR-142-3p is simultaneously overexpressed compensated the deregulated ability of the cells to confer these features. Thus, miR-142-3p directly targets CD133 to regulate its ability to confer cancer and stem cell-like features in HCC **(*Chai S et al, Oncotarget 2014*)**

Role of EBV-encoded miRNAs in regulating DNA damage response in NPC

To gain insight into the expression pattern of EBV microRNAs in NPC, we measured the copy number of EBV miRNAs by qRT-PCR. Interestingly, the average copy number of BART miRNAs expressed in NPC is higher than other EBV-associated cancer types. Some miR-BARTs are predominantly expressed in NPC cell line (C666-1) such as BART5-5p, BART76-3p, BART9-3p and BART14-3p. These highly expressed miR-BARTs could directly regulate the expression of endogenous ATM, a critical DNA double-strand break responder gene. Moreover, manipulation of these individual miR-BART expression in NPC cells could alter their sensitivity to γ-irradiation and the behavior during lytic cycle induction. We also demonstrated that BART12 works cooperatively with miR-182 in the control of other important DNA repair gene expression, such as BRCA1. Our findings may contribute to the optimization of therapeutic regimens to combat NPC by using DNA damaging agents and PARP inhibitors. (***Lung RE et al, manuscript in preparation***)

Upstream epigenetic regulation of miRNA expression

Chronic hepatitis B virus (HBV) infection is the major risk factor for HCC in most Asian countries. The X protein of HBV (HBx) can transactivate the polycomb protein EZH2, which catalyzes H3K27me3 for epigenetic gene silencing in cancer development. Using integrated genome-wide binding and expression analysis, we uncovered a set of miRNAs that were epigenetically regulated by DNA methylation and H3K27me3. We further discovered an epigenetic connection between

miRNA deregulation and NF-κB activation in HCC, which was mediated by the transcription factor YY1. Our data uncover novel epigenetic routes by which chronic HBV infection promotes hepatocarcinogenesis. (***Tsang DP et al, J Pathol 2016***).

6.2 Potential for further development of the research and the proposed course of action *(maximum half a page)*

Stemmed from this CRF research, we comprehensively profiled RNA and protein contents of exosomes secreted from motile and non-motile HCC cell lines. We found novel interaction between HCC tumor cells and immortalized hepatocyte via exosomes. Our study also showed multiple oncogenic molecules carried in tumor-derived exosomes that may be responsible for exosomes-induced hepatocyte migration and invasion. Our proteome analysis suggested proteins that might be associated with exosomes formation. Among them, syndecan–syntenin–ALIX is known to support biogenesis of exosomes and the segregation of signaling cargo to these vesicles. Rab GTPase family members, which are capable to manipulate different steps of the exosomes secretion pathway, were also identified. Our data hence supports, in addition to promoting cancer progression, necessary proteins for biogenesis and secretion are also present in exosomes. Data derived from this study will be of value in understanding of cell-cell interaction through exosomes. Studies on cellular and EBV-encoded miRNAs revealed novel therapeutic targets for NPC, particularly future developments in manipulating miR-BARTs expressions with DNA damaging agents and PARP inhibitor for optimization of therapeutic regimens in patients with NPC. Collectively, we have also demonstrated that miRNAs in conferring stemness characteristics in CSCs. miR-1246 overexpression substantially activates and sustains Wnt signaling in CD133+ liver CSCs and HCC by simultaneously suppressing multiple Wnt inhibitors of the β-catenin destruction complex (AXIN2 and GSK3β), providing a new layer of understanding on the molecular mechanism by which the Wnt-mediated stem cell-like properties of HCC cells are developed. Our data from the epigenetic analysis of miRNA expressions highlight the potentials on pharmacological reversion of H3K27me3 epigenome may have important implications for prevention of HCC, which is an urgent priority due to its prevalence and grave prognosis.

