4회

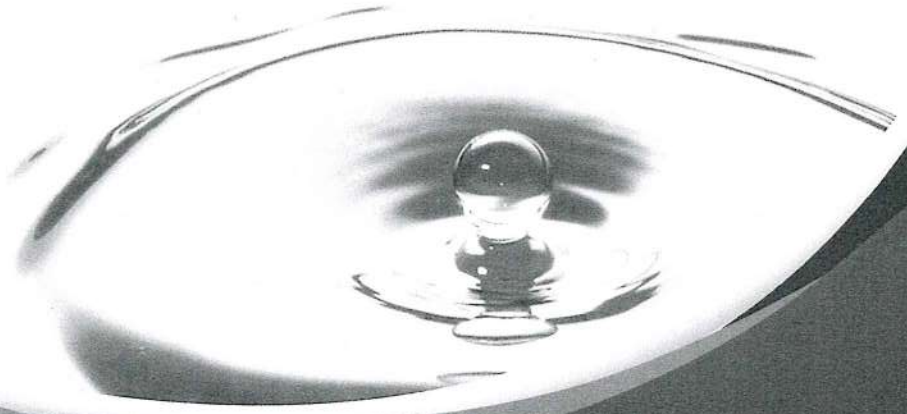
水 2012 festival

제주물의 가치와 글로벌 브랜드화

2012. 6. 7. (목)

제주국제컨벤션센터(서귀포시 중문관광단지 내)

발/표/자/료/집



주 최 | Jeju 제주특별자치도개발공사 Jeju Special Self-Governing Province Development Corporation

후 원 | MKE 지식경제부 Ministry of Knowledge Economy · Jeju 제주특별자치도 Jeju Special Self-Governing Province · KIAT Korea Institute for Advancement of Technology 한국산업기술진흥원 · LeadER 제주광역경제권 선도산업 지원단

水 2012 festival

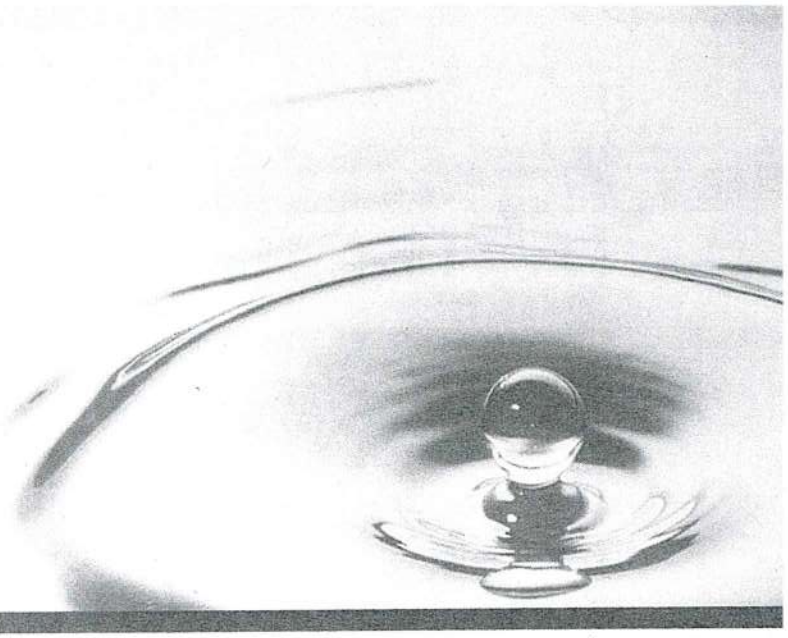
제주물의 가치와 글로벌 브랜드화

2012. 6. 7.(목)
제주국제컨벤션센터(서귀포시 중문관광단지 내)

발/표/자/료/집

주 최 | 제주특별자치도개발공사 Jeju Special Self-Governing Province Development Corporation

후 원 | 지식경제부 Ministry of Knowledge Economy · 제주특별자치도 Jeju Special Self-Governing Province · KIAT Korea Institute for Advancement of Technology 한국산업기술진흥원 · LEADER 제주광역경제권 선도산업 지원단



CONTENTS

2012 水페스티벌 2012 Water Festival

배경 및 목적

- 제주물의 가치를 대중들에게 전달하는 홍보적 요소와 동시에 국내 · 외 제주워터 유망상품 거래선을 발굴하는 마케팅적 요소를 결합한 형태의 페스티벌 진행
- 제주물의 신제품 소개와 신제품에 대한 대내외적 홍보의 장으로 페스티벌을 활용
- 제주물 산업의 미래와 비전을 도민이 함께 참여하며 이해할 수 있도록 공감대를 형성하고, 제주물 산업의 진흥과 미래를 도모하는 종합 축제의 장으로 마련
- 제주물 산업의 현재와 미래 비전, 지역공헌에 대한 다양한 내용을 전시, 발표, 시연함으로 도민들에게 사회공헌에 대한 인식 개선

행사 개요

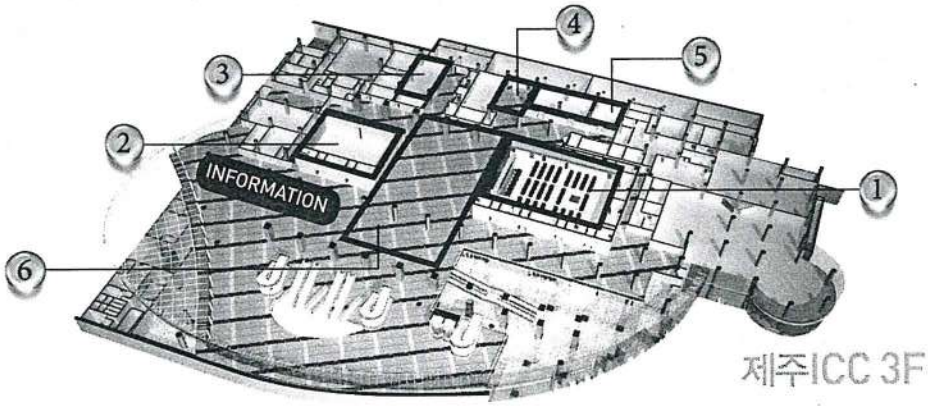
- 행사명 : 水 2012 festival (2012 Water Festival)
- 주 제 : **제주물의 가치와 글로벌 브랜드화**
- 기 간 : 2012년 6월 7일 ~ 8일 (2일간)
- 장 소 : ICC JEJU (제주국제컨벤션센터)
- 주 최 : Jeju 제주특별자치도개발공사 (Jeju Special Self-Governing Province Development Corporation)
- 후 원 : MKE 지식경제부 (Ministry of Knowledge Economy), Jeju 제주특별자치도 (Jeju Special Self-Governing Province), KIAT (Korea Institute for Advancement of Technology 한국산업기술진흥원), LEADER (제주청학경제권 선도산업 지원단)
- 참가자 : 물 관련 기관 및 학회, 전문가, 지역주민, 일반인 등
- 행사내용
  - 개회식 및 제주워터 신규 브랜드 시제품 설명회
  - 제주 물 세계포럼
  - 유망상품 기업 전시 및 바이어상담
  - 오찬, 만찬

전체 일정표

장소 / 일정	6월 7일 (목)				
	탐라홀	한라홀	삼다홀	3층 로비	303호
08:00		제주워터 신규 브랜드 시제품 전시			
09:00					
10:00	개회식&제주워터 신규 브랜드 시제품 설명회			유망상품 기업 전시 & 기업 IR / 캘리 작가 작품 전시	바이어 상담회
11:00					
12:00	오 찬				
13:00					
14:00			제주 물 세계포럼		
15:00					
16:00					
17:00					
18:00					
18:30	만 찬				
19:00					
20:00					

장소 / 일정	6월 8일 (금)			
	한라홀	삼다홀	3층 로비	303호
08:00	제주워터 신규 브랜드 시제품 전시			
09:00				
10:00			유망상품 기업 전시 & 기업 IR / 캘리 작가 작품 전시	바이어 상담회
11:00				
12:00				
13:00				
14:00		폐회식 (15:30 ~ 16:00)		
15:00				
16:00				
17:00				
18:00				
18:30				
19:00				
20:00				

행사 장소



1 제주워터 신규 브랜드 시제품 전시
위치 ICC 3층 한라홀
일시 2012년 6월 7일 ~ 8일

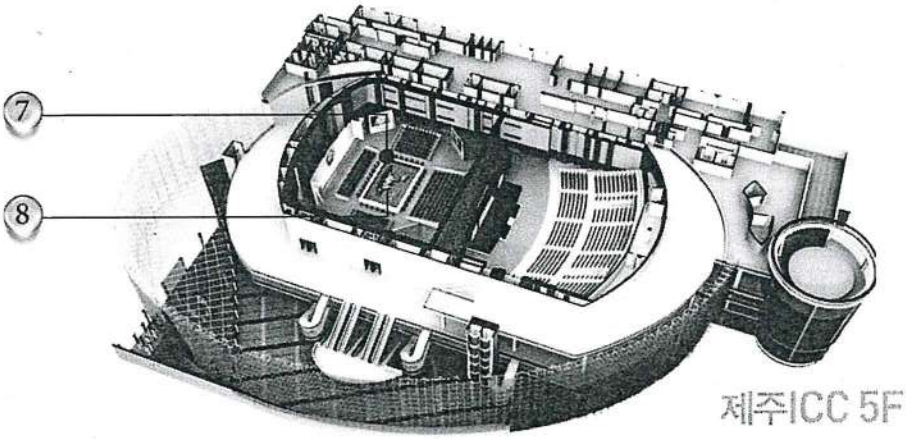
2 제주 물 세계포럼
위치 ICC 3층 삼다홀
일시 2012년 6월 7일
14:00 ~18:00

