科技部補助專題研究計畫成果報告
期末報告

探討蛋白質精胺酸甲基轉移腖8之生理和病理角色(第3年)

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中 文 摘 要 ： 蛋白質精胺酸甲基化由蛋白質精胺酸甲基轉移酶所催化，和訊息傳遞、 轉錄調控、 RNA處理和DNA修補等相關。本研究將焦點放在唯一神經細胞特異性表達的PRMT8上。PRMT8是度保留最高的PRMT1脊椎動物中的平行同源基因。二者主要差異在不同物種中PRMT8均含多出60-90個胺基酸長度的N端。本研究希望回答PRMT8為何及如何不同於PRMT1，以及PRMT8的生理功能為何，並將聚焦於其可能參與的神經疾病及癌症。為探討PRMT8的相關課題，我們將對其基因結構、剪接模式及可能的轉錄調節單元進行生物資訊分析，以追蹤PRMT8在演化中改變。我們將分析PRMT8和部分 PRMT1 異構體的甲基轉移酶活性以及其於神經細胞中的交互作用體，以描繪PRMT8特有的交互作用網。我們將訂出不同PRMT8/(PRMT1)異構體在一般及壓力條件下的表現形式，以檢查他們可否能參與神經退化性疾病。我們也將研究PRMT8可否在癌症中表現並扮演某些角色。我們還將分析PRMT8的轉錄調節。最後我們會以斑馬魚為系統來驗證或補充在哺乳動物細胞中所得結果。由本研究所提實驗獲致的結果，我們將能勾勒出較細節的PRMT8特有精胺酸甲基化網絡以及PRMT8在生理和病理上的角色

中 文 關 鍵 詞 ： 蛋白質精胺酸甲基轉移酶1， 蛋白質精胺酸甲基轉移酶8，神經母細胞瘤細胞，酵母菌雙雜合， 蛋白質精胺酸甲基化， 神經退化性疾病， 癌症

英 文 摘 要 ： Protein arginine methylation catalyzed by protein arginine methyltransferases (PRMTs) is involved in various cellular processes including signal transduction, transcriptional regulation, RNA processing, and DNA repair. In this study we will focus on PRMT8, the only neuron-specific PRMT. PRMT8 is a vertebrate-specific paralogue of the most conserved PRMT1. The major difference between the two is that PRMT8 contains an extra N-terminus for about 60-90 amino acids in different species. In this study we would like to answer why and how PRMT8 is different from PRMT1 and what is the physiological function of PRMT8, with the focus on its putative participation in the pathogenesis of neural disorders or cancers. We will pursue the issues of PRMT8 by conducting bioinformatic analyses of the gene structure, splicing pattern, the putative transcriptional regulatory elements of the prmt8 gene, and tracing the changes of the segments in the N-terminus of PRMT8 through evolutionary. We then will analyze the methyltransferase activity of PRMT8 and specific PRMT1 isoforms, and also the interactome of human PRMT8 in the neuronal cells to picture the PRMT8-specific interaction network. We will determine the expression pattern of different PRMT8/(PRMT1) isoforms under normal and stress conditions to examine their putative involvement in neural degenerative disease. We will also study the putative expression and roles of PRMT8 in cancer. We will also analyze transcriptional regulation of prmt8. Finally, we will use zebrafish as the biological

system to validate and complement the results from studies of the mammalian cell cultures. With the results of the experiments proposed in this project, we can outline a more detailed PRMT8-specifc arginine methylation network and the physiological and pathological roles of PRMT8.

英文關鍵詞：PRMT1, PRMT8, neuroblastoma cells, yeast two hybridprotein arginine methylation, neural degenerative disease, cancer

Final report of MOST103-2320-B-040-022-MY3

Investigation of the physiological and pathological roles of protein arginine methyltransferase 8

Introduction and Specific aims

In the post-genomic era, posttranslational modification (PTM) of proteins becomes the key issue for understanding gene expression, epigenetic regulation as well as pathogenesis of many diseases. Of these modifications, protein arginine methylation catalyzed by protein arginine methyltransferases (PRMTs) is involved in various cellular processes including signal transduction, transcriptional regulation, RNA processing, and DNA repair (Krause et al., 2007; Wang and Li, 2012). Nine different human PRMTs have been identified. In this study we will focus on the unsolved biological function and the putative involvement in neurodegenerative diseases and cancers of the only neuron-specific PRMT, PRMT8.