6.3 Research collaboration achieved *(please give details on achievement and its relevant impact)*

Members of the CRF project have been actively engaged in research activities and much collaborations have been undertaken in investigating the different aspects of miRNA deregulations in cancers, including signaling transductions and tumor phenotypes. These activities can be reflected by the many co-authorship publications between team members as listed in Section 8. In this 3-yr investigative period, team members have met 3-4 times per year. During each meeting, updates on each other's research progress and discussions on data generated were made. Collaborative projects have been initiated and the logistics involved in the transfer of research materials discussed. Described here are few major collaborative activities that resulted in publications described in this report: (1) To determine the protein content of HCC and NPC secreted exosomes, ***NW, KWL*** and ***TCP*** are collaborating to explore Mass Spectrometry analysis for proteome by MALDI-TOF and computational target predictions. (2) ***KWL*** and ***KFT*** worked closely on the studies of cellular and EBV-encoded microRNAs on NPC tumorigenesis. ***KYY*** contributed informatic analysis of NPC transcriptomes and target predictions of various cellular and EBV-microRNAs. (3) Integrative analysis of genome-wide occupancy from ChIP-seq and bioinformatics of HCC epigenome was conducted through the efforts between ***ASC*** and ***KYY***. (4) A joint effort between ***KLC*** and ***ASC*** continued in the generation of a liver-specific and temporal-controlled transgenic mouse model. There have also been exchanges of research material between team members, such as the transfer of wild-type and carboxyl-terminal truncated HBx over-expression plasmids from ***ASC*** to ***SM***.

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)

MicroRNAs (miRNAs) of cellular and viral origin hold importance in regulating gene expression by repressing translation of mRNA into protein. Supported by this Collaborative Research Fund, the present investigative team has intensely researched and reported on deregulated cellular and viral miRNAs of two locally prevalent cancers, namely Nasopharyngeal Carcinoma (NPC) and Hepatocellular Carcinoma (HCC), and the Epstein-Barr virus (EBV) which is a strong risk factor for the development of NPC. In this study, we initiated new research areas that are vital in establishing firm understandings on the miRNA-modulated NPC and HCC biology. Recent data emphasized on the content of cancer-secreted exosomes in the intercellular communications and promotion of cell motility. Based on previous experience in deciphering viral miRNAs, we identified in this study additional EBV miRNAs that are particular to NPC, and defined their functional implications in disease pathogenesis. We have also broadened our knowledge on miRNAs that governor cancer stem cell characteristics in HCC and NPC, and realized the upstream epigenetic mechanisms (namely, histone modifications and DNA methylation) that regulate expression of cancer-associated miRNAs. In sum, the collaborative effort fostered in this project has promoted understandings on the biological effects of miRNAs in both HCC and NPC developments.

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Part C: Research Output

8. Peer-reviewed journal publication(s) arising directly from this research project

(Please attach a copy of the 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) *(denote the corresponding author with an asterisk*)*	Title and Journal/Book *(with the volume, pages and other necessary publishing details specified)*	Submitted to RGC *(indicate the year ending of the relevant progress report)*	Attached to this report *(Yes or No)*	Acknowledged the support of RGC *(Yes or No)*	Accessible from the institutional repository *(Yes or No)*
Year of publication	Year of Acceptance (For paper accepted but not yet published)	Under Review	Under Preparation (optional)						
			2016	Lung RE, Hau TP, Chak WP, Tong JH, Yu KH, Tsao SW, Yip KY, To KF, Lo KW*	The role of Epstein-Barr virus-encoded miRNAs in ATM regulating DNA damage response in nasopharyngeal carcinoma	No	No	Yes	No
			2016	To SK, Mak AS, Fung YM, Li SS, Che CM, Deng W, Wong AS*	β-catenin mediated downregulation of microRNA biogenesis determines ovarian tumor aggressiveness	No	No	Yes	No
		2016		Ip CK, Li SS, Tang MY, Sy SK, Ren Y, Shum HC, Wong AS*	Stemness and chemoresistance in epithelial ovarian carcinoma cells under shear stress. *Scientific Reports* (in revision)	No	No	Yes	No
		2016		Chai S, Ng KY, Tong M, Lau EY, Lee TK, Chan KW,	Functional interplay of microRNA-1246 and Wnt/β-catenin in the	No	No	Yes	No