3 VIP 및 연사 대기실
위치 ICC 3층 302호
일시 2012년 6월 7일 ~ 8일

4 사 무 국
위치 ICC 4층 401호
일시 2012년 6월 6일 ~ 8일

5 기업 IR 및 비즈니스 상담공간
위치 ICC 3층 303호
일시 2012년 6월 7일 ~ 8일

6 유망상품 기업 전시장
위치 ICC 3층 한라홀 앞 로비
일시 2012년 6월 7일 ~ 8일



7 개회식 및 제주워터 신규 브랜드 시제품 설명회
위치 ICC 5층 탐라홀 B
일시 2012년 6월 7일 10:00 ~ 11:30

8 오찬, 만찬
위치 ICC 5층 탐라홀 B
일시 2012년 6월 7일
- 오찬 11:30 ~ 13:00
- 만찬 18:30 ~ 20:00

제주 물 세계포럼 Jeju Water Forum

2012. 6. 7.(목) 14:00 ~ 18:00 제주국제컨벤션센터(ICC JEJU) 3층 삼다홀

프로그램 구성

항 목	시 간	내 용
개 회	14:00 ~ 14:10	인사말 : 오재윤(제주특별자치도개발공사 사장) 발표 진행 순서 안내 및 좌장소개
발표1	14:10 ~ 14:30	강 연 자 : 윤성택(고려대학교 이과대학 교수) 발표주제 : 제주 지하수의 수질 특성과 차별화 방안
발표2	14:30 ~ 14:50	강 연 자 : 현진원(제주대학교 의학전문대학원 교수) 발표주제 : 제주 지하수의 항산화 시스템에 대한 효과
발표3	14:50 ~ 15:10	강 연 자 : 유호진(조선대학교 의과대학 교수) 발표주제 : 제주 지하수의 항비만 효과
휴 식	15:10 ~ 15:25	휴 식
발표4	15:25 ~ 15:45	강 연 자 : 고관표(제주대학교병원 내분비대사내과 교수) 발표주제 : 당뇨병 환자에서 혈당에 대한 제주 지하수의 효능
발표5	15:45 ~ 16:05	강 연 자 : 지영흔(제주대학교 수의과대학 교수) 발표주제 : 제주 지하수의 면역활성 효능 및 그 메커니즘
발표6	16:05 ~ 16:25	강 연 자 : 히로시 마쓰다(동경농공대 수의과대학 교수) 발표주제 : 제주 천연 지하수의 아토피성 피부염증에 대한 효능
발표7	16:25 ~ 16:45	강 연 자 : 장현욱(영남대학교 약학대학 교수) 발표주제 : 제주 지하수의 혈당 조절 및 알러지 반응 조절 효과
휴 식	16:45 ~ 17:00	휴식 및 자리정돈
종합토의	17:00 ~ 17:50	제주 지하수를 이용한 먹는샘물 글로벌 브랜드화 방안

참가자 소개

좌장 김 현 구 | 한국식품연구원 책임연구원

| 학위 | 동국대학교 공학박사 / 미국 New Jersey 주립대 Post-Doc.
| 경력 | Marquis Who's Who in the World / 세계인명사전 등재 / 제13회 과학기술우수논문상 수상 / 한국식품영양과학회 부회장 / 한국식품저장유통학회 회장 등 역임
| 현재 | 한국식품연구원 책임연구원 / 제주광역경제권선도산업지원단 자문위원 / 경북해양바이오산업연구원 자문위원 / 한국거래소 코스닥시장 상장 심사 자문위원 / 사랑의 화폭 등 산행 수필가

발표 1 윤 성 택 | 고려대학교 이과대학 교수

| 학위 | 고려대학교 이학박사
| 경력 | 세명대학교 자원공학과 교수 / 학술진흥재단 자연과학단 Project Manager / 환경부 먹는물자문회의 위원 / 환경부 중앙환경보전자문위원 / 국가연구개발사업 중기예산편성자문위원 등 역임
| 현재 | 캐나다 캘거리대학교 Adjunct Professor / 서울특별시 지하수 및 물 재이용 관리위원회 위원 / 고려대학교 그린스쿨대학원 및 지구환경과학과 교수

발표 2 현 진 원 | 제주대학교 의학전문대학원 교수

| 학위 | 서울대학교 약학박사
| 경력 | 서울대학교 의과대학 BK21 조교수 / 프랑스 파스퇴르 대학 박사 후 연구원 / 서울대학교 의과대학 암연구소 선임연구원
| 현재 | 제주대학교 의학전문대학원 생화학교실 교수

발표 3 유 호 진 | 조선대학교 의과대학 교수

| 학위 | 조선대학교 의과대학졸업 학사학위 / 서울대학교 대학원 졸업 의학박사학위
| 경력 | 미국 에모리 의과대학 포스트닥 / 조선대학교 의과대학 부교수
| 현재 | 조선대학교 의과대학 약리학 교수

발표 4 고 관 표 | 제주대학교병원 내분비대사내과 교수

| 학위 | 경희대학교 의과대학 의학과 의학사 / 경희대학교 일반대학원 의학과 내과학 석사 / 경희대학교 일반대학원 의학과 내과학 박사
| 경력 | 경희의료원 내분비내과 임상조교수 / 건양대학교 의과대학 내과 전임강사
| 현재 | 제주대학교 의학전문대학원 내과 교수

발표 5 지 영 흔 | 제주대학교 수의과대학 교수

| 학위 | 경북대학교 수의과대학 수의학과 수의학박사
| 경력 | 동경신경과학연구소 면역병리학연구실 박사후 연구원 / Barrow Neurological Institute / Adjunct researcher
| 현재 | 제주대학교 수의과대학 수의학과 교수 / 환경자원연구원 운영위원 / 수자원본부 평가위원

발표 6 히로시 마쓰다 | 동경농공대 수의과대학 교수

| **학위** | 오사카 대학 농학박사
| **경력** | Research Fellow, McMaster University, Canada. / Yale University 방문교수
| **현재** | 일본동경농공대 수의과대학 교수

발표 7 장 현 욱 | 영남대학교 약학대학 교수

| **학위** | 일본 동경대학 약학부 (박사, 1987)
| **경력** | 미국 MIT (Post-Doc.) / 미국 Medical College of Virginia (visiting scientist), Department of Allergy and Immunology / 영남대학교 약학대학 학장
| **현재** | 영남대학교 약학대학 교수

토론 손 혜 원 | 크로스포인트 대표

| **학위** | 홍익대학교 응용미술학 전공 / 홍익대학교 미술대학원 석사
| **경력** | 현대양행, 디자인포커스 근무 / 홍익대 산업미술대학원 교수 역임 / 참이슬, 정관장, LG트롬, 엔젤리너스커피, 힐스테이트, 그린핑거 등 다수 브랜딩 활동
| **현재** | 사단법인 한국디자인협회 회원 / 사단법인 한국문명교류 연구소 이사 / 사단법인 통영지속가능발전교육재단 이사 / 국가브랜드위원회 위원 / 국제 한식문화재단 이사

토론 김 대 희 | 대통령직속 국가브랜드 위원회 전문위원

| **학위** | 한양대 기계공학 / KAIST MBA, 경희대 경영학박사 수료
| **경력** | 국가브랜딩 중장기 전략 개발 / 국가브랜드 지수개발 등
| **현재** | 국가브랜드위원회 전문위원(브랜딩 전략 / 국가브랜드 지수)

토론 김 희 재 | 올댓스토리 대표

| **학위** | 한양대 연극영화과 대학원 수료 / 추계예술대 영상시나리오 석사 / 세종대 에니메이션학과 대학원 박사과정
| **경력** | 만화스토리 작가, 영화시나리오 작가 / 실미도, 국화꽃 향기, H, 공공의적 2, 한반도, 포화속으로, 글로브, 이끼 등 다수 영화 시나리오 작품 활동 / 마법천자문, 세상에 하나뿐인, 브로커 등 다수 만화 작가 활동
| **현재** | (주)올댓스토리 대표 / 추계예술대 영상시나리오 학과 교수 / EBS라디오 "김희재의 영화음악실" 진행

토론 황 용 철 | 제주대학교 경상대학 교수

| **학위** | 중앙대학교 경영학 석사(마케팅 전공) / 중앙대학교 경영학 박사(마케팅 전공)
| **경력** | 미국 일리노이 주립대 방문교수 / 중앙대학교 교류 교수 / 한국마케팅학회 상임이사 / Marquis Who's Who 세계인명대사전 등재
| **현재** | 제주대학교 경영학과 교수 / 한국상품학회 부회장 / 한국소셜미디어협회 이사장 / 한국소비문화학회 부회장 및 조직위원장 / 국제경상학회 상임이사

토론 고 기 원 | 제주특별자치도수자원본부 수자원개발부장

| **학위** | 부산대 수문지질 이학박사
| **경력** | 하와이주 호놀룰루시 파견연구원 / 한국지하수협회 전문위원 / 대한지질학회 전문위원 / 행정자치부 전문위원 / 제주특별자치도 물산업육성부장 / 제주광역경제권선도산업지원단장
| **현재** | 제주특별자치도 수자원 개발부장 / 제주특별자치도 문화재 위원

발/표/자/료/집

제주물의 가치와 글로벌 브랜드화

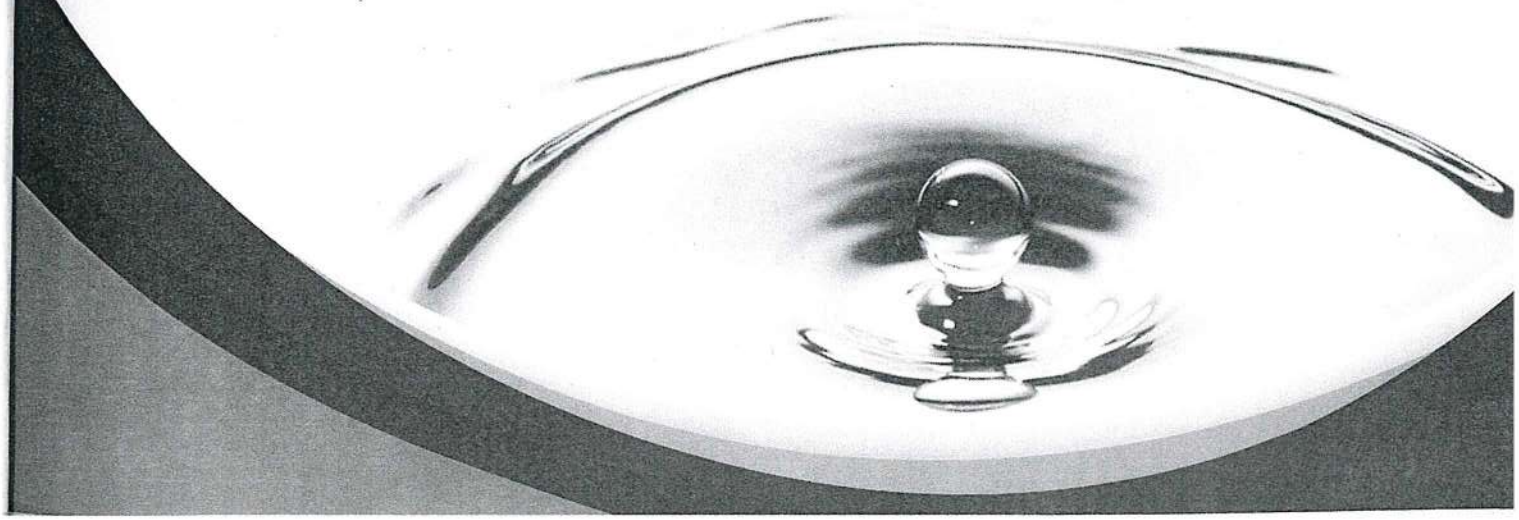
Value of Jeju Groundwater and Strategy for Global Brand