PRMT8 appears to be a paralogue of PRMT1 in vertebrates and is highly homologous to PRMT1 with about 90% sequence identity (Hung and Li, 2004). Its expression is restricted to brain and neuron cells and is the only PRMT with tissue-restricted expression pattern. Brain-specific expression pattern was first shown by Northern blotting (Lee et al., 2005). Neuron-specific somatosensory distribution was further demonstrated by *in situ* hybridization (Taneda et al., 2007). The major difference between the two PRMTs is that PRMT8 contains an extra N-terminus of about 60-90 amino acids in different species. We showed that *prmt8* plays important roles non-overlapping with *prmt1* in embryonic and neural development depending on its specific N-terminus (Lin et al., 2013). Plasma membrane localization through N-myristoylation of PRMT8 at the second glycine residue has been shown by transfection (Lee et al., 2005). However, dominant nuclear localization of PRMT8 was observed in mouse central nervous neurons by a PRMT8-specific antibody (Kousaka et al., 2009), arguing against the dominant plasma membrane localization of PRMT8.

High sequence identity as well as conserved substrate preference of PRMT8 and PRMT1 indicate similar catalytic activity and implicate putative redundancy. For example, specific association and modification of Ewing sarcoma (EWS) by PRMT8 has been reported (Kim et al., 2008). However, EWS is also an excellent substrate of PRMT1. Nevertheless, PRMT8 is the only mammalian PRMT with tissue specificity. The neuron-specific expression of PRMT8 as well as its restricted distribution in vertebrates may suggest a novel function of PRMT8 in the vertebrate nervous system. We showed the early embryonic expression pattern of Prmt8 and observed *prmt8*-knockdown phenotypes in zebrafish. We performed rescue experiments with *prmt*8 or *prmt1* cRNAs to the *prmt*8 or *prmt1* AMO-injected embryos (morphants) and showed that the function of Prmt8 is not redundant with Prmt1 (Lin et al., 2013).

Mouse *prmt8* mutants grew and reproduced normally but displayed abnormal motor

behaviors. Moreover, *prmt8*$^{-/-}$ mice and TALEN-induced zebrafish *prmt8* mutants showed abnormal phenotypes, including the development of dendritic trees in Purkinje cells and altered cerebellar structure. It is shown that PRMT8 also has the phospholipase activity to hydrolyze phosphatidylcholine thus regulates Purkinje cell dendritic arborization and motor coordination (Kim et al., 2015). Another zebrafish *prmt8* knockdown and rescue experiment showed that full-length *prmt8* but not *prmt1* cRNA can rescue the defects of prmt8 morphants and vice versa. Interestingly, cRNA encoding Prmt1 fused with the N-terminus of Prmt8 can rescue the *prmt8* morphants. Moreover, N-terminus- deleted but not full-length *prmt8* cRNA can rescue the *prmt1* morphants. Therefore, *prmt8* plays important roles non-overlapping with *prmt1* depending on its specific N-terminus in fish (Lin et al., 2013).

Interestingly, PRMT8 is highly up-regulated in the induced regeneration competent cells (iRC) that has increased cellular lifespan without cancerous permanent self-renewal. These human dermal fibroblast cells derived by addition of fibroblast growth factor FGF2 and cultured in reduced oxygen concentration expressed a novel PRMT8 mRNA variant. This novel variant was required for proliferation of human dermal fibroblasts (hDFs) and grade IV glioblastomas (Hernandez et al., 2016).

Prmt8 is identified to be expressed in mouse embryonic stem cells (ESC) and in induced pluripotent stem cells, and modulated along differentiation to neural precursor cells. Prmt8 promoter activity is induced by the pluripotency transcription factors Oct4, Sox2 and Nanog. Prmt8 mRNA levels were reduced in ESC transfected with Sox2 shRNA vector. Thus besides its known function in nervous system, Prmt8 could play a role in pluripotent stem cells (Solari et al., 2016).