				Yuan YF Cheung TT, Cheung ST, Wong N, Lo CM, Man K, Guan XY, Ma S*	pathogenesis of CD133+ hepatocellular carcinoma. *Gasteroenterol. (under review)*				
		2016		Lam SN, Ip CK, Mak AS, Wong AS*.	A novel p70 S6 kinase-microRNA biogenesis axis mediates multicellular spheroid formation in ovarian cancer progression. *Oncotarget* (in press)	No	No	Yes	No
	2016			Cheung CC, Lun SW, Chung GT, Lo C, Choy KW, Lo KW*	MicroRNA-183 as tumor suppressor in EBV-associated nasopharyngeal carcinoma by suppressing cancer stem-like cell properties. *BMC Cancer (in press)*	No	Yes	Yes	No
2016				Tsang DP, Wu WK, Kang W, Lee YY, Wu F, Yu Z, Xiong L, Chan AW, Tong JH, Yang W, Li MS, Lau SS, Li X, Lee SD, Yang Y, Lai PB, Yu DY, Xu G, Lo KW, Chan MT, Wang H, Lee TL, Yu J, Wong N, Yip KY,	Yin Yang 1-mediated epigenetic silencing of tumour-suppressive microRNAs activates nuclear factor-κB in hepatocellular carcinoma *J Pathol. 2016; 238:651-64.*	No	Yes	Yes	No

				To KF, Cheng AS*					
2016				Zhu R, Mok MT, Kang W, Lau SS, Yip WK, Chen Y, Lai PB, Wong VW, To KF, Sung JJ, Cheng AS*, Chan HL	Truncated HBx-dependent silencing of GAS2 promotes hepatocarcinogenesis through deregulation of cell cycle, senescence and p53-mediated apoptosis. *J Pathol. 2015; 237:38-49.*	No	Yes	Yes	No
2015				He M, Qin H, Poon TC, Sze SC, Ding X, Co NN, Ngai SM, Chan TF, Wong N*.	Hepatocellular carcinoma-derived exosomes promote motility of immortalized hepatocyte through transfer of oncogenic proteins and RNAs *Carcinogenesis 2015;36:1008-18*	No	Yes	Yes	No
2015				Leung WK, He M, Chan AW, Law PT, Wong N*	Wnt/β-Catenin activates MiR-183/96/182 expression in hepatocellular carcinoma that promotes cell invasion. *Cancer Lett. 2015;362:97-105*	No	Yes	Yes	No
2015				Tsao SW, Tsang CM, To KF, Lo KW*	The role of Epstein-Barr virus in epithelial malignancies. *J Pathol, 2015; 235:323-33*	No	Yes	Yes	No

2015				Tsao SW, Tsang CM, Lo KW	Nasopharyngeal carcinoma. In: EBV, edited by Takada K, 2015 (Japanese)	No	No	Yes	No
2014				Chai S, Tong M, Ng KY, Kwan PS, Chan YP, Fung TM, Lee TK, Wong N, Xie D, Yuan YF, Guan XY, Ma S*.	Regulatory role of miR-142-3p on the functional hepatic cancer stem cell marker CD133. *Oncotarget 2014; 5: 5725-35.*	No	Yes	Yes	No
2014				Cheung CC, Chung GT, Lun SW, To KF, Choy KW, Lau KM, Siu SP, Guan XY, Ngan RK, Yip TT, Busson P, Tsao SW, Lo KW*	miR-31 is consistently inactivated in EBV-associated nasopharyngeal carcinoma and contributes to its tumorigenesis. *Mol Cancer, 2014; 7;13:184*	No	Yes	Yes	No
2014				Tsao SW*, Yip YL, Tsang CM, Pang PS, Lau VM, Zhang G, Lo KW	Etiological factors of nasopharyngeal carcinoma. *Oral Oncol, 2014; 50:330-8.*	No	Yes	Yes	No
2014				Lun SW, Cheung ST, Lo KW*	Cancer stem-like cells in Epstein-Barr virus-associated nasopharyngeal carcinoma. *Chin J Cancer, 2014; 33:529-38*	No	Yes	Yes	No
2014				Lam SN, Mak AS, Yam JW, Cheung AN, Ngan HY, Wong AS*	Targeting estrogen-related receptor alpha inhibits epithelial to mesenchymal	No	Yes	Yes	No