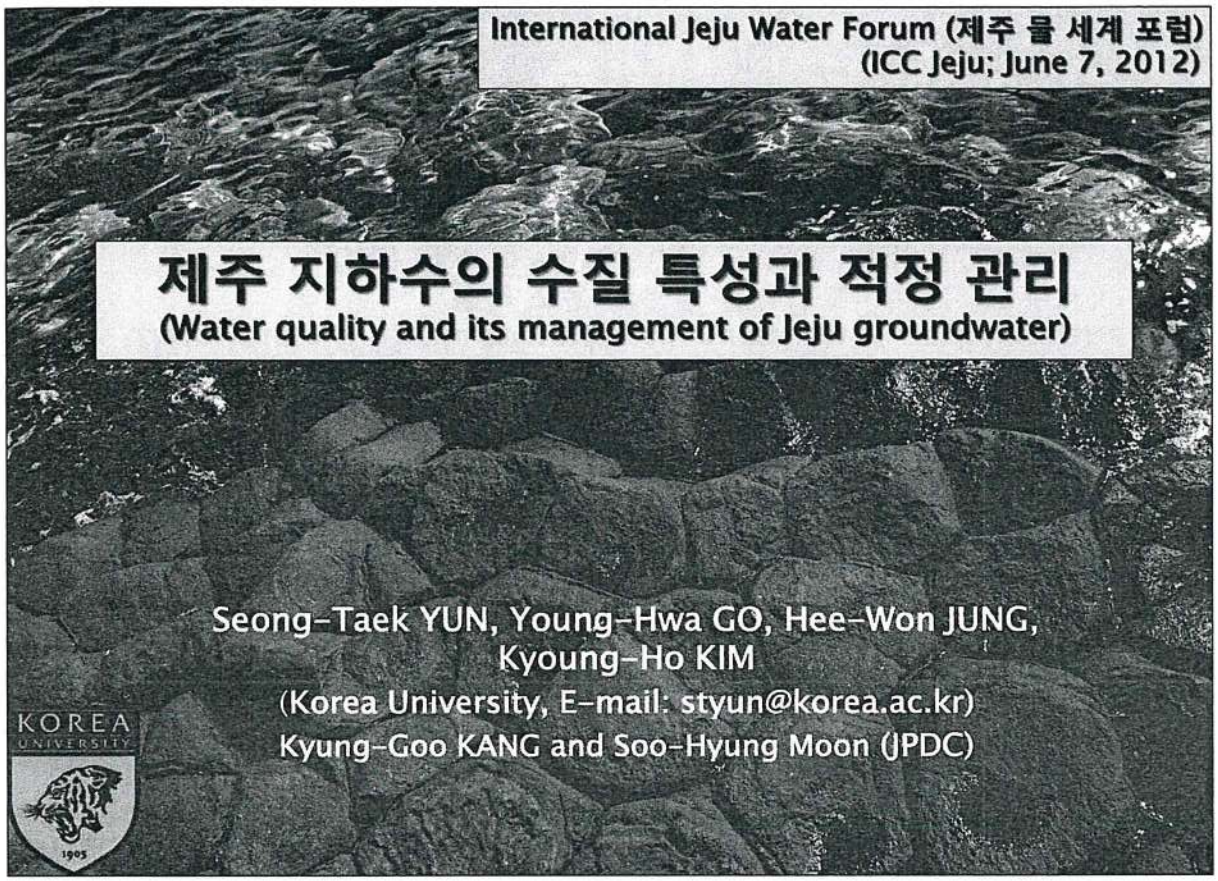
제주 지하수의 수질 특성과 적정 관리

Water quality and its management of Jeju groundwater

윤성택 고려대학교 이과대학 교수

Seong-Taek Yun, Korea University




International Jeju Water Forum (제주 물 세계 포럼)
(ICC Jeju; June 7, 2012)
제주 지하수의 수질 특성과 적정 관리
(Water quality and its management of Jeju groundwater)
Seong-Taek YUN, Young-Hwa GO, Hee-Won JUNG,
Kyoung-Ho KIM
(Korea University, E-mail: styun@korea.ac.kr)
Kyung-Goo KANG and Soo-Hyung Moon (JPDC)
KOREA UNIVERSITY
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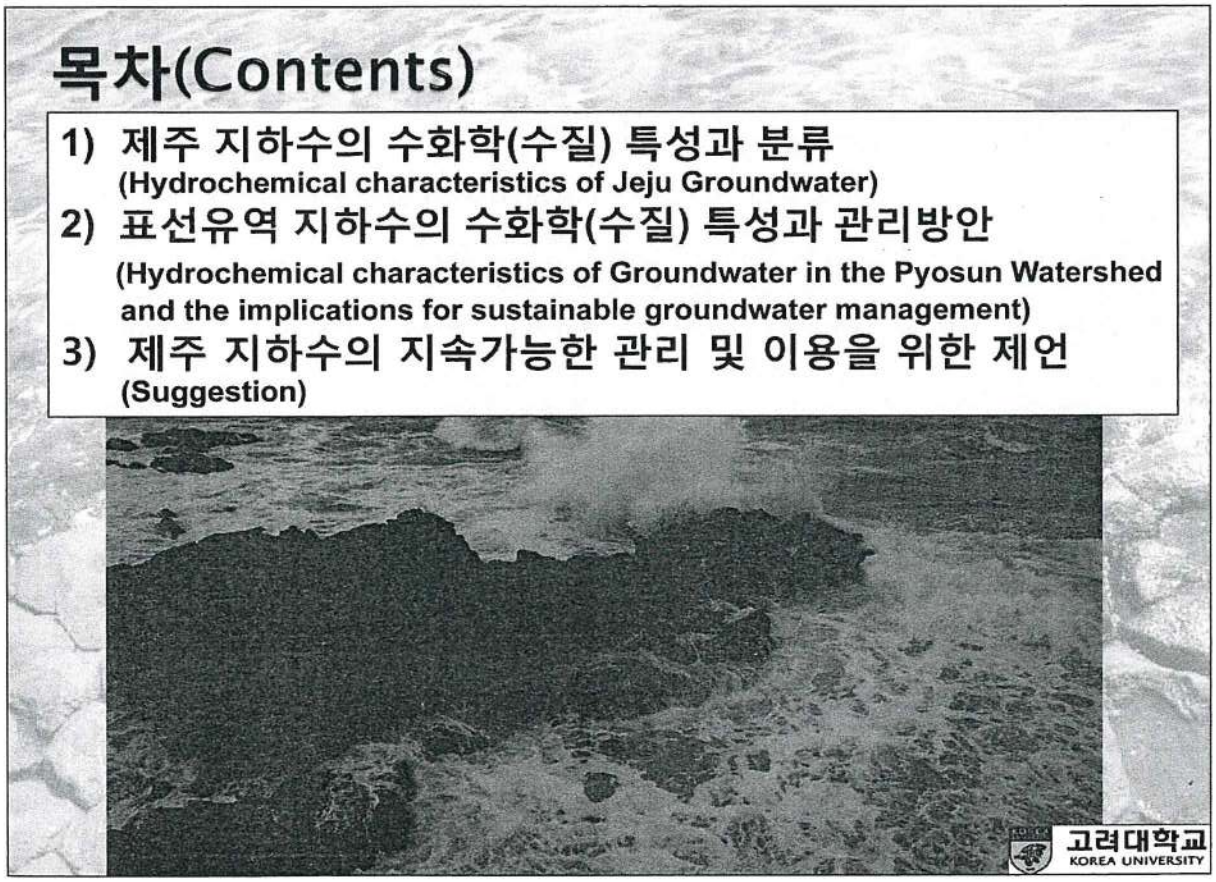
목차(Contents)
1) 제주 지하수의 수화학(수질) 특성과 분류
(Hydrochemical characteristics of Jeju Groundwater)
2) 표선유역 지하수의 수화학(수질) 특성과 관리방안
(Hydrochemical characteristics of Groundwater in the Pyosun Watershed and the implications for sustainable groundwater management)
3) 제주 지하수의 지속가능한 관리 및 이용을 위한 제언
(Suggestion)
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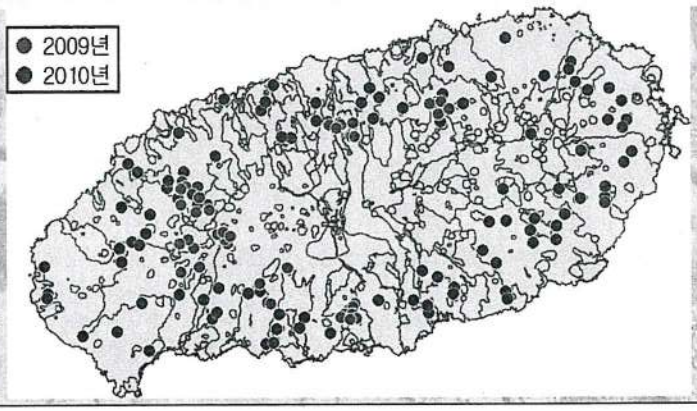
1. Hydrochemistry of Jeju Groundwater

주제 1) 제주 지하수의 수화학(수질) 특성과 분류
(Hydrochemical characteristics of Jeju Groundwater)

1) 제주 지하수의 수화학 특성과 분류 및 수질 현황
(Hydrochemistry and quality status of Jeju GW)
2) 제주도 지하수 내 기능성 성분의 분포 특성
(Occurrence of functional constituents in Jeju groundwater)
3) 국내 먹는샘물의 수화학 특성과의 비교 (Bottled Water in Korea)
4) 해외 먹는샘물의 수화학 특성과의 비교 (Bottled water in abroad countries)



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1. Hydrochemistry of Jeju Groundwater

1) 제주 지하수의 수화학 특성과 분류 및 수질 현황
(Hydrochemistry and quality status of Jeju GW)

- 제주도 지하수 수질관측망 자료 해석(Yun et al., in prep.

2009~2010 Total (N=392)							
Variables	Unit	Mean	Std.Dev	Maximum	Median	Minimum	C.V (%)
pH	-	7.7	0.5	8.8	7.7	6.3	7.0
EC	μs/cm	139.0	93.8	965.0	117.0	8.6	67.5
TDS	mg/L	138.7	69.0	691.1	123.0	64.0	49.8
Ca	mg/L	7.0	4.4	55.0	6.0	2.0	62.1
Mg	mg/L	5.5	4.3	33.8	4.5	1.4	78.3
Na	mg/L	11.5	9.1	83.1	9.0	4.2	79.0
K	mg/L	3.5	3.0	42.8	2.8	0.9	84.4
SiO2	mg/L	**32.0**	4.6	51.8	**32.1**	1.8	14.4
F	mg/L	**0.1**	0.1	0.6	**0.1**	0.0	49.4
Cl	mg/L	11.0	8.7	85.3	8.1	4.0	79.7
NO3	mg/L	10.3	17.7	250.2	5.1	0.1	172.5
SO4	mg/L	3.4	3.1	23.2	2.4	0.6	88.6
HCO3	mg/L	53.9	41.1	460.3	45.0	20.0	76.2

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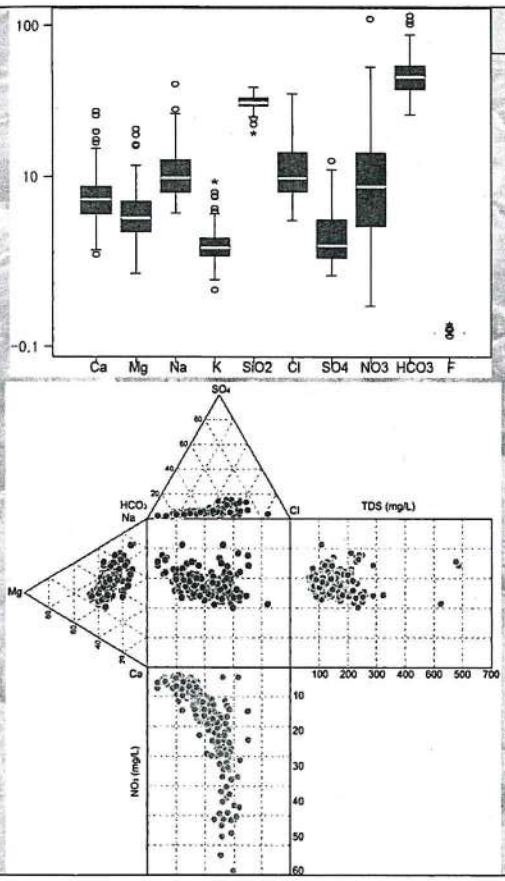
1. Hydrochemistry of Jeju Groundwater



1) 수화학 특성은 전반적으로 Na(-Ca-Mg)-HCO_3 유형으로부터 Ca-Mg(-Na)-Cl(-HCO_3) 유형에 걸쳐 폭넓게 변화
2) TDS는 대체적으로 낮아 90% 이상의 지하수에서 250 mg/L 이하
3) 일부 지역 시료에서는 인위오염에 의해 특히 NO_3의 농도 증가가 나타남. 따라서 지하수 수질관리를 위하여 농업활동과 관련한 비료와 분뇨 사용의 효율적 관리가 요망됨

(Yun et al., in prep.)

