<붙임 4>

기관고유연구사업 최종보고서

연구분야(코드)		과제번호	1210450	지원 프로그램	*ex)창의 (일반연구)과제*
과제성격(기초,응용,개발)		실용화 대상여부	실용화/ 비실용화	공개가능여부 (공개,비공개)	
연구과제명	PPARɣ 활성화에 의한 위암 억제기전에서 galectin-9과 CCL4의역할 PPARɣ activated-galectin-9 induction and CCL4 repression suppresses gastric cancer progression				
과제책임자	소 속	위암연구과	직 위	선임연구원	
	성 명	조수정	전 공	내과	

세부과제	구분	세부과제명	세부과제책임자		
			성명	소속(직위)	전 공
	1				
	2				
	3				

총 연구기간	2012년 3월~ 2013년 12월(총 2 년)	참여연구원수 (단위: 명, MY)	

연구기간 및 연구비 (단위:천원)	구분	연 구 기 간	계	국 립 암센터	기 업 부 담 금		
					소계	현금	현물
	계	2012년 3월~2013년 12월	100.000	100,000			
	제1차	2012년2월~2012년12월	50,000	50,000			
	제2차	2013년1월~2013년12월	50,000	50,000			
	제3차	~					

참 여 기 업	명 칭		전화		FAX	

기관고유연구사업관리규칙에 따라 본 연구개발사업을 성실히 수행하였으며 아래와 같이 최종보고서를 제출합니다.

2013년 10월 31 일

과제책임자 조 수 정 (서명)

국 립 암 센 터 원 장 귀 하

(첨부서류)

작 성 요 령

○ 반드시 편집순서에 따라 작성하여야 함

○ 전년도 연차실적을 포함하여 전체 사업기간에 대한 연구결과와 성과를 중심으로 기술함

○ 필요한 경우 소제목을 설정하여 체계적인 형식을 갖추도록 함

○ 요약문은 연구목표, 연구내용 및 방법, 연구성과 등을 중심으로 작성함

○ 요약문중 중심단어(key words)는 5개 이내로 반드시 기재해야 함

○ 번호나 기호를 사용한 보고서 형태로 작성하고 표나 그림을 이용할 수 있음. 단, 동 보고서와 함께 제출하는 전산파일에도 같은 표와 그림이 첨부되어 있어야 함

목 차

※ 여러개의 세부과제로 과제가 구성된 경우 위 목차와 동일하게 세부과제별로 작성함

(I. 총괄과제, II. 제1세부과제, III. 제2세부과제.....)

< 요 약 문 >

<table>
<tr><td>연구목표
(200자 이내)</td><td colspan="4"><최종목표>
- PPARG활성화에 의한 galectin-9의 유도 및 CCL4의 억제에 의해 위암의 침윤 및 전이가 억제됨을 증명하며, 위암 예후인자 및 맞춤형 치료의 표적을 개발한다.

<당해연도목표>
-1차년도에 이어 PPARG활성화에 의한 SPRY-4의 유도가 위암 침윤 전이 억제함을 in vitro 실험을 통해 증명한다.
-Galectin-9, SPRY-4 과발현시 위암의 침윤 및 전이가 억제되는 것을 in vivo model에서 증명 동물모델(nude mice, xebrfafish)에서 PPARG, galectin-9, SPRY4 발현에 따른 전이 진행여부 확인한다.
-PPARG-related chemoresistance in AGC 연구 예정
- 통계분석, 논문작성, 위암 예후인자 screening 방법</td></tr>
<tr><td>연구내용 및 방법
(500자 이내)</td><td colspan="4">-PPARG 과발현 시스템 확립(lenti-virus)
-위암세포주에 PPARG 과발현시킨후 RT-PCR, western blot으로 galectin-9, SPRY4, CCL4 발현확인
-Galectin-9, SPRY4, CCL4 과발현, 억제시 invasion, migration assay 시행
-Galectin-9, SPRY4, CCL4 과발현, 억제시 EMT 억제 여부 확인(EMT 관련 인자들(N-cadherin, E-cadherin, fibronectin, snail)의 mRNA발현을 RT-PCR로 확인)
-2006-2007년 위암수술한 환자의 조직으로 TMA제작
-IRB 제출 및 승인</td></tr>
<tr><td>연구개발에 따른
기대성과</td><td colspan="4"><정량적 성과[1)]>
<table><tr><th>구분</th><th>달성치/목표치[1)]</th><th>달성도(%)</th></tr><tr><td>SCI 논문 편수</td><td>1</td><td>100</td></tr><tr><td>IF 합</td><td>5</td><td>100</td></tr><tr><td>기타 성과</td><td>학술대회에서 수차례 수상함</td><td>100</td></tr></table>1) 총연구기간 내 목표연구성과로 기 제출한 값
<정성적 성과>
-주요연구성과를 개조식으로 간단히 작성(5줄 이내)
1) 논문 작성 완료 Peroxisome Proliferator-Activated Receptor ɣ Inhibits Cell Invasion, Migration and Epithelial-Mesenchymal Transition through Up-regulating Galectin-9, and Predicts the Prognosis in Intestinal-Type of Gastric Cancer --> Int J Cancer (under revision)
2) 논문 작성 완료 Long-term metformin use reduces gastric cancer risk in type 2 diabetic patients without insulin treatment: a nationwide cohort study--> Alimentary Pharmacology and Therapeutics, under review (grant number; 1210450-2)
3) 논문 작성중 Tumoral expression of galectin-9 is associated with good prognosis in patients with intestinal-type gastric cancer -->600명의 TMA로 결과 분석 완료됨. 논문 작성완료, 영문 교정중</td></tr>
<tr><td rowspan="6">색인어</td><td rowspan="3">국문</td><td>PPARɣ</td><td>galectin-9</td><td>CCL-4</td></tr>
<tr><td>위암</td><td></td><td></td></tr>
<tr><td></td><td></td><td></td></tr>
<tr><td rowspan="3">영문</td><td>PPARɣ</td><td>galectin-9</td><td>CCL-4</td></tr>
<tr><td>gastric cancer</td><td></td><td></td></tr>
<tr><td></td><td></td><td></td></tr>
</table>

※ 요약문의 총분량은 2page 이내로 제한함

Project Summary

Title of Project	PPARγ activated-galectin-9 induction and CCL4 repression suppresses gastric cancer progression
Key Words	PPARγ, galectin-9, CCL4, gastric cancer
Project Leader	Soo-Jeong Cho
Associated Company	

Background: The importance of PPARγ (peroxisome proliferator-activated receptor γ) in gastric cancer (GC) is unclear. We investigated the role of PPARγ in GC cells and an animal model, and its prognostic significance of PPARγ in GC patients.