Because the predicted initiation methionine of human PRMT8 followed by a glycine residue is a myristoylation signal, PRMT8 was proposed to associate with plasma membrane through myristoylation of the N-terminal glycine after the elimination of the initiating methionine (Lee et al., 2005). Plasma membrane localization and myristoylation of transfected GFP-PRMT8 were shown in HeLa cells (Lee et al., 2005). The results may implicate a putative upstream role of PRMT8 in certain signaling pathways. However, dominant nuclear localization of PRMT8 was observed in mouse central nervous neurons by a PRMT8-specific antibody (Kousaka et al., 2009), arguing against the plasma membrane localization of PRMT8. Initiation from the third AUG and no myristoylation of PRMT8 were proposed (Kousaka et al., 2009). In this way, the possibility that PRMT8, like PRMT1 and most other PRMTs, participates in epigenetic histone modification increases.

PRMT8 can form homodimers as well as heterodimers with its highly conserved paralogue PRMT1 (Lee et al., 2005). PRMT1 and PRMT8 share high sequence identity and the major difference is that PRMT8 has an extra N-terminal sequence for about 76 amino acid

in human. Deletion of the N-terminal 60 amino acids increased the methyltransferase activity of PRMT8 *in vitro*, indicating that the region might be involved in regulating the enzyme activity (Sayegh et al., 2007). The proline-rich sequence in the N-terminus has been shown to bind to SH3 domain of PRMT2 and Fyn, pIcγ and p85, but the binding did not alter the methyltransferase activity. Beside, automethylation of two argininyl resides in the N-terminus has been identified and can reduce PRMT8 activity by increasing the Km of AdoMet (Dillon et al., 2013). Recent studies showed that two PRMT8 dimers interact mainly through β15 beta strand interactions to form a homotetramer. The open or closed conformations were observed for PRMT8 without SAH or SAH bound (Lee et al., 2015 Biochemistry). In another structural study, human PRMT8 has been shown to form an octameric structure critical for its plasma localization and methyltransferase activity (Toma-fukai, 2016, JMB). However, the N-terminal segment was not included in these studies.

Thus in this study we would like to answer two major issues of PRMT8: Why and how PRMT8 is different from its paralogue PRMT1 and what is the physiological function of PRMT8, with the focus on its putative participation in the pathogenesis of neural disorders or cancers. We proposed to pursue the issues of PRMT8 by conducting bioinformatic analyses of the gene structure, splicing pattern, the putative transcriptional regulatory elements of the *prmt8* gene, and tracing the changes of the segments in the N-terminus of PRMT8 through evolutionary. We proposed to analyze the methyltransferase activity of PRMT8 and specific PRMT1 isoforms, and also the interactome of human PRMT8 in the nervous system to picture the PRMT8-specific interaction network. We proposed to determine the expression pattern of different PRMT8/(PRMT1) isoforms under normal and stress conditions to examine their putative involvement in neural degenerative disease. We also proposed to study the expression and roles of PRMT8 in certain cancer.

In this study, we completed most of the experiments we proposed. We had published three papers based on this study. Several manuscripts are still under submission, modification and preparation. However, some studies did not have positive or confirmative results and thus were disclosed.

PART 1. Published paper

I. Analyses of gene structures and splicing variants of prmt1 and its vertebrate paralogue prmt8 suggest their molecular evolution. Wang, YC, Chuang, LC, Lee, YJ, Chang, CP and **Li, C** (2016) Chung Shan Medical Journal 27:39-50

Abstract:
Protein arginine methylation is a posttranslational modification involved in transcriptional regulation, RNA processing and many different cellular processes. There are nine different