					transition and stem cell properties of ovarian cancer cells. *Mol Ther 2014; 22: 743-751.*				
2014				Yip DK, Pang IK, Yip KY*	Systematic exploration of autonomous modules in noisy microRNA-target networks for testing the generality of the ceRNA hypothesis *BMC Genomics 2014, 15:1178*	No	Yes	Yes	No
2013				Chung GT, Lou WP, Chow C, To KF, Choy KW, Leung AW, Tong CY, Yuen JW, Ko CW, Yip TT, Busson P, Lo KW*	Constitutive activation of distinct NF-κB signals in EBV-associated nasopharyngeal carcinoma. *J Pathol. 2013; 231:311-22*	2013	No	Yes	No
2013				Ma S*	Biology and clinical implications of CD133(+) liver cancer stem cells. *Exp Cell Res. 2013; 319:126-32*	2013	No	Yes	No
2013				Chau WK, Ip CK, Mak AS, Lai HC, Wong AS*	C-KIT mediates chemoresistance and tumor-initiating capacity of ovarian cancer cells through activation of Wnt/β-catenin-	2013	No	Yes	No

					ATP-binding cassette G2 signaling. *Oncogene 2013; 32: 2767-81.*				
2013				Tso KK, Yip KY, Mak CK, Chung GT, Lee SD, Cheung ST, To KF, Lo KW*	Complete genomic sequence of Epstein-Barr virus in nasopharyngeal carcinoma cell line C666-1. *Infect Agent Cancer. 2013;8:29*	2013	No	Yes	No
2013				Yu Z Cheng AS*	Epigenetic Deregulation of MicroRNAs: new opportunities to target oncogenic signaling pathways in hepatocellular carcinoma *Curr Pharm Des. 2013; 19:1192-200*	2013	No	Yes	No
2013				Chai S, Ma S*	Clinical implications of miRNA in liver cancer stem cells. *Chin J Cancer 2013; 32:419-26*	2013	No	Yes	No
2013				Lin SW, Cheung CC, Chow C, Chung GT, Lo KW*	Molecular Genetics of Nasopharyngeal Carcinoma *Book Chapter In: eLS. John Wiley & Sons Ltd, Chischester*	2013	No	Yes	No

2012				Lun SW, Cheung ST, Cheung PF, To KF, Woo JK, Choy KW, Chow C, Cheung CC, Chung GT, Cheng AS, Ko CW, Tsao SW, Busson P, Ng MH, Lo KW*	CD44+ cancer stem-like cells in EBV-associated nasopharyngeal carcinoma. *PLoS One, 2012; 7(12): e52426.*	2013	No	Yes	No

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

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 RGC *(Yes or No)*	Accessible from the institutional repository *(Yes or No)*
Aug, 2012, Philadelphia USA	Inactivation of miR-31, a tumor suppressor microRNA at 9p21.3 homozygous deletion region in EBV-associated nasopharyngeal carcinoma	International Congress on Oncogenic Herpesviruses and Associated Diseases	2013	No	Yes	No
Oct, 2012, Amsterdam, Netherlands	Yin Yang-1-mediated epigenetic silencing of tumor-suppressive microRNAs activates NF-kappa B signaling to promote hepatocarcinogenesis	United European Gastroenterology Week 2012	2013	No	Yes	No
Nov, 2012, Guangzhou, China	Dissecting liver cancer stem cells – CD133 and beyond. *Oral Presentation*	2012 Merck Millipore Asia Bio-Forum,	2013	No	Yes	No
June, 2013, Sydney, Australia	Biology and clinical implications of liver cancer stem cells. Featured Symposia – Liver Regenerative Medicine. *Oral Presentation*	International Liver Transplantation Society 19th Annual International Congress	2013	No	Yes	No