Methods: We controlled PPARγ and galectin-9 expression by using siRNAs and lenti-viral constructs. Interaction between PPARγ and galectin-9 was evaluated using luciferase and ChIP assays. PPARγ expression of GCs was determined by immunohistochemical staining of tissue microarrays. COX proportional hazards regression was used for survival analysis.

Results: Overexpression of PPARγ was accompanied by increased galectin-9. Enhanced PPARγ or galectin-9 expression increased E-cadherin expression, decreased expression of N-cadherin, fibronectin, snail, twist and slug; and reduced cell invasion and migration. PPARγ bound to the galectin-9 promoter region. Galectin-9 activity increased in PPARγ overexpressing cells but decreased in PPARγ siRNA-treated cells. In a zebrafish xenograft model, the number of migrated cancer cells and number of fish with AGS cells in the tail vein were reduced in PPARγ-overexpressing GC cells. PPARγ was expressed in 462 of the 688 patients (69.2%) with GC. In 306 patients with intestinal-type GC, those with PPARγ-positive tumors had lower overall and cancer-specific mortalities than those with PPARγ-negative tumors. PPARγ expression was an independent prognostic factor for overall and GC-specific mortality in patients with intestinal-type GC (adjusted HR, 0.42; 95% CI, 0.22-0.81).

Conclusions: PPARγ inhibits cell invasion, migration, and epithelial-mesenchymal transition through up-regulation of galectin-9 *invitro*and*invivo*.Tumor PPARγ expression is associated with higher survival for intestinal-type GC patients.

1. 연구의 최종목표

○ 당초 연구계획을 참고하기 위한 자료임. 선정당시 「과제계획서」와 전년도 제출하였던 「연차실적·계획서」상의 내용과 동일하게 작성해야 함. 연구사업의 목적, 범위 등에 대해 기술

<최종목표>

- PPARG활성화에 의한 galectin-9의 유도 및 CCL4의 억제에 의해 위암의 침윤 및 전이가 억제됨을 증명하며, 위암 예후인자 및 맞춤형 치료의 표적을 개발한다.

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2. 연구의 내용 및 결과

○ 연구의 이론적, 실험적 연구 방법, 연구 내용 및 결과를 객관적으로 기술

<1차년도>

- 위암세포주에서 PPARG 활성에 의해 galectin-9이 유도되고 CCL4가 억제되는 것을 증명; 위암세포주에 PPARG-expressing lenti-virus로 transfection시킨 후 RT-PCR, immunoblotting으로 galectin-9, CCL4 발현을 확인

- Galectin-9 과발현, CCL4 발현 억제시 위암의 침윤 및 전이가 억제되는 것을 in vitro에서 증명; invasion, migration study, EMT관련 gene/protein study (E-cadherin, N-cadherin, vimentin, fibronectin, snail-1), MMPs expression assay

- 위암조직에서 galectin-9, CCL4, CCR5 발현을 환자의 임상 data로 예후와의 관련성을 증명; 위암수술한 환자의 조직으로 TMA제작, 수술 받은 환자들의 슬라이드를 제작, 면역염색(Galectin-9, CCL4, CCR5)

<2차년도>

-PPARɣ에의한 Galectin-9 과발현, 발현 억제시 위암의 침윤 및 전이가 억제되는 기전 증명

;실험완료 및 논문 투고 완료되었으며, revision중으로 현재 추가실험 중임.

-위암세포주에서 PPARG 활성에 의해 SPRY4 발현 감소를 증명; PPARG 과발현벡터 확립 및 SPRY4발현 감소 확인

-SPRY4 과발현시 위암의 침윤 및 전이가 억제되는 것을 in vitro에서 증명;SPRY4 과발현벡터 확립, in vitro 진행중

-SPRY4 발현 억제시 위암의 침윤 및 전이가 증가되는 것을 in vitro에서 증명;SPRY4 과발현벡터 확립, in vitro 진행중

-위암조직에서 SPRY4 발현을 환자의 임상 data로 예후와의 관련성을 증명;IRB승인받은 600명의 환자에 대한 tissue microarray 제작완료. Ab conditioning중임.

- 위암세포주에 PPARG-expressing lenti-virus로 transfection시킨 후 RT-PCR, immunoblotting

Figure1. Rosiglitazone으로 cell proliferation 확인

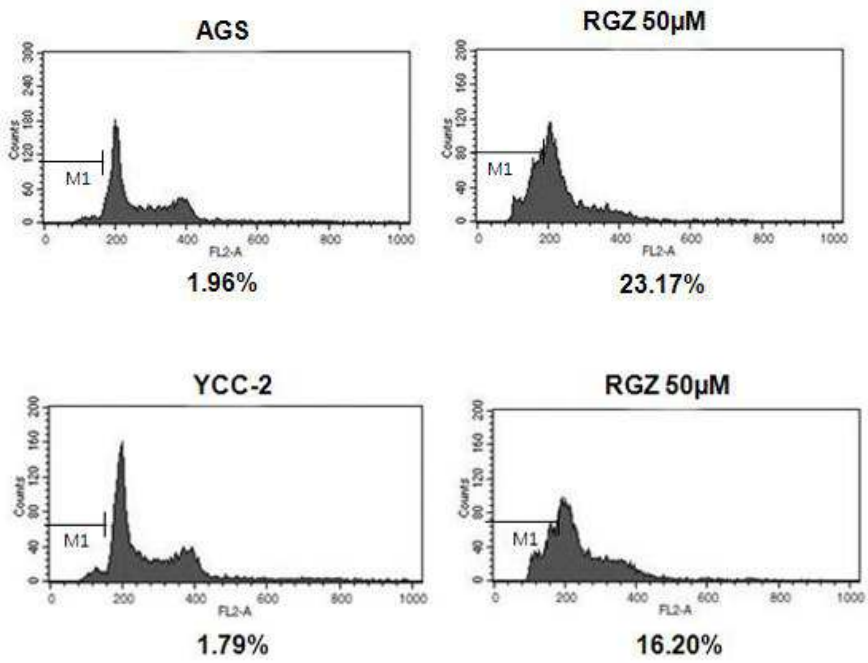

Figure2. AGS, YCC-2 cell에서 rosiglitazone으로 cell cycle 확인.