protein arginine methyltransferases (PRMTs) genes in mammals. PRMT1 is the most conserved and widely distributed PRMT in eukaryotes. PRMT8 is a vertebrate-specific paralogue of PRMT1 and the major difference between the two PRMTs is that PRMT8 contains an extra N-terminus of about 60-90 amino acids in different species. We collected the *prmt1* as well as *prmt8* genomic and cDNA sequences from typical vertebrate and animal species and constructed the gene structure diagram. A basic 10-exon configuration with exactly the same intron/exon junctions was observed for vertebrate *prmt1* and *prmt8* as well as some chordate *prmt1*. Multiple sequence alignments of the amino acid sequences of PRMT1 and PRMT8 clearly illustrated the major differences in N-terminal variable region through evolution. We also collected RNA variants of the two genes. Most of the *prmt1* variants in human and mice encode different N-termini due to alternative splicing. However, similar *prmt1* variants with missing sequences close to the C-terminus in human (variant 4) and mouse (variant 3) have not been reported in previous publications. A *prmt8* variant 2 in primates with an alternative exon 1 was identified in the data base and similar variants can be predicted in primates with conserved protein sequences and genomic localization. We also constructed phylogenetic tree of the *prmt1* and *prmt8* mRNAs and showed clear vertebrate duplication pattern. Our analyses of the genomic structures and the putative transcriptional variants of *prmt1* and *prmt8* will help to trace the evolution origin of *prmt8* and provide critical information for future experimental designs of these genes.

II. PRMT1 expression is elevated in head and neck cancer and inhibition of protein arginine methylation by adenosine dialdehyde or PRMT1 knockdown affect proliferation and migration of oral cancer cells. Chuang, CY, Chang, CP, Lee, YJ, Lin, WL, Chang, WW, Wu, JS, Cheng, YW, Lee, H and **Li, C** (2017) **Oncology Reports**, 38:1115-1123

Abstract:
Protein arginine methylation is a post-translational modification that has been implicated in signal transduction, gene transcription, DNA repair and RNA processing. Overexpression or deregulation of protein arginine methyltransferases (PRMTs) have been reported to be associated with various cancers but have not been studied in head and neck cancer (HNC). We investigated the involvement of the modification in HNC using oral cancer cell lines (SAS, OECM-1 and HSC-3) and an immortalized normal oral cells (S-G). The expression levels of the predominant PRMT1 were generally consistent with the levels of asymmetric dimethylarginine (ADMA), highest in SAS and OECM1, then S-G and low in HSC-3. Upon the treatment with an indirect methyltransferase inhibitor adenosine dialdehyde (AdOx), the ADMA levels in SAS and OECM1, but not that in S-G and HSC-3, decreased significantly. SAS and OECM with high ADMA levels grew faster than HSC-3 and S-G. The growth rate of the fast growing SAS and OECM, but not that of the other two cell lines, decreased significantly upon AdOx treatment. The migration activity of SAS and HSC-3, two cell lines

with migration ability also decreased after the AdOx treatment. Immunohistochemical analyses of specimens from typical HNC patients showed strong PRMT1 expression in the tumor cells compared with neighboring normal cells. Knockdown of PRMT1 in SAS cells decreased the levels of PRMT1 and ADMA-containing proteins significantly. These cells showed decreased growth rate, reduced migration activity but increased expression of the epithelial marker E-cadherin. The present study thus provides fundamental background for evaluation of the PRMT1 gene as the therapeutic targets of HNC.

III. Identification, chromosomal arrangements and expression analyses of the evolutionarily conserved *prmt1* gene in chicken in comparison with its vertebrate paralogue *prmt8*. Wang, YC, Wang CW, LC, Lee, Lin WC, Tsai YJ, Chang, CP, Lee YJ, Lin MJ and **Li, C** (2017) **PLOS One**. 12(9):e0185042 https://doi.org/10.1371/journal.pone.0185042

Abstract:
Nine protein arginine methyltransferases (PRMTs) are conserved in mammals and fish. Among these, PRMT1 is the major type I PRMT for asymmetric dimethylarginine (ADMA) formation and is the most conserved and widely distributed one. Two chicken *prmt1* splicing variants were assembled and confirmed by RT-PCR experiments. However, only two scaffolds containing single separate *prmt1* exon with high GC contents are present in the current chicken genome assembly. Besides, *prmt1* exons are scattered in separate small scaffolds in most avian species. Complete *prmt1* gene has only been predicted from two falcon species with few neighboring genes. Crocodilians are considered close to the common ancestor shared by crocodilians and birds. The gene arrangements around *prmt1* in American alligator are different from that in birds but are largely conserved in human. Orthologues of genes in a large segment of human chromosomal 19 around *PRMT1* are missing or not assigned to the current chicken chromosomes. In comparison, *prmt8*, the *prmt1* paralogue, is on chicken chromosome 1 with the gene arrangements downstream of *prmt8* highly conserved in birds, crocodilians, and human. However, the ones upstream vary greatly in birds. Biochemically, we found that though *prmt1* transcripts were detected, limited or none PRMT1 protein was present in chicken tissues. Moreover, a much higher level of PRMT8 protein was detected in chicken brain than in mouse brain. While PRMT8 is brain specific in other vertebrate species studied, low level of PRMT8 was present in chicken but not mouse liver and muscle. We also showed that the ADMA level in chicken was similar to that in mouse. This study provides the critical information of chicken PRMT1 and PRMT8 for future analyses of the function of protein arginine methyltransferases in birds.