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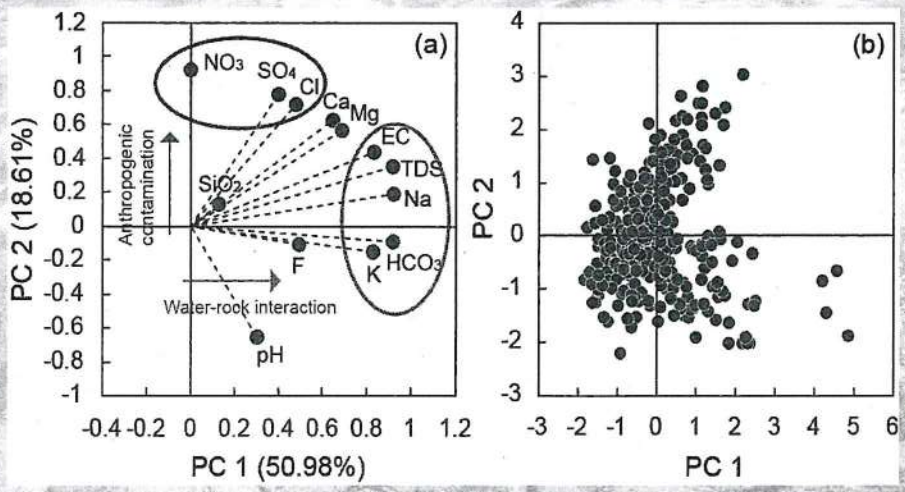
1. Hydrochemistry of Jeju Groundwater



<제주 전지역 지하수의 주성분(요인) 분석 결과. (a) 요인적재량, (b) 요인점수>

- 수질 형성 요인을 좌우하는 두 가지 주성분이 도출됨 (설명력 약 70%)
- 주성분1(PC1)는 자연적인 물-암석 반응으로 설명되는데, 이 과정은 특히 HCO_3, Na, K, TDS 등의 농도 증가로 표현됨.
- 주성분2(PC2)은 인위오염으로 설명되는데, 특히 다양한 성분을 갖는 화학비료와 분뇨 사용에 의한 NO_3, SO_4, Cl 등의 농도 증가로 표현됨.

(Yun et al., in prep.)

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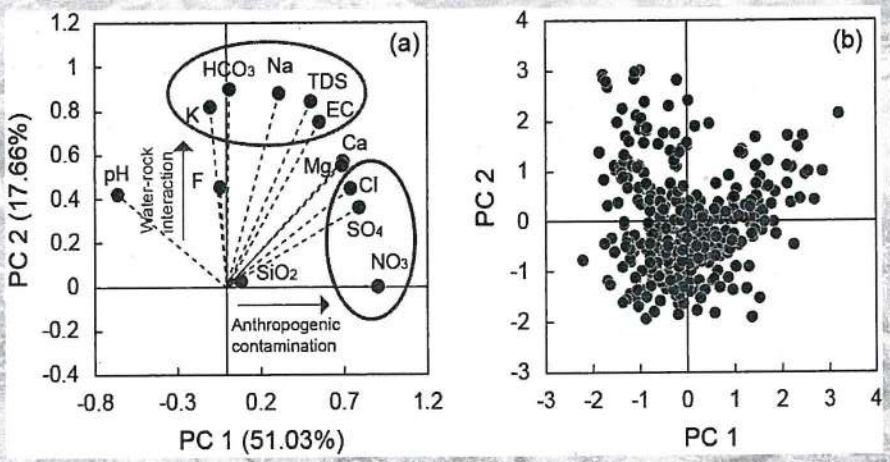
1. Hydrochemistry of Jeju Groundwater



<이상치를 제외한 제주 전지역 지하수의 주성분(요인) 분석 결과. (a) 요인적재량, (b) 요인점수>

- 수질 형성 요인을 좌우하는 두 가지 주성분이 도출됨 (설명력 약 69%)
- 주성분1(PC1)은 인위오염으로, 주성분2(PC2)는 자연기원(물-암석 반응)으로 설명됨.

(Yun et al., in prep.)

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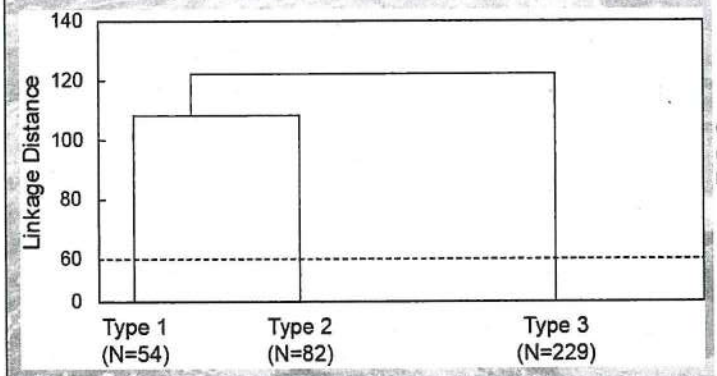
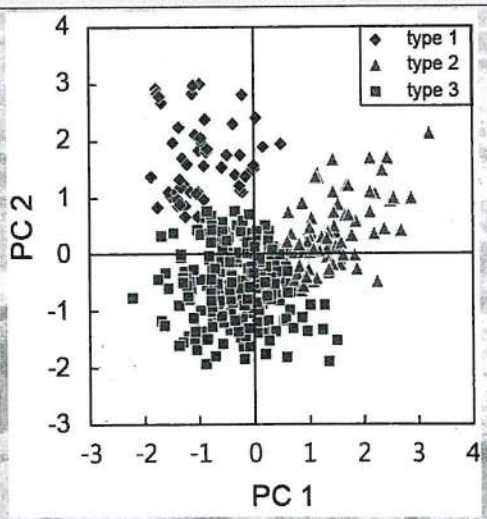
1. Hydrochemistry of Jeju Groundwater





<제주 전지역 지하수의 계층적 군집분석 결과>

- Type 1: 주성분 2에 많은 영향을 받는 시료들로 Na 사장석의 풍화로 수질 특성이 결정되는 물
- Type 2: 주성분 1에 많은 영향을 받는 시료들로 인위적 오염에 의해 수질 특성이 결정되는 물
- Type 3: 주성분 1과 2 각각에 대해 큰 영향을 받지 않는 물들로 제주 지역의 청정한 지하수(Fresh water)를 나타냄

(Yun et al., in prep.)

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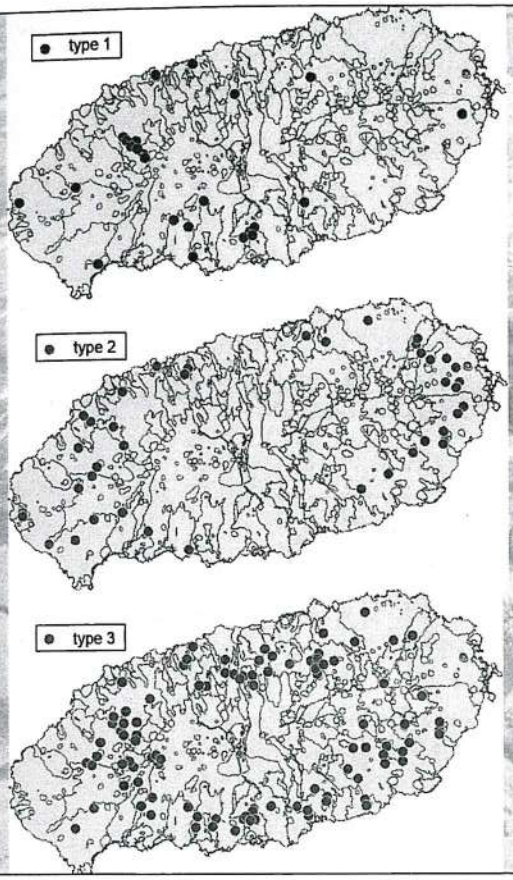
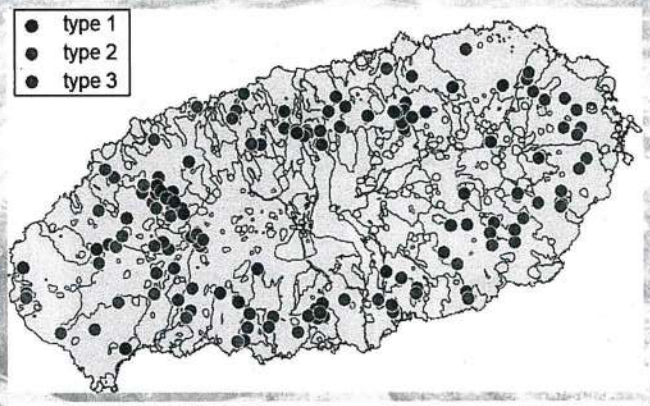
1. Hydrochemistry of Jeju Groundwater





<제주 전지역 지하수의 수화학 그룹 및 분포를 보여주는 계층군집 분석 결과>

- 유형 1과 3: 자연적인 물-암석반응에 영향을 받는 지하수 (청정성)
  * 유형 1은 사장석 용해반응이 지배
  * 유형 3은 상류에 우세하게 분포하며, 물-암석 반응 정도가 상대적으로 낮음.
- 유형 2: 인위적인 오염 영향을 나타내는 지하수로 하류에 우세 분포 (수질관리가 필요)

(Yun et al., in prep.)