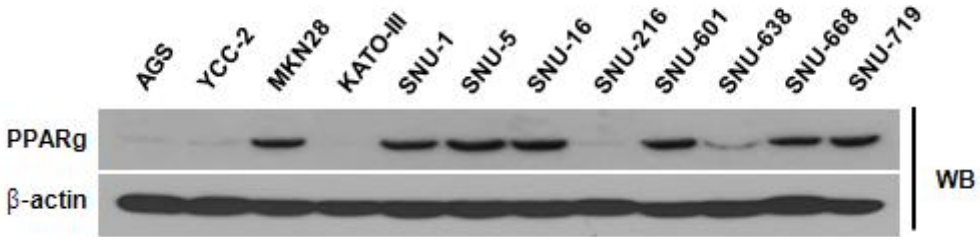

Figure3. PPARg 발현을 western blot으로 확인

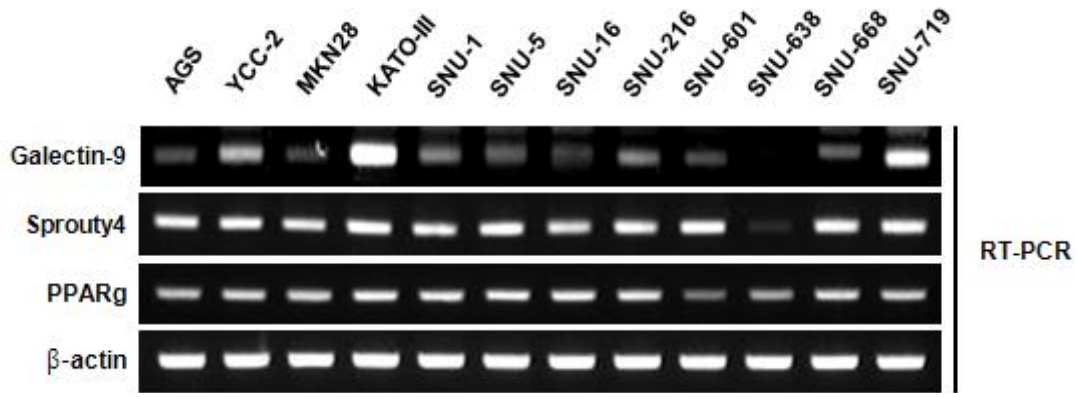

Figure4. PPARg, galectin 9 발현을 RT-PCR로 확인

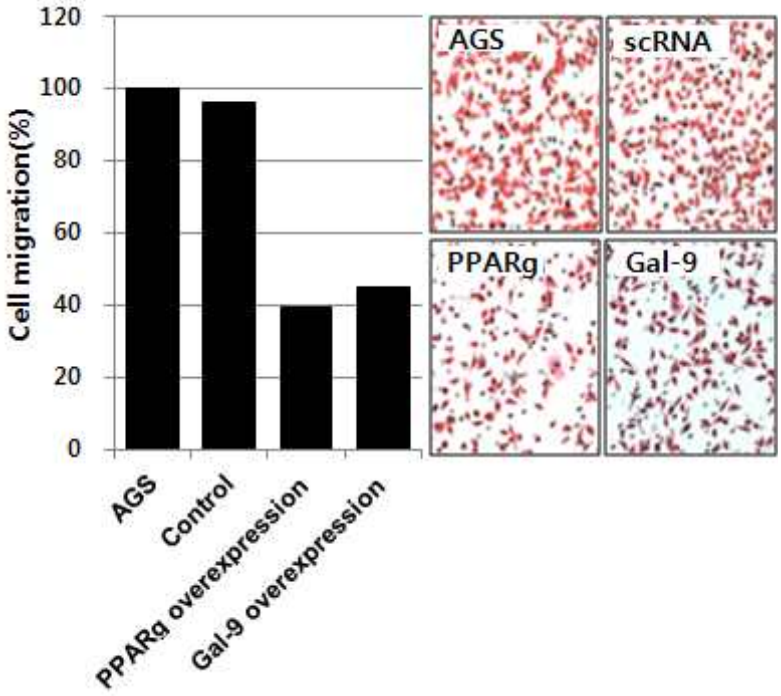

Figure5. PPARg, galectin 9 lenti-virus로 transfection시킨 후 migation

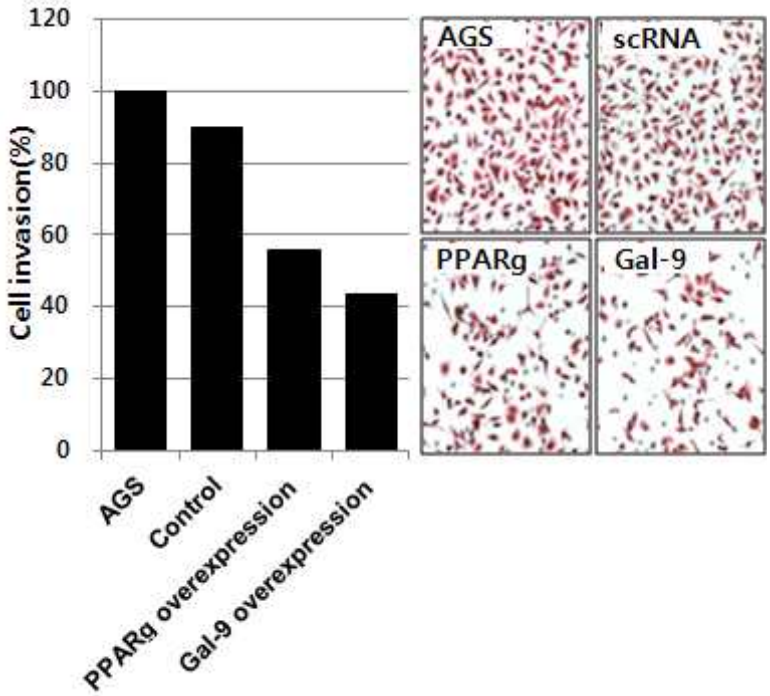

Figure6. PPARg, galectin 9 lenti-virus로 transfection시킨 후 invasion

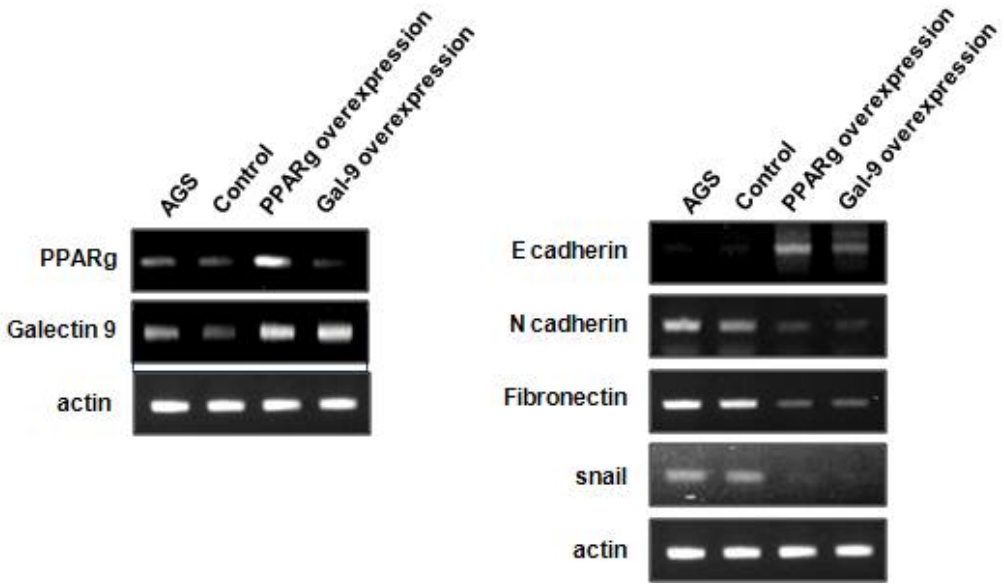

Figure7. PPARg, galectin 9 lenti-virus로 transfection시킨 후 EMT 관련 gene assay

- Invasion, migration study, EMT관련 gene/protein study (E-cadherin, N-cadherin, vimentin, fibronectin, snail-1) expression assay를 통해 확인하였음