PART2. Manuscript submitted or in preparation

I. Down-regulation of PRMT1 in neuroblastoma SK-N-SH cells leads to senescence and

reveals a PRMT1-p53-p21/PAI-1 axis. Lee, YJ, Chang, WW, Chang, CP, Liu, TY, Chuang, CY, Qian, K, Zheng, YG and **Li, C.** (2018) FEBS J submitted.

Abstract

Protein arginine methyltransferase 1 (PRMT1) is the predominant enzyme catalyzing the formation of asymmetric dimethylarginines in proteins. PRMT1 has been implicated in cancer development, metastasis, and prognosis. In this study, we investigated the roles of PRMT1 in a non-MYCN overexpressed neuroblastoma SK-N-SH cell model. Compared with the control lenti-vector infected cells, stable *PRMT1*-knockdown (*PRMT1*-KD) cells were larger with a prolonged doubling-time with cell cycle arrest at G2/M. The *PRMT1*-KD SK-N-SH cells showed senescent phenotypes and increased expression of p53, p21 and PAI-1. We observed increased gamma-H2AX signals indicating elevated DNA damage in the *PRMT*1-KD cells and the cells were slightly more sensitive to cisplatin. The ROS levels increased marginally and the cells became less sensitive to hydrogen peroxide after PRMT1 KD. Induced PAI-1 was related to the increased migration activity of the *PRMT1*-KD SK-N-SH cells. Blocking p53 transactivation activity or PRMT1 methyltransferase activity could partially release the induction of p21 and PAI-1. Thus in the SK-N-SH cells, PRMT1 expression level or activity is critical for cell proliferation and migration activity through a PRMT1-p53-p21/PAI-1 axis. These results suggest the multifaceted complexity of PRMT1 as a biological regulator of neuroblastoma.

II. PRMT1 regulates neurite outgrowth and microtubules in SK-N-SH neuroblastoma cells
III. The N-terminus of PRMT8 interfere with PRMT8 dimer formation and may favor PRMT1/PRMT8 dimer formation in vivo
IV. N-terminus of PRMT8 is critical for zebrafish prmt8 and interferes the interaction with mammalian binding partners

PART 3. Manuscript in preparation but with published similar results

The study about a novel C-terminal deletion isoform of human PRMT1:

A specific PRMT1 mRNA variant 4 (GI:359338973, protein GI:333360913) without exon 6 and 7 present in the NCBI database was reported in our previous study (Chuang et al., 2016). Although blasting against EST database identified only limited supports of the variant in neuroblastoma and prostate carcinoma (BX403078, BX352789 and BM043971), in mouse a similar variant with a splicing acceptor in exon 5 and a donor in exon 8 was identified (gi:357197160). We used PRMT1v4 as NCBI to indicate the PRMT1 isoform with middle deletion. The N-terminus of this isoform is the same as PRMT1v1. Exon 6 and 7 encode

residues 168-235 in PRMT1v1 including the whole dimerization arm (residues 188-222) with the end of the AdoMet binding domain and the beginning of the beta-barrel domain. We showed no dimer formation of PRMT1 v4 with by yeast two hybrid analyses. Furthermore, there were no methyltransferase activity or interfering of the methyltransferase activity of PRMT1v4. While we are preparing the manuscript, a paper "A novel splicing isoform of protein arginine methyltransferase 1 (PRMT1) that lacks the dimerization arm and correlates with cellular malignancy" based on similar results has been published (Patounas et al., 2017).