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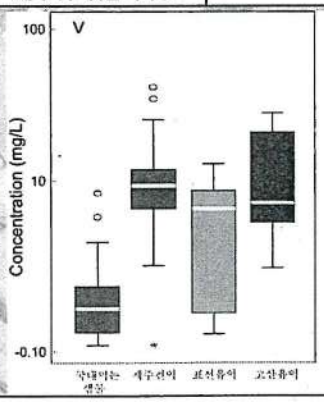
1. Hydrochemistry of Jeju Groundwater

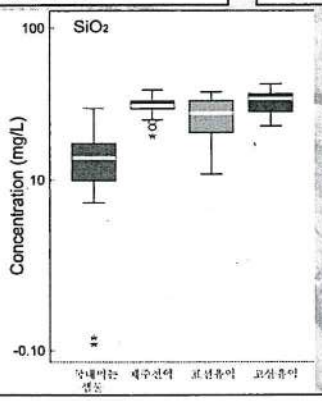
2) 제주도 지하수 내 기능성 성분의 분포 특성 (Occurrence of functional constituents in Jeju groundwater)

용존 실리카와 바나듐의 농도 비교

SiO_2 (ppm)	Min	Max	Median
국외 병입수	6.2	26.53	10.95
국내 병입수	0.47	30.33	7.07
제주 전역 지하수	31.53	39.85	31.62
표선 지역 지하수	32.87	38.69	33.77
고산 지역 지하수	35.03	43.7	33.98
제주워터(삼다수)	평균 28.52		

V (ppb)	Min	Max	Median
국외 병입수	<0.02	13	0.113
국내 병입수	0.41	5.51	0.71
제주 전역 지하수	0.01	0.04	0.01
표선 지역 지하수	N.A		
고산 지역 지하수	7.01	28.78	12.22
제주워터(삼다수)	평균 8.14		





- 용존 실리카는 골격의 칼슘화에 작용하여 뼈의 생성을 돕고 혈관을 강하게 하여 고혈압 예방에 좋다고 알려져 있음.
- 바나듐은 제주워터 내에 현저히 높은데, 당뇨질환에 관련되는 인슐린 조절에 관련된다고 보고되고 있음.

(Yun et al., in prep.)

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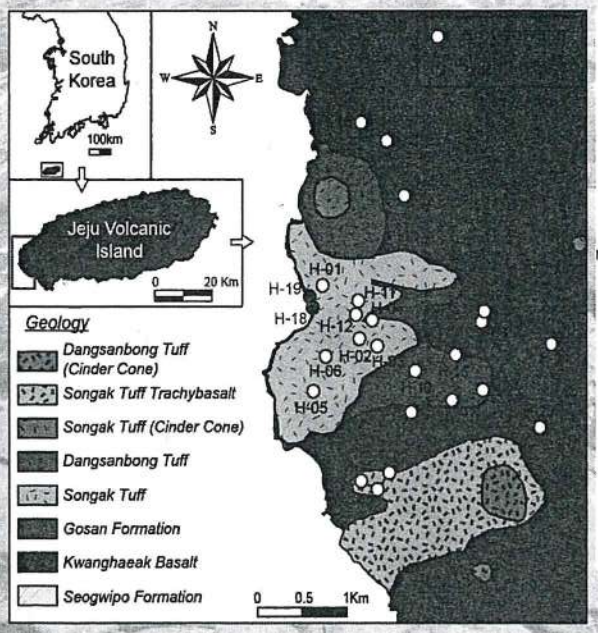
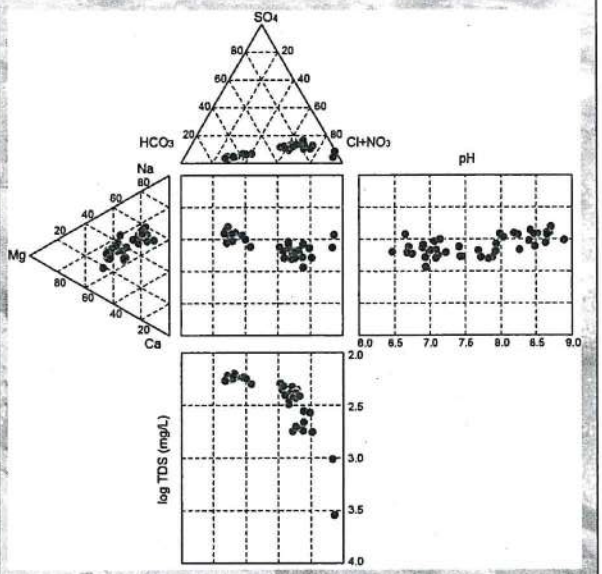
1. Hydrochemistry of Jeju Groundwater

고산지역 함 바나듭 지하수 연구





(Yun et al., in prep.)

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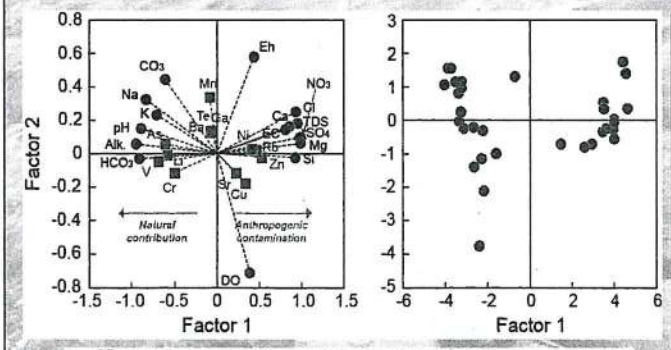
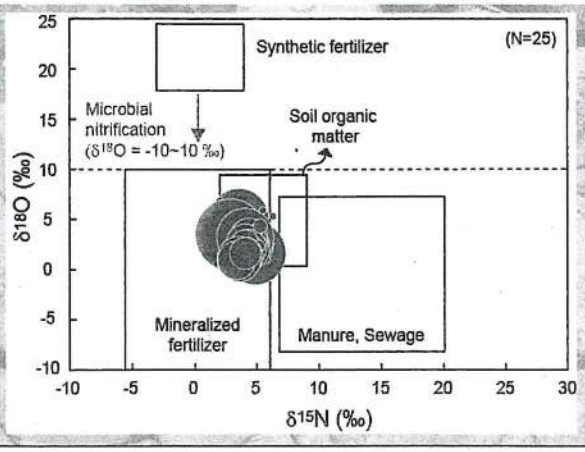
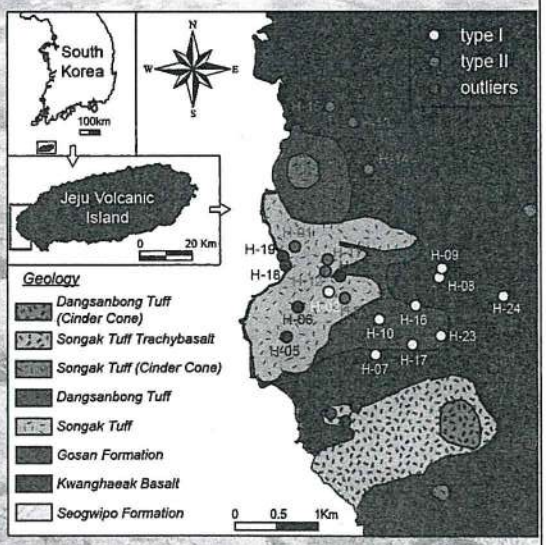
1. Hydrochemistry of Jeju Groundwater







Results of robust PCA

(Yun et al., in prep.)

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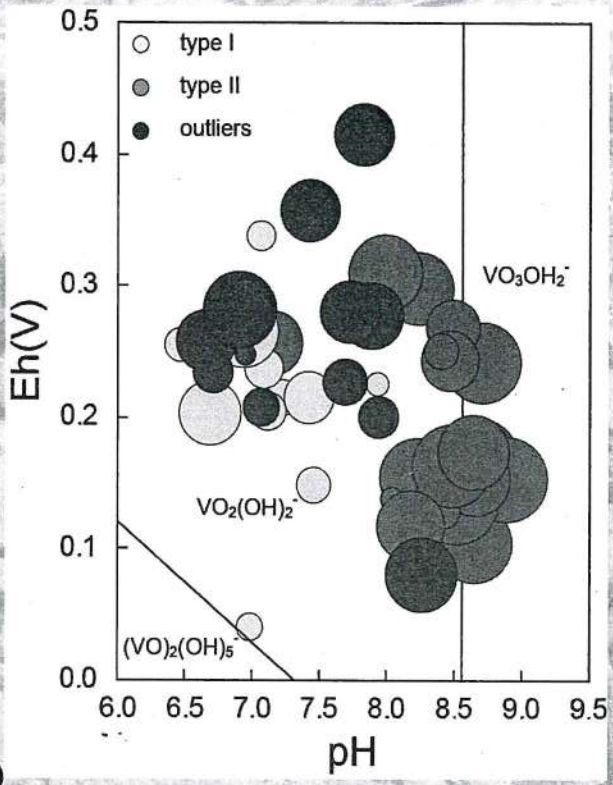
1. Hydrochemistry of Jeju Groundwater



(Yun et al., in prep.)

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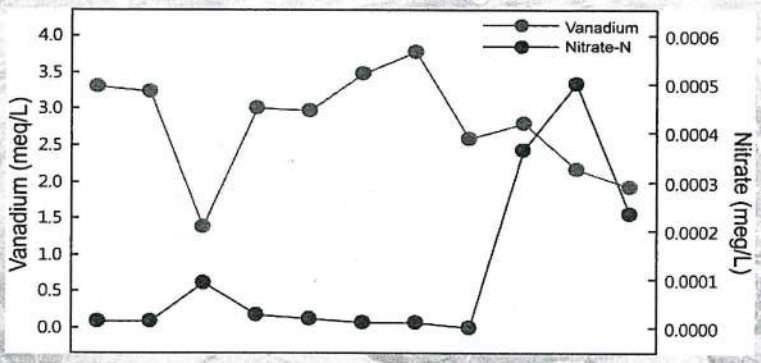
1. Hydrochemistry of Jeju Groundwater



고산지역 지하수의 바나듐 분석 결과:

- V 농도가 20 μg/L 이상으로 매우 높을 때는 대부분의 시료는 최저 수준의 질산성질소 농도 (0.1 ~ 1.8 mg/L)를 나타냄. 이는, 농업활동 지역에서 직접 함양되는 지하수의 유입량이 증가하는 경우에 바나듐의 농도는 감소함을 지시
- 고함량 바나듐 지하수는 광역 순환을 하는 전형적인 지하수(다분히 환원 상태가 큼)이며, 이 지하수계에 농업지역 토양을 통해 직접 함양되는 지하수의 유입량이 증가할수록 바나듐 함량은 희석에 의해 감소함.
- 따라서 고농도 바나듐 지하수의 부존지를 확인하여 경제적으로 개발 이용하기 위해서는 본 지역 지하수계의 수리 혼합 특성을 자세히 고찰해야 함.

(Yun et al., in prep.)