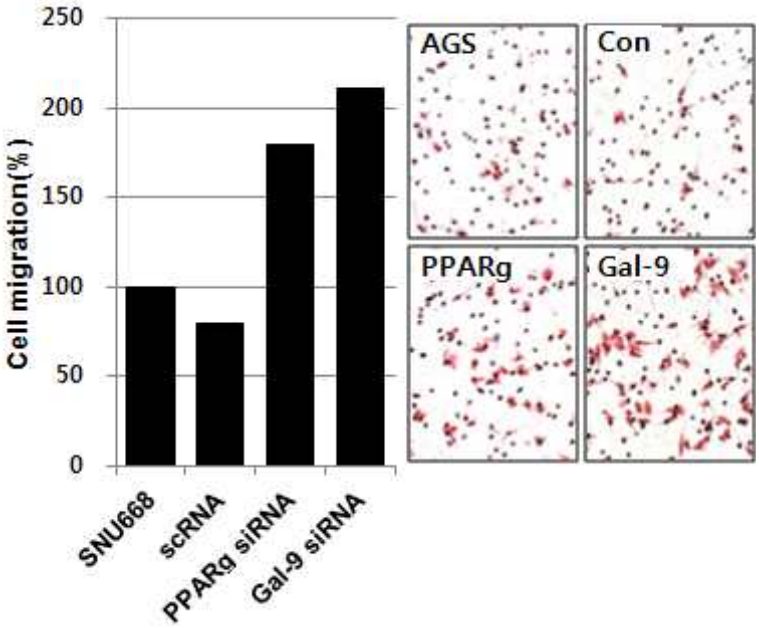

Figure8. PPARg siRNA, Gal-9 siRNA에 대한 migration

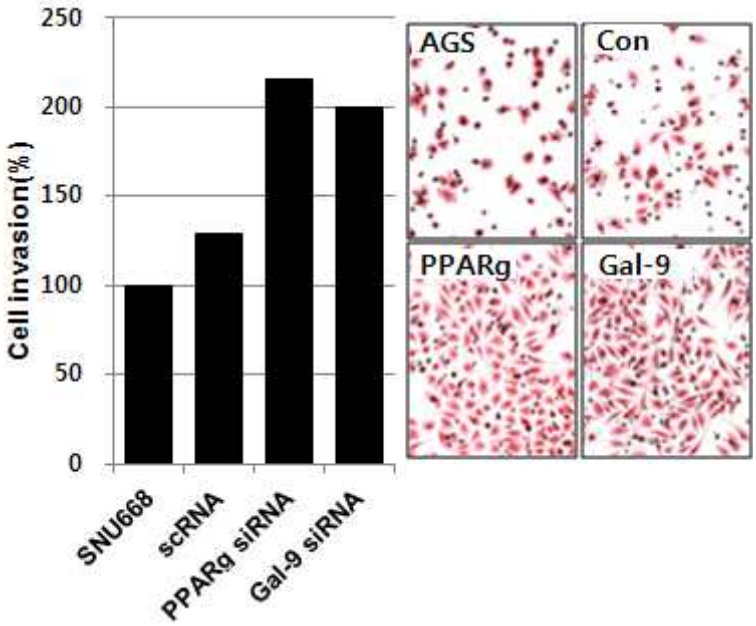

Figure9. PPARg siRNA, Gal-9 siRNA에 대한 invasion

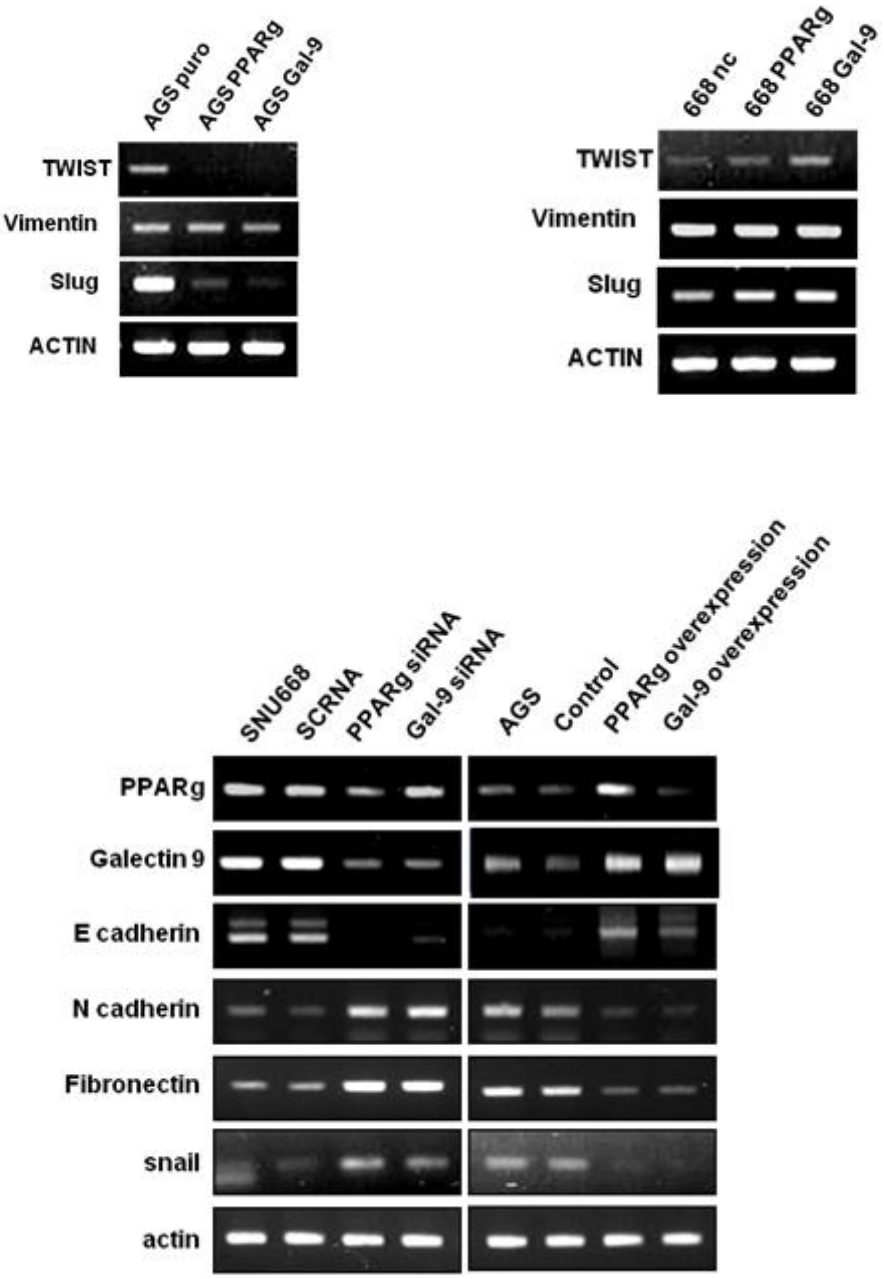

Figure10. PPARg siRNA, Gal-9 siRNA에 대한 EMT gene study

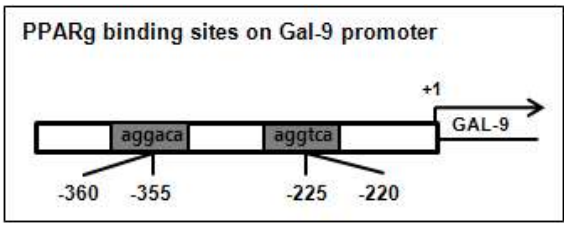

Figure11. Gal-9 promoter gene assay

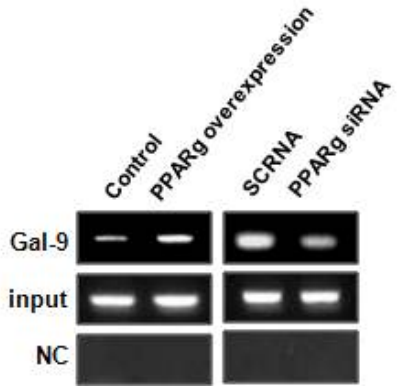

Figure12. ChiP assay로 PPARg-galectin9의 direct binding 증명

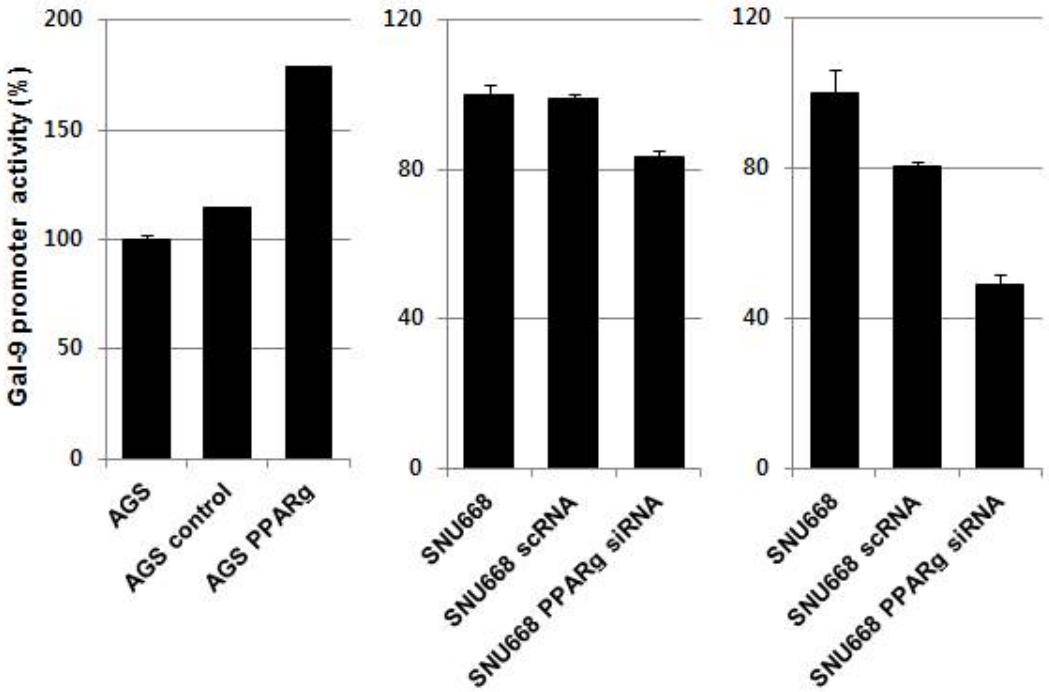

Figure13. Luciferase assay를 통한 Gal-9 promoter activity 측정

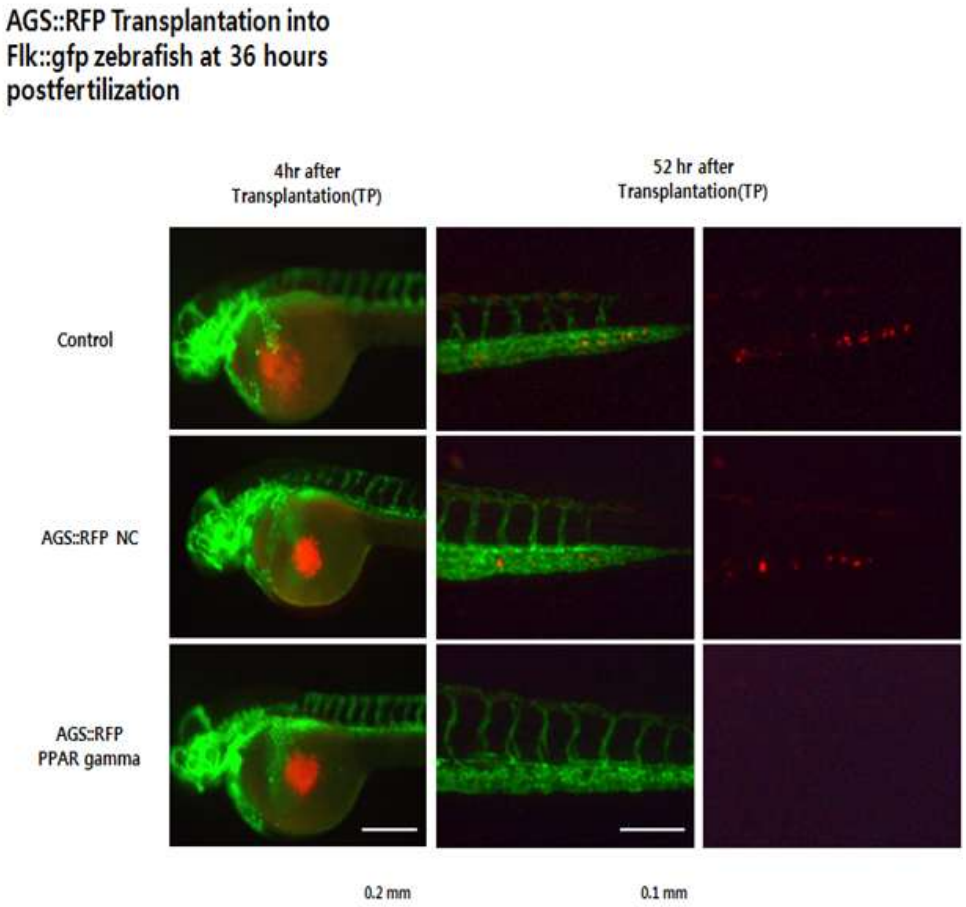

Figure14. Zebrafish xenograft model

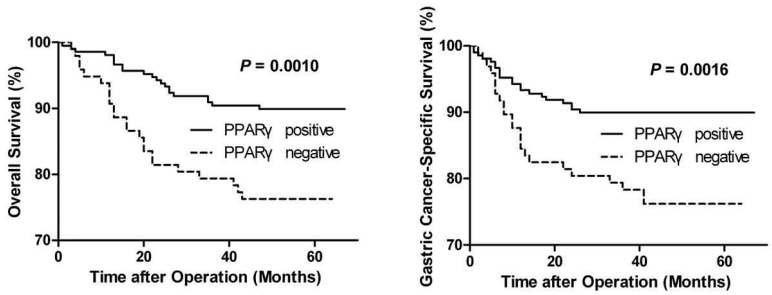

Figure15. Survival analyses according to PPARg positivity

3. 연구결과 고찰 및 결론

○ 국내·외 관련분야의 기술개발 현황과 연구결과가 국내·외 기술개발 분야에서 차지하는 위치 등을 기술