July, 2013, Busan, Korea	Role of liver cancer stem cells in HCC metastasis. *Oral Presentation*	The 4th Asia Pacific Primary Liver Cancer Expert Meeting (APPLE)	2013	No	Yes	No
Sept, 2013, Amsterdam, Netherlands	MicroRNA-145, a p70 S6 kinase-activated microRNA, regulates N-cadherin expression and epithelial-mesenchymal transition *Awarded Fellowship Grant*	17thECCO - 28thESMO - 32ndESTRO European Cancer Congress	2013	No	Yes	No
Nov, 2013, Hong Kong	Regulatory role of miR-142-3p on the functional liver cancer stem cell marker CD133. *Selected for Oral Presentation*	20th Hong Kong International Cancer Congress	2013	No	Yes	No
April, 2014, San Diego, USA	p70 S6 kinase signals tristetraprolin/Dicer-mediated maturation of microRNA-145 to regulate tumor metastasis.	American Association for Cancer Research Annual Meeting	No	Yes	Yes	No
April, 2014, San Diego, USA	Regulatory role of miR-1246 and Wnt/β-catenin pathway interaction in CD133+ liver cancer stem cells-driven hepatocellular carcinoma.	American Association for Cancer Research Annual Meeting	No	Yes	Yes	No
April, 2014, San Diego, USA	Whole-transcriptome analyses of EBV-associated nasopharyngeal carcinoma using next-generation transcriptome sequencing.	American Association for Cancer Research Annual Meeting	No	Yes	Yes	No

Oct, 2014, Hong Kong	miR-31 functions as tumor suppressors and targets FIH1 and MCM2 in EBV-associated nasopharyngeal carcinoma	CANCER 2014: Advances in EBV and Nasopharyngeal Carcinoma Research.	No	Yes	Yes	No
Nov, 2014, Hong Kong	Whole transcriptome study of EBV-associated nasopharyngeal carcinoma	The Croucher Foundation – Advanced Study Institute: Advances in Nasopharyngeal Carcinoma Studies	No	Yes	Yes	No
April, 2015, Philadelphia, Pennsylvania, USA	Regulatory role of miRNA-1246 and Wnt/β-catenin pathway interaction in CD133+ liver cancer stem cells-driven hepatocellular carcinoma. Minisymposium (Non-Coding RNAs in Cancer Biology 2) *Selected for Oral Presentation*	American Association for Cancer Research Annual Meeting	No	Yes	Yes	No
April, 2015, Philadelphia, Pennsylvania, USA	Truncated HBx-dependent Silencing of Growth Arrest-specific 2 Promotes Hepatocarcinogenesis through Inhibition of p53-mediated Apoptosis	American Association for Cancer Research Annual Meeting	No	Yes	Yes	No
Sept, 2015, Vancouver, Canada	Proteomic study revealing roles of MET and caveolins in exosome-induced hepatoma motility	14th Human Proteome Organization World Congress (HUPO)	No	Yes	Yes	No
April, 2016, New Orleans, Louisiana, USA	The role of Epstein-Barr virus-encoded miRNAs in ATM regulating DNA damage response in nasopharyngeal carcinoma	American Association for Cancer Research Annual Meeting	No	Yes	Yes	No

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
Ching Mei, CHEUNG	Ph.D.	August 2009	July 2013
Pui Ying, CHOI	MPhil	August 2011	August 2013
Mian, HE	Ph.D.	August 2011	October 2015
Ka Yan, MAK	MPhil	August 2012	August 2014
Sophia So Ngo, LAM	PhD	August 2011	2016 (expected)
Ying-Ying, LEE	MPhil	August 2012	2016 (expected)

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

- Paper published by PhD student He Mian et al, Carcinogenesis 2015 was recommended as Editor's Choice in the published issue
- PhD student, Sophia So Ngo, LAM, received a Fellowship Grant to the 17th ECCO - 28th ESMO - 32nd ESTRO European Cancer Congress, Sept 2013, Amsterdam.
- Prof. Alfred Cheng was awarded a Travel Grant of EUR 1,000 for Basic Scientists to the United European Gastroenterology Week 2012, Oct 2012, Amsterdam.
- Prof. Alfred Cheng was awarded Oral Free Paper Prize at the United European Gastroenterology Week 2012, Oct 2012, Amsterdam.
  Session: HCC and liver transplantation
  Free paper entitled: *Yin Yang-1-Mediated Epigenetic Silencing of Tumor Suppressive MicroRNAs Activates NF-Kappa B Signaling to Promote Hepatocarcinogenesis*
- PhD student, Ching Mei CHEUNG, received a Poster Presentation award from the SYSU-CUHK 2012 Retreat Conference

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Project Coordinator

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