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1. Hydrochemistry of Jeju Groundwater

3) 국내 먹는샘물의 수화학 특성과의 비교 (Hydrochemistry of bottled water in Korea)

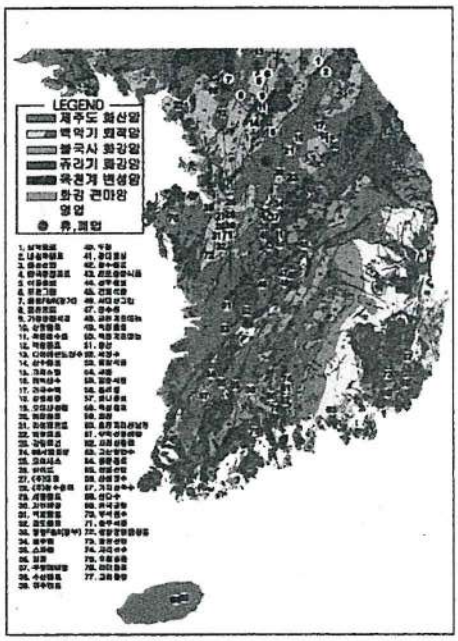

그림 1-1. 전국 먹는샘물 업체의 위치도

화학 조성 (n=60)

Unit: mg/L	K	Na	Ca	Mg	SiO_2	Cl	SO_4
Mean	1.01	7.35	17.36	3.55	18.41	4.10	10.05
Maximum	2.91	21.10	43.40	15.00	45.50	15.10	42.50
Minimum	0.07	1.63	3.15	0.36	2.09	1.06	0.96

F	NO_3	HCO_3	Al	TDS	EC (μS/cm)	pH
0.36	0.87	77.42	0.00	114.8	151.4	7.35
1.91	4.33	207.4	0.10	221.0	314.0	8.17
0.00	0.00	24.4	0.00	35.0	43.9	6.08

From MOE & KIGAM (2000)

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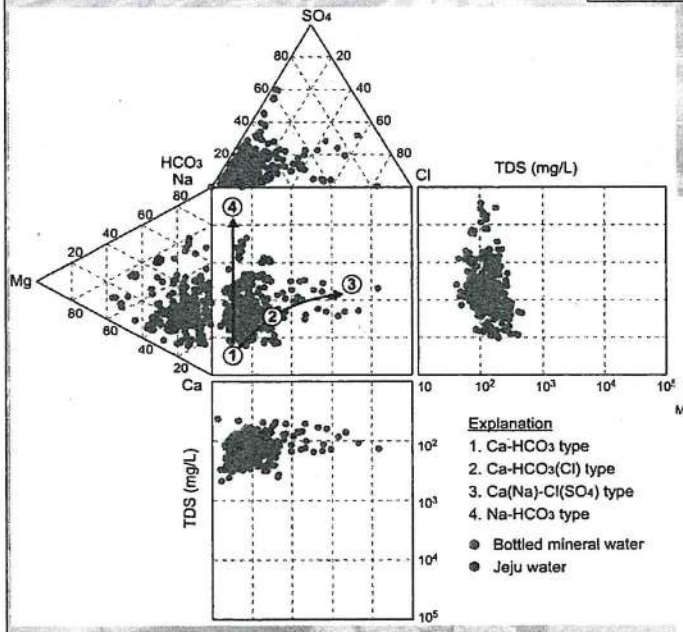
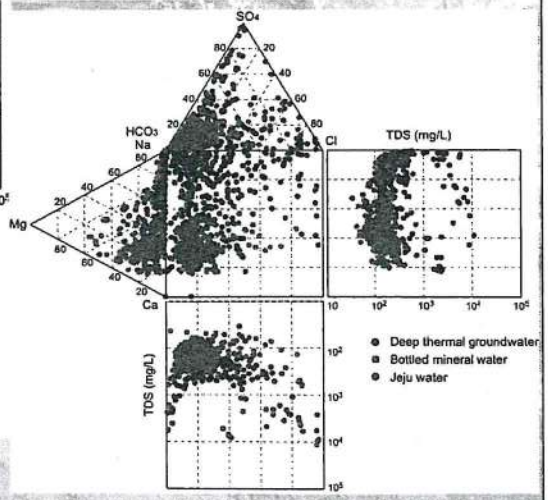
1. Hydrochemistry of Jeju Groundwater

- 국내 병입수는 심부 지하수에 비해 용질 함량이 현저히 낮으며, 대부분 Ca-HCO_3 유형
- 제주워터(삼다수)는 특징적으로 Na-HCO_3 유형



국내 병입수의 화학 조성 (Yun et al., in prep.)



국내 심부지하수(온천수)와 병입수의 화학 조성 (Yun et al., in prep.)

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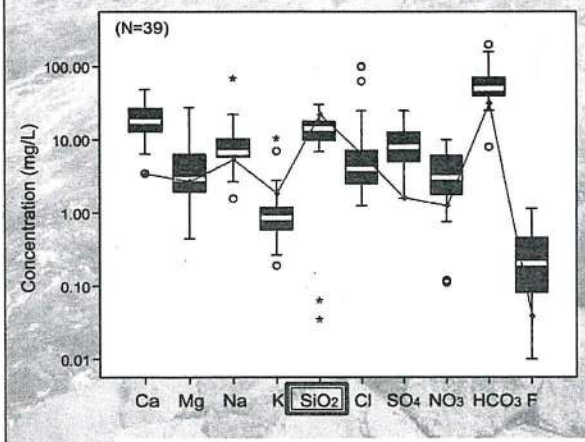
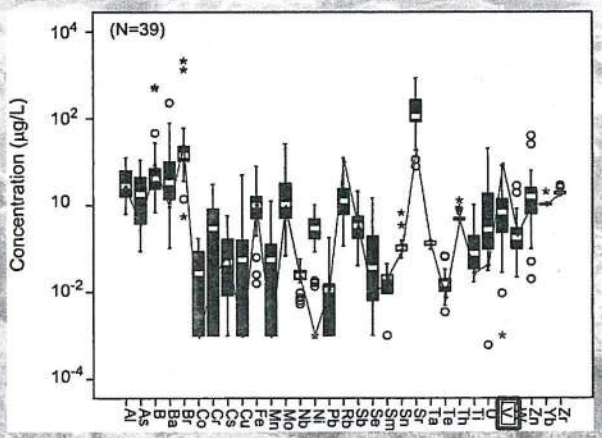
1. Hydrochemistry of Jeju Groundwater

◆ **Major ions**



◆ **Minor and trace elements**



<국내 병입수의 주성분 이온 및 미량원소 조성 (Yun et al., in prep.)>
- 붉은 선은 제주워터(삼다수) 자료임

제주워터(삼다수)의 수화학 특징 요약
- 양이온: Lower Ca & Higher K and Si
- 음이온: Lower SO_4 & NO_3 (청정성)
- 미량원소: Higher V, Rb & Br

(Yun et al., in prep.)

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1. Hydrochemistry of Jeju Groundwater

4) 해외 먹는샘물의 수화학 특성과의 비교 (Hydrochemistry of bottled water in abroad countries)

Types, qualities, and geologic settings of European bottled mineral waters

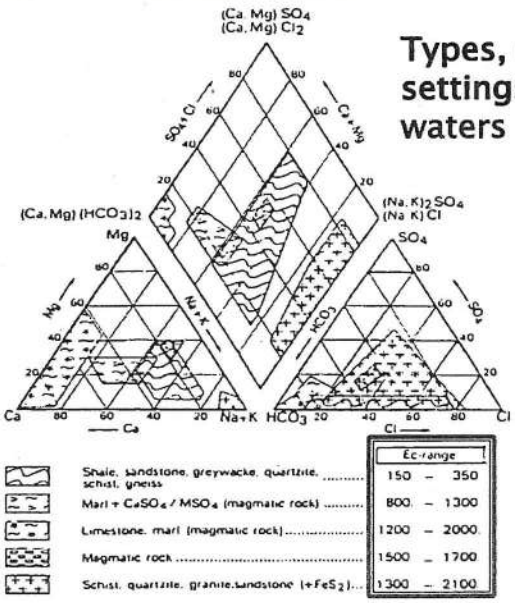

Figure 2.12. A Piper plot of European bottled mineral waters and their relation to the rock type from which the water has been extracted (modified from Zuurdeeg and Van der Weiden, 1985).

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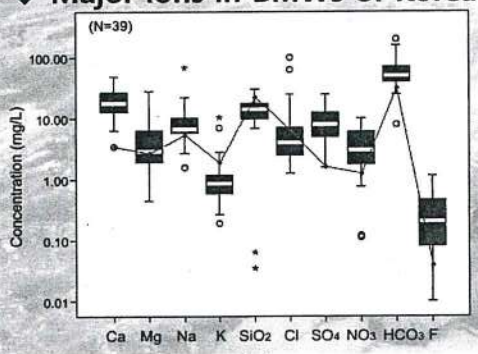
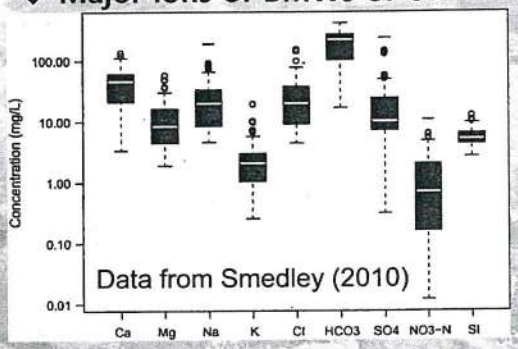
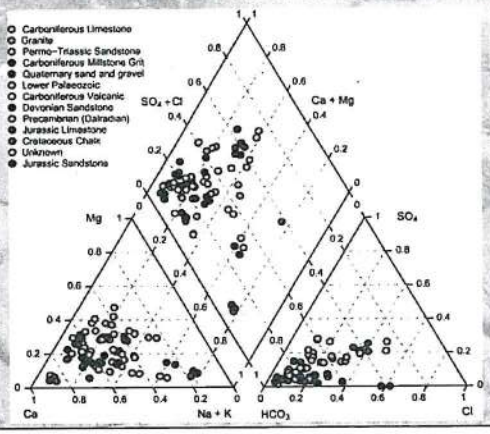
1. Hydrochemistry of Jeju Groundwater

◆ Major ions in BMWs of Korea



◆ Major ions of BMWs of UK





국내 병입수는 영국의 병입수와 유사한 조성을 보여주나, TDS와 alkalinity는 다소 낮다.

Piper plot of bottled mineral waters of the British Isles (Smedley, 2010)

(Yun et al., in prep.)