○ 연구결과 해석 및 다른 결과와의 비교분석 등에 대해 고찰하고 결론을 서술함

Overexpression of PPARγ was accompanied by increased galectin-9. Enhanced PPARγ or galectin-9 expression increased E-cadherin expression, decreased expression of N-cadherin, fibronectin, snail, twist and slug; and reduced cell invasion and migration. PPARγ bound to the galectin-9 promoter region. Galectin-9 activity increased in PPARγ overexpressing cells but decreased in PPARγ siRNA-treated cells. In a zebrafish xenograft model, the number of migrated cancer cells and number of fish with AGS cells in the tail vein were reduced in PPARγ-overexpressing GC cells. PPARγ was expressed in 462 of the 688 patients (69.2%) with GC. In 306 patients with intestinal-type GC, those with PPARγ-positive tumors had lower overall and cancer-specific mortalities than those with PPARγ-negative tumors. PPARγ expression was an independent prognostic factor for overall and GC-specific mortality in patients with intestinal-type GC (adjusted HR, 0.42; 95% CI, 0.22-0.81).

In this study, we evaluated the anti-metastatic ability of PPARγ *in vitro* and *in vivo* and examined the relationship between PPARγ expression and patient survival in a large number of patients with GC. We demonstrated that enhanced PPARγ activity reduced GC cell migration, invasion, and EMT factors of GC cells throughup-regulation of galectin-9, a downstream product in the PPARγ pathway. We also found that PPARγ expression was associated with less advanced disease overall and improved survival in patients with intestinal-type GC, thereby suggesting that PPARγ is a marker of less aggressive GC.