PART 4. Studies without positive confirmative results

I. Yeast two-hybrid analyses for PRMT1 and PRMT8 interacting proteins in human neural system

We performed yeast two-hybrid analyses using full-length or N-terminal PRMT8 and PRMT1 as a bait to fish a human brain cDNA libraries for yeast two-hybrid analyses. The Matchmaker Gold Yeast Two-Hybrid System uses the GAL-4 system. Full-length or N-terminal PRMT8 were cloned in frame with the *GAL4* DNA-BD of the bait plasmid pGBKT7 and libraries of prey proteins are expressed as fusions to the Gal4 AD. We obtained about 10-80 different positive clones from three screens for the N-terminus of human PRMT8. However, no clones can be obtained for the PRMT8 full-length screen. After PCR screening, Y2H auto-activation analysis, we sequenced the targets. The putative targets are summarized in Fig. 3. The targets were cloned into a myc-tagged vector to conduct co-immunoprecipitation with FLAG-tagged full-length or N-terminal PRMT8 for confirmation. The Y2H system was also used for evaluating the binding strength of PRMT1-PRMT8 interaction and for the cross-species examination of the unique PRMT8 N-terminal sequences in fish and mammals.

Part 6. Master theses based on support of this work

1. Chien-Ping Chang, Investigation of protein arginine methylation in oral cancer cell lines. Master thesis, Department of Biomedical Sciences, Chung Shan medical University, July, 2015.
2. Cheng-Kang Tsai, Specific interacting proteins of the N-terminus of protein arginine methyltransferase PRMT8. Master thesis, Department of Biomedical Sciences, Chung Shan medical University, July, 2016.
3. Chien-Wen Wang, Analyses of the deletion of the most evolutionarily conserved protein arginine methyltransferase PRMT1 in avian. Master thesis, Department of Biomedical Sciences, Chung Shan medical University, July, 2016.

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Patounas, O., Papacharalampous, I., Eckerich, C., Markopoulos, G.S., Kolettas, E., and Fackelmayer, F.O. (2017). A novel splicing isoform of Protein Arginine Methyltransferase 1 (PRMT1) that lacks the dimerization arm and correlates with cellular malignancy. J Cell Biochem.

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non-mammalian animal systems. FEBS Journal *279*, 932-945.

103年度專題研究計畫成果彙整表

計畫主持人：李娟			**計畫編號：**103-2320-B-040-022-MY3		
計畫名稱：探討蛋白質精胺酸甲基轉移酶8之生理和病理角色					
成果項目			量化	單位	質化 （說明：各成果項目請附佐證資料或細項說明，如期刊名稱、年份、卷期、起訖頁數、證號...等）
國內	學術性論文	期刊論文	1	篇	I.Analyses of gene structures and splicing variants of prmt1 and its vertebrate paralogue prmt8 suggest their molecular evolution. Wang, YC, Chuang, LC, Lee, YJ, Chang, CP and Li, C (2016) Chung Shan Medical Journal 27:39-50
		研討會論文	5		Tsai, Y.-R. , and Li, C. (2014) The expression and critical roles of protein arginine methyltransferase prmt6 in zebrafish early embryonic development. Poster presentation in 2014 Taiwan Zebrafish Symposium. December 13, NHRI, Zhunan/Miaoli, Taiwan. Chien-Ping Chang, Chun-Yi Chuang , Chuan Li (2015) Investigation protein arginine methylation in oral cancer cell lines. Poster presentation in 30th Joint Annual Conference of Biomedical Sciences. March 21-22, 2015, Taipei, Taiwan Chien-Wen Wang, Prof. Chuan Li, Asst. Prof. Yi-Chun Wang (2016) Analyses of the deletion of evolutionarily conserved protein arginine methyltransferase genes in avian. Poster presentation in 31th Joint Annual Conference of Biomedical Sciences. March 26-27, 2016, Taipei, Taiwan Cheng-Kang Tsai, Yu-Jen Lee, Li, C.(2016) Specific interacting proteins of the N-terminus of protein arginine methyltransferase PRMT8. Poster presentation in 31th Joint Annual Conference of Biomedical Sciences. March 26-27, 2016, Taipei, Taiwan Yu-Jen Lee, Cheng-Kang Tsai, Li, C.(2016) Knockdown of PRMT1 in neuroblastoma SK-N-SH cells leads to senescent phenotypes and