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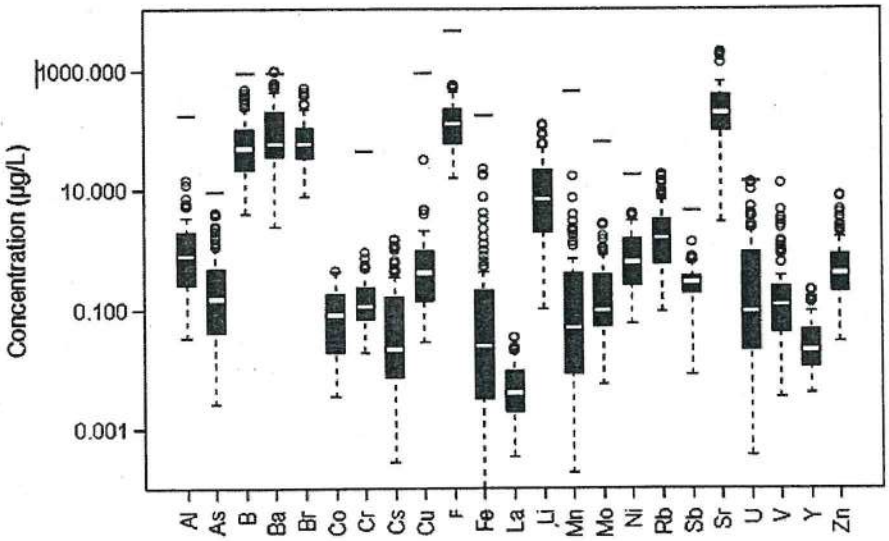
1. Hydrochemistry of Jeju Groundwater

◆ Trace elements in BMWs of UK



제주 워터(삼다수)의 바나듐 함량(평균 8 ppm)은 영국 병입수에 비해 매우 높다.

(Yun et al., in prep.)

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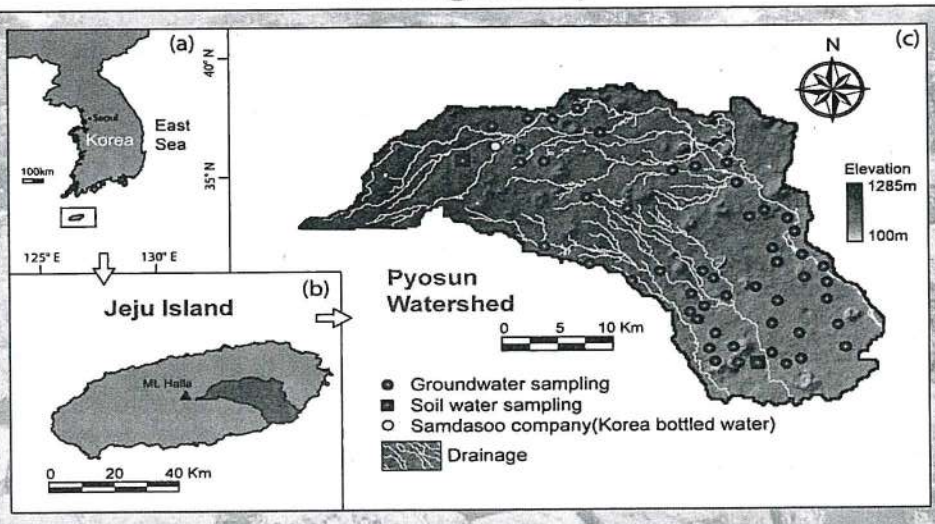
2. Pyosun Groundwater

주제 2) 표선유역 지하수의 수화학(수질) 특성과 관리방안
(Hydrochemical characteristics of Groundwater in the Pyosun Watershed and the implications for sustainable groundwater management)



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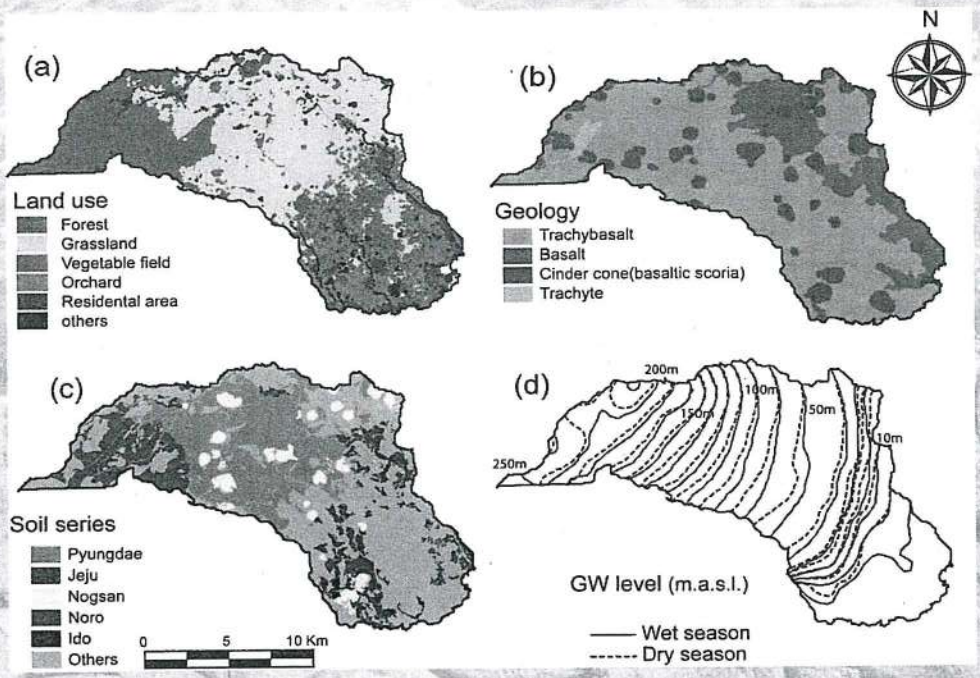
2. Pyosun Groundwater



(Yun et al., in prep.)

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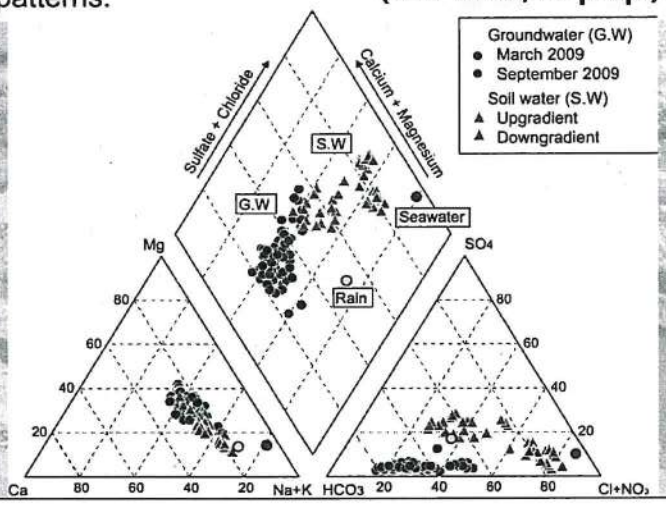
2. Pyosun Groundwater

1) General hydrochemistry: water type

- The groundwater shows a cluster of the Na+Mg(Ca)-HCO_3 type. However, there is a trend of the progressive increase of Cl and NO_3, due to larger degrees of anthropogenic contamination toward downstream sites.
- Soil water samples are different in chemistry from groundwater. Upstream samples are characteristically SO_4-rich, while downstream samples are rich in Cl and NO_3. Therefore, observed changes of water chemistry are generally coincident with land use patterns.

(Yun et al., in prep.)

- **Groundwater**
  - ***Na+Mg(Ca)-HCO_3 type***
- **Soil water**
  - ***Na+Mg(Ca)-HCO_3 type*** **at an upstream site**
  - ***Na-Cl type*** **at a downstream site**



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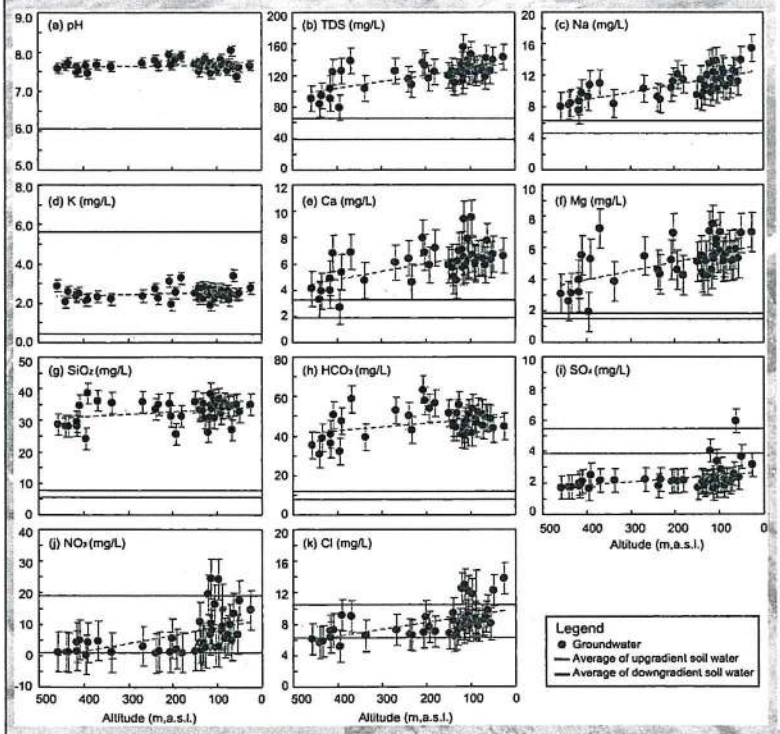
2. Pyosun Groundwater



2) Spatial change of GW quality

1) Soil waters show the remarkable increases of TDS, NO_3, Cl, SO_4, K, Ca and Na at downstream sites, due to the influences from agrochemicals and domestic sewage.
2) Groundwater also show the similar trends. In particular, increases of NO_3 and Cl are remarkable at the sites with elevations below about 150 m are distinct.
3) Compared with soil waters, groundwater is very high in pH, SiO_2, HCO_3, Ca and Mg, due to w/r interaction.

(Yun et al., in prep.)