The role of PPARγ in GC has not been firmly established. Experimental studies have suggested that PPARγ functions in cell cycle regulation, suppression of cyclooxygenase-2, inhibition of the antiapoptotic bcl-2/bcl-xl family, and activation of p53 in GC cells (17, 29), supporting its antineoplastic effect. In GC cell lines, PPARγ ligands inhibit cell growth by G1 cell cycle arrest, induce apoptosis in a dose-dependent manner, and inhibit GC cell invasion, migration, and matrix metallopeptidase-2 secretion (17, 27). PPARγ ligands also impede neovascularization, thus suppressing cancer growth (27). Likewise, endogenous PPARγ ligands, such as 15-deoxy-$\triangle^{2,14}$-prostaglandin J2, may negatively affect invasion, metastasis, or neoangiogenesis of cancer cells in PPARγ-expressing tumors. Mice with PPARγ deficiency (PPARγ (+/−) are more susceptible to N-methyl-N-nitrosourea-induced gastric carcinogenesis (28). A recent study showed that hypermethylation of the PPARγ promoter was associated with poor prognosis in colorectal cancer (35). Epigenetic silencing of PPARγand consequent lower expression of PPARγ in GC patients may suggest that PPARγ involved early in gastric carcinogenesis and expression of PPARγcan be altered during tumor progression by epigenetic silencing.

Although the prognostic value of PPARγ has been previously established for colorectal cancer (29, 30), ours is the firststudy to demonstrate that PPARγ is an independent prognostic factor in patients with GC. However, PPARγ was an independent prognostic factor only in intestinal-type GC, which may be attributable to the putative origin of this type of GC. It is thought that intestinal-type GC often arises from an *H. pylori*-induced inflammatory process involving atrophic gastritis, intestinal metaplasia, and ultimately GC (9). PPARγ suppresses *H. pylori*-induced apoptosis in gastric epithelial cells by direct inhibition of *H. pylori*-induced NF-κB activation (31), thereby suggesting that PPARγ may interfere with the initial inflammatory process. As expression of NF-κB/p65 and its target genes are higher in intestinal-type GC than diffuse-type GC, and rates of NF-κB/p65 positivity are higher in

cagA-positive *H. pylori* infected patients than in cagA-negative patients (32), the crosstalk between PPARγ and NF-κB may explain PPARγ's survival effects being limited to intestinal-type GC.

By contrast, diffuse-type GC is influenced more by genetic factors than *H. pylori* infection. It is thought to originate from gastric epithelial stem cells and/or precursors in the isthmus region of the middle portion of the epithelium (33). Although the expression rate of PPARγ in diffuse type GC was similar to that of intestinal type GC in our study (70.7% vs. 68.3%), the mortality of diffuse-type GC was not affected by the PPARγ status. This may be explained by the different carcinogenesis of these GCs.

Galectin-9 is a member of the β-galactoside-binding galectin family of proteins (39), which suppresses invasion of tumor cells in colon cancer and melanoma cell lines by inhibiting the binding of tumor cell adhesive molecules to ligands on vascular endothelium and extracellular matrices (40). Galectin-9 is also a prognostic factor in breast cancer (41). Along with our findings, these observations suggest that galectin-9 may be a potential therapeutic target to inhibit EMT and thus reduce metastases in GC.

Byconferring migratory and invasive abilities ontumor cells, EMT increasesresistance to apoptosis, leading to acquired drug resistance (42) enables evasion of host immune surveillance (43) and endows cells with stem cell traits (44). Although tumor recurrence is not associated with PPARγ expression in our study, PPARγ expression was significantly associated with reduced overall and GC-specific mortalities, which are mostly influenced by distant metastases (not local recurrence) in GC (2-4). Meanwhile, EMT has also been implicated in the acquisition of drug resistance to chemotherapeutic agents (45). These observations emphasize why strategies to block EMT by activating PPARγ may be particularly useful in the clinical management of patients with GC.

Although this study evaluated a substantial number of patients with GC, thereby enabling robust survival analyses, it had limitations. First, the study was performed at a single institution, preventing external validation. Second, other tumor-related proteins were not studied. Third, we did not determine the *H. pylori* status of the patients in the study. However, the ability to detect *H. pylori* at this stage may have been limited; although *H. pylori* can act as an early initiating agent in carcinogenesis, it may have disappeared by the time GC develops (8).

In summary, we have shown that enhanced PPARγ activity reduced GC cell migration, invasion, and EMT through up-regulation of galectin-9. We have also demonstrated that PPARγ expression is independently associated with a good prognosis in intestinal-type GC. These findings suggest the possibility of PPARγ, or perhaps galectin-9, as a potential therapeutic target for GC.

4. 연구성과 및 목표달성도

(1) 연구성과

가. 국내 및 국제 전문학술지 논문 게재 및 신청

논문명	저자 (저자구분[1])	저널명(I.F.)	Year; Vol(No):Page	구분[2]	지원과제번호[3]
Peroxisome Proliferator-Activated Receptor ɣ Inhibits Cell Invasion, Migration and Epithelial-Mesenchymal Transition through Up-regulating Galectin-9, and Predicts the Prognosis in Intestinal-Type of Gastric Cancer	교신저자; 조수정, 제1저자; 조수정	International Journal of Cancer (6.198)	under revision	국외 SCI	1210450
Long-term metformin use reduces gastric cancer risk in type 2 diabetic patients without insulin treatment: a nationwide cohort study--> Alimentary Pharmacology and Therapeutics, under review	교신저자; 조수정, 제1저자; 김영일, 김소영	Alimentary Pharmacology and Therapeutics (4.548)	under review	국외 SCI	1210450
Prognostic Value of Tumoral Expression of Galectin-9 in Gastric Cancer	교신저자; 조수정, 제1저자;서기우		영문교정중		1210450

1) 저자구분 : 교신, 제1, 공동
2) 구분 : 국내, 국내 SCI, 국내 SCIE, 국외, 국외SCI, 국외SCIE 등
3) 지원과제번호(Acknowledgement)
- 과제번호를 연차 표시(-1, -2, -3 등)를 생략하고 7자리로 기재하고, 과제와 관련성은 있으나 불가피하게 Acknowledgement가 누락된 경우에는 '없음'으로 기재