							suppresses neurite outgrowth. March 26-27, 2016, Taipei, Taiwan
		專書			0	本	
		專書論文			0	章	
		技術報告			0	篇	
		其他			0	篇	
	智慧財產權及成果	專利權	發明專利	申請中	0	件	
				已獲得	0		
			新型/設計專利		0		
		商標權			0		
		營業秘密			0		
		積體電路電路布局權			0		
		著作權			0		
		品種權			0		
		其他			0		
	技術移轉	件數			0	件	
		收入			0	千元	
國外	學術性論文	期刊論文			2	篇	PRMT1 expression is elevated in head and neck cancer and inhibition of protein arginine methylation by adenosine dialdehyde or PRMT1 knockdown affect proliferation and migration of oral cancer cells. Chuang, CY, Chang, CP, Lee, YJ, Lin, WL, Chang, WW, Wu, JS, Cheng, YW, Lee, H and Li, C (2017) Oncology Reports, 38:1115-1123 Identification, chromosomal arrangements and expression analyses of the evolutionarily conserved prmt1 gene in chicken in comparison with its vertebrate paralogue prmt8. Wang, YC, Wang CW, LC, Lee, Lin WC, Tsai YJ, Chang, CP, Lee YJ, Lin MJ and Li, C (2017) PLOS One. 12(9):e0185042
		研討會論文			0		
		專書			0	本	
		專書論文			0	章	
		技術報告			0	篇	
		其他			0	篇	
	智慧財產權及成果	專利權	發明專利	申請中	0	件	
				已獲得	0		

			新型/設計專利	0		
		商標權		0		
		營業秘密		0		
		積體電路電路布局權		0		
		著作權		0		
		品種權		0		
		其他		0		
	技術移轉	件數		0	件	
		收入		0	千元	
參與計畫人力	本國籍	大專生		1	人次	高銓佑
		碩士生		2		蔡政剛 王千文
		博士生		0		
		博士後研究員		1		李侑蓁
		專任助理		1		蔡沄容
	非本國籍	大專生		0		
		碩士生		0		
		博士生		0		
		博士後研究員		0		
		專任助理		0		
其他成果 （無法以量化表達之成果如辦理學術活動、獲得獎項、重要國際合作、研究成果國際影響力及其他協助產業技術發展之具體效益事項等，請以文字敘述填列。）						

科技部補助專題研究計畫成果自評表

請就研究內容與原計畫相符程度、達成預期目標情況、研究成果之學術或應用價值（簡要敘述成果所代表之意義、價值、影響或進一步發展之可能性）、是否適合在學術期刊發表或申請專利、主要發現（簡要敘述成果是否具有政策應用參考價值及具影響公共利益之重大發現）或其他有關價值等，作一綜合評估。

1. 請就研究內容與原計畫相符程度、達成預期目標情況作一綜合評估
   ■達成目標
   □未達成目標（請說明，以100字為限）
   　□實驗失敗
   　□因故實驗中斷
   　□其他原因
   說明：

2. 研究成果在學術期刊發表或申請專利等情形（請於其他欄註明專利及技轉之證號、合約、申請及洽談等詳細資訊）
   論文：■已發表　□未發表之文稿　□撰寫中　□無
   專利：□已獲得　□申請中　■無
   技轉：□已技轉　□洽談中　■無
   其他：（以200字為限）
   Oncology Reports, 38:1115-1123
   PLOS One. 12(9):e0185042

3. 請依學術成就、技術創新、社會影響等方面，評估研究成果之學術或應用價值（簡要敘述成果所代表之意義、價值、影響或進一步發展之可能性，以500字為限）
   We have published two papers in SCI journals and one in non-SCI peer-reviewed journal. We still have one manuscript in submission and 2-3 manuscript in preparation. This study provides the critical information of PRMT1 and PRMT8 for future analyses.

4. 主要發現
   本研究具有政策應用參考價值：■否　□是，建議提供機關
   （勾選「是」者，請列舉建議可提供施政參考之業務主管機關）
   本研究具影響公共利益之重大發現：□否　□是
   說明：（以150字為限）
   NA