나. 국내 및 국제 학술대회 논문 발표

논문명	저자	학술대회명	지역[1]	지원과제번호
Peroxisome Proliferator-Activated Receptor ɣ expression is associated with good survival in patients with intestinal type-gastric carcinoma	Soo-Jeong Cho	American Association of Cancer Research	미국, 시카고	1210450
Receptor ɣ Inhibits Cell Invasion, Migration and Epithelial-Mesenchymal Transition through Up-regulating Galectin-9 in Gastric Cancer Cells and in Zebrafish Xenograft Model	Soo-Jeong Cho	Seoul International Digestive Disease Symposium **우수포스터상 수상**	국제학회,서울	1210450
Peroxisome Proliferator-Activated Receptor ɣ Inhibits Cell Invasion, Migration and Epithelial-Mesenchymal Transition through Up-regulating Galectin-9 in Gastric Cancer Cells and in Zebrafish Xenograft Model	Ji-Young Shin, Soo-Jeong Cho	Research festival, NCC **우수구연상 수상**	국내	1210450
Peroxisome Proliferator-Activated Receptor ɣ Inhibits Cell Invasion, Migration and Epithelial-Mesenchymal	Ji-Young Shin,	10th Japan-Korea Joint Symposium	국제학회,	1210450

Transition through Up-regulating Galectin-9	Soo-Jeong Cho 우수포스터상 수상	on Helicobacter **우수포스터상 수상**	서울	
Long-term metformin use reduces gastric cancer risk in type 2 diabetic patients without insulin treatment: a nationwide cohort study	Young Il Kim, Soo-Jeong Cho	10th Japan-Korea Joint Symposium on Helicobacter **Plenary session** 발표, **우수구연상 수상**	국제학회, 서울	1210450
Prognostic Value of Tumoral Expression of Galectin-9 in Gastric Cancer	Ki-woo Seo, Soo-Jeong Cho	2013년도 대한소화기학회 추계학술대회 구연발표	국내	1210450
Long-term metformin use reduces gastric cancer risk in type 2 diabetic patients without insulin treatment: a nationwide cohort study	조수정, 김영일	United European Gastroenterology Week 2013 구연발표 **Travel grant 수상**	국제학회	1210450

1) 지역 : 국내, 국외

다. 산업재산권

구분[1)]	특허명	출원인	출원국	출원번호

1) 구분 : 발명특허, 실용신안, 의장등록 등

라. 저 서

저서명	저자	발행기관(발행국, 도시)	쪽수	Chapter 제목, 쪽수 (공저일 경우)

마. 연구성과의 정부정책 기여

보고서명	정부정책	기여내용

바. 기타연구성과

(2) 목표달성도

가. 연구목표의 달성도

최종목표	연차별목표	달성내용	달성도(%)	
			연차	최종

PPARG활성화에 의한 galectin-9의 유도 및 CCL4의 억제에 의해 위암의 침윤 및 전이가 억제됨을 증명하며, 위암 예후인자 및 맞춤형 치료의 표적을 개발한다.	1차년도	위암세포주에서 PPARG 활성에 의해 galectin-9이 유도되고 CCL4 발현 감소를 증명	위암세포주에서 PPARG 활성에 의해 galectin-9이 유도되고 SPRY4 발현 감소를 증명하였음	1	100
		Galectin-9 과발현, CCL4 발현 억제시 위암의 침윤 및 전이가 억제되는 것을 in vitro에서 증명	Galectin-9 과발현, SPRY4 발현 억제시 위암의 침윤 및 전이가 억제되는 것을 in vitro에서 증명하였음	1	100
		위암조직에서 galectin-9, CCL4 발현을 환자의 임상 data로 예후와의 관련성을 증명	위암조직에서 galectin-9, SPRY4 발현을 환자의 임상 data로 TMA완료 후 면역염색중임.	1	100
	2차년도	PPARγ에의한 Galectin-9 과발현, 발현 억제시 위암의 침윤 및 전이가 억제되는 기전 증명	실험완료 및 논문 투고 완료	2	100
		위암세포주에서 PPARG 활성에 의해 SPRY4 발현 감소를 증명	PPARG 과발현벡터 확립 및 SPRY4발현 감소 확인	2	100
		SPRY4 과발현시 위암의 침윤 및 전이가 억제되는 것을 in vitro에서 증명	SPRY4 과발현벡터 확립, in vitro 진행중	2	100
		SPRY4 발현 억제시 위암의 침윤 및 전이가 증가되는 것을 in vitro에서 증명	SPRY4 과발현벡터 확립, in vitro 진행중	2	100
		위암조직에서 SPRY4 발현을 환자의 임상 data로 예후와의 관련성을 증명	IRB승인받은 600명의 환자에 대한 tissue microarray 제작완료.	2	100

나. 평가의 착안점에 따른 목표달성도에 대한 자체평가

평가의 착안점	자 체 평 가
위암세포주에서 PPARG 활성에 의해 galectin-9이 유도되고 CCL4 발현 감소를 증명	위암세포주에서 PPARG 활성에 의해 galectin-9이 유도되고 SPRY4 발현 감소하는 것을 RT-PCR, western blot을 하였다.
Galectin-9 과발현, CCL4 발현	Galectin-9 과발현, SPRY4 발현 억제시 위암의 침윤 및

억제시 위암의 침윤 및 전이가 억제되는 것을 in vitro에서 증명	전이가 억제되는 것 gene assay, luciferase assay를 하였다.
위암조직에서 galectin-9, CCL4 발현을 환자의 임상 data로 예후와의 관련성을 증명	위암조직에서 galectin-9, SPRY4 발현을 환자의 임상 data로 예후와의 관련성을 증명하였다.

5. 연구결과의 활용계획

(1) 연구종료 2년후 예상 연구성과

구 분	건 수	비 고
학술지 논문 게재	3	International Journal of Cancer (6.198), Alimentary Pharmacology and Therapeutics (4.548), Annals of surgical oncology (4.12)
산업재산권 등록		특허 등록 예상 국가, 예상 특허명 등
기 타		

(2) 연구성과의 활용계획

연구시작전부터 체계적으로 어떤 연구를 할지에 대해 생각했기 때문에 짧은 시간동안 적은 비용으로 많은 성과를 낼 수 있었습니다. Independent large-scale cohort study에서도 비교적 일관되게 PPARg의 prognostic value가 나타나는 바, 향후 external validation study가 필요하겠습니다. 짧은 기간으로 pilot study만 수행했던 여러 topic(chemoresistance, down-stream pathway)들에 대해 후속연구가 필요합니다.

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7. 첨부서류

논문 별첨