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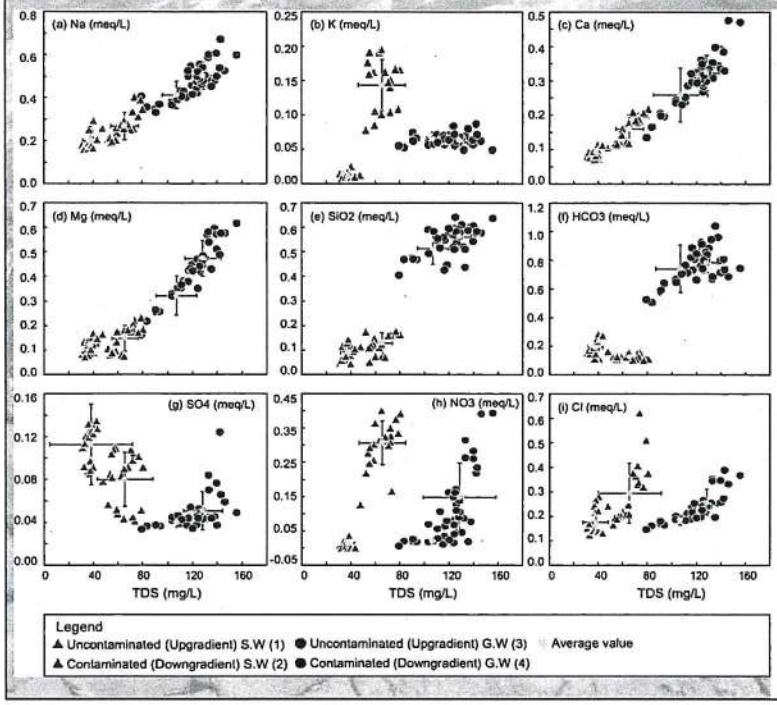
2. Pyosun Groundwater

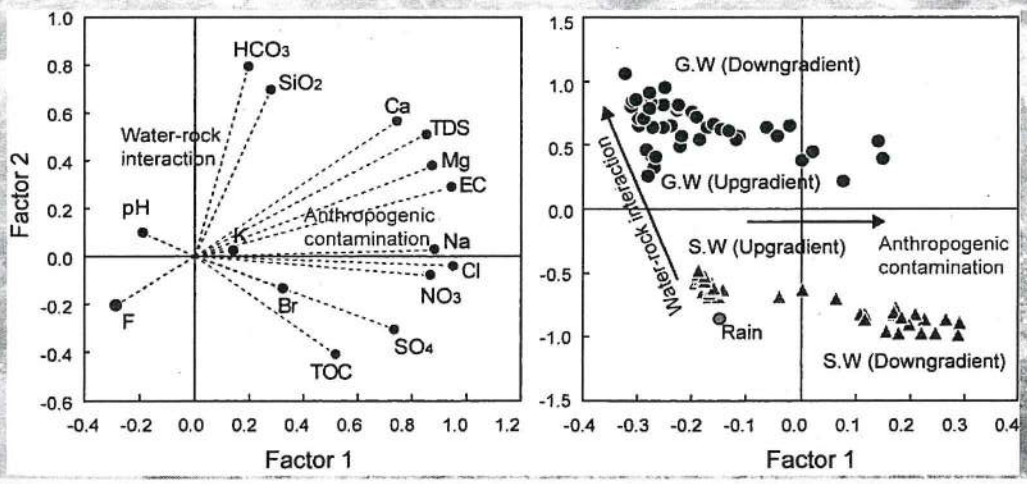
3) Relationships between TDS and ions: Estimation of hydrogeochemical processes (Yun et al., in prep.)



1) Overall, there is a general increase of the concentrations of solutes with increasing TDS, except for K, SO_4, NO_3 and Cl.
2) SO_4 is higher in soil water (esp. at an upstream site) than in groundwater, suggesting its preferential removal (by sorption) during infiltration through soils.
3) K is very high in soil water samples from a downstream site, suggesting its enrichment by dissolving agrochemicals.
4) NO_3 and Cl are highest in soil water samples from a downstream site. Similarly, their enrichments in downstream groundwater samples indicate anthropogenic contamination.
5) More enrichments of most solutes such as Na, K, Ca, Mg, SiO_2 and HCO_3 indicate their origin from w/r interaction. Thus, K is clearly of both natural and anthropogenic origin.

2. Pyosun Groundwater

4) Factor analysis: estimation of main hydrochemical processes



- Factor 1 : Discriminating between natural versus anthropogenic effects; In particular, Na, Cl and SO_4 are of typically anthropogenic origin.
- Factor 2 : Discriminating the group controlled dominantly by water-rock interaction; Especially, HCO_3 and SiO_2 are of typically natural origin;

The other solutes are of both natural and anthropogenic origin with variable contribution.
The estimated two factors nicely classify the samples according to main hydrogeochemical processes.

(Yun et al., in prep.)

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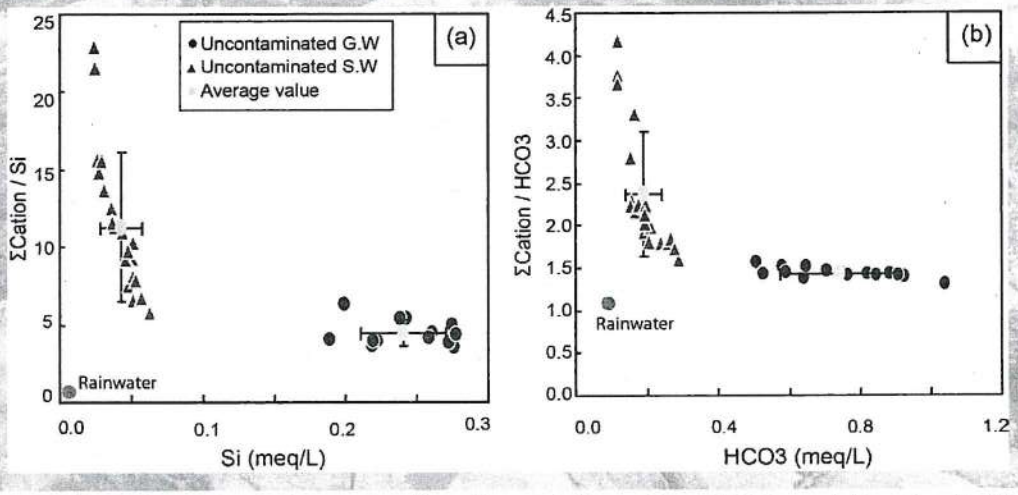
2. Pyosun Groundwater

5) Quantitative estimation of rock-silicates weathering



The generation of most solutes, as well as the enrichments of HCO_3 and dissolved silica in groundwater, can be successfully explained by water-rock interaction as follow:

Primary (Na, Ca, Mg) silicates + H_2CO_3 →
Secondary silicates (clays) + ions (Na, Ca, Mg) + HCO_3 + H_4SiO_4

(Yun et al., in prep.)

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2. Pyosun Groundwater

Calculated mass transfer to generate the observed GW chemistry

Phases	Wet precipitation - groundwater (mmol)	Chemical formula
Forsterite	0.076	Mg2SiO4
Albite	0.164	NaAlSi3O8
Anorthite	0.120	CaAl2Si2O8
K-feldspar	0.054	KAlSi3O8
Halite	0.140	NaCl
Kaolinite	-0.229	Al2Si2O5(OH)4

positive values indicates dissolution and negative values precipitation.

Primary (Na, Ca, Mg) silicates + H_2CO_3 → Secondary silicates + ions (Na, Ca, Mg) + HCO_3 + H_4SiO_4
Assuming the formation of kaolinite as a secondary mineral,

- ***Albite composition***

$0.164NaAlSi_3O_8 + 0.2453H_2O + 0.164CO_2 = 0.082\ Al2Si_2O_5(OH)_4 + 0.164Na + 0.327\ SiO_2 + 0.164HCO_3$

- ***Anorthite composition***

$0.120CaAl_2Si_2O_8 + 0.3596H_2O + 0.239CO_2 = 0.120\ Al2Si_2O_5(OH)_4 + 0.120Ca + 0.239HCO_3$

- ***K-feldspar***

$0.054KAlSi_3O_8 + 0.0812H_2O + 0.054CO_2 = 0.027\ Al2Si_2O_5(OH)_4 + 0.054K + 0.108\ SiO_2 + 0.054HCO_3$

- ***Forsterite***

$0.076Mg_2SiO_{24} + 0.1523H_2O + 0.305CO_2 = 0.152\ Mg^{2+} + 0.076\ SiO_2 + 0.305HCO_3$

0.511 mmoles

Results

Na	Ca	K	Mg	SiO2	HCO3
0.164	0.120	0.054	0.152	0.511	0.762

(Yun et al., in prep.)

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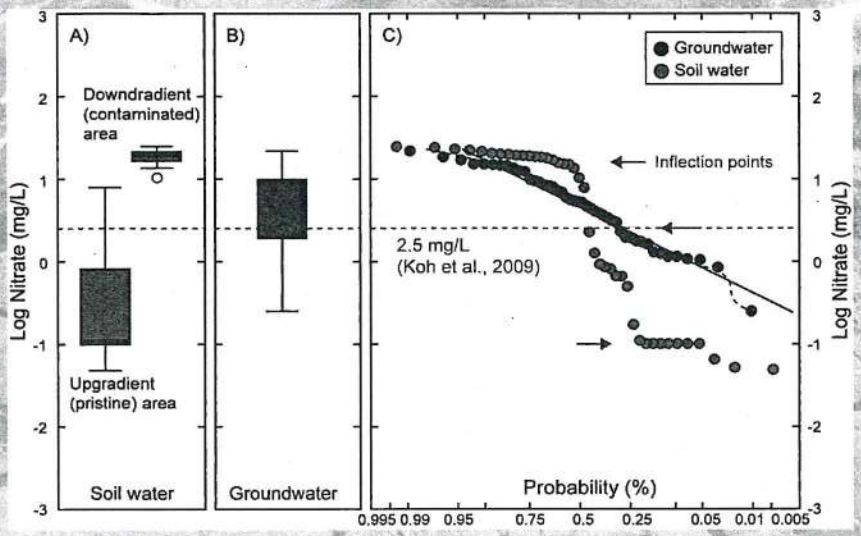
2. Pyosun Groundwater

6) Assessment of background (natural) levels of nitrate

The cumulative probability curves for nitrate concentrations in groundwater and soil water
- To estimate the nitrate levels as a guideline for GW quality management



❖ Group II
Anthropogenically impacted group in agricultural area

Inflection point is about *2.5 mg/L NO_3*

❖ Group I
Natural background group in pristine area

(Yun et al., in prep.)

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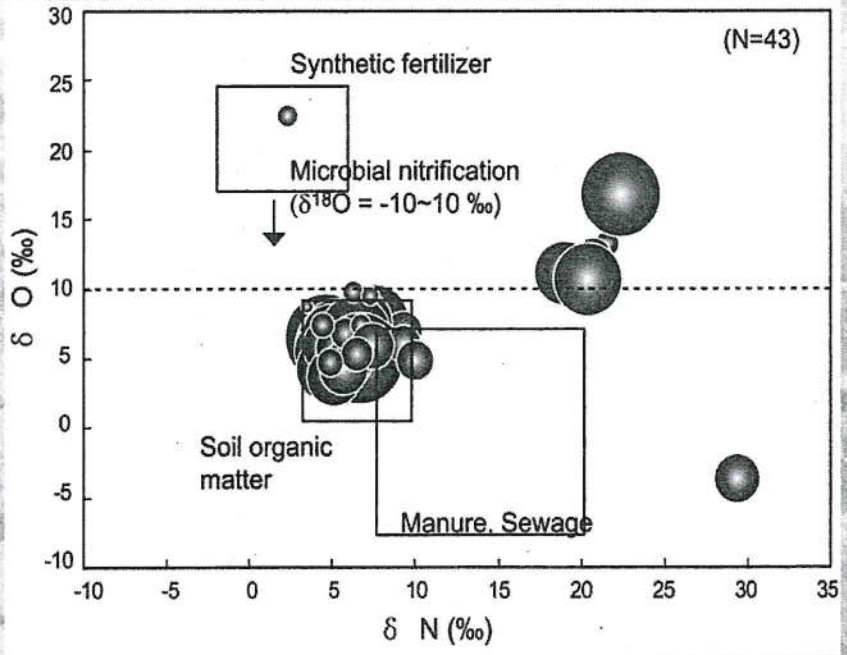
2. Pyosun Groundwater

7) Identification of nitrate sources



(Yun et al., in prep.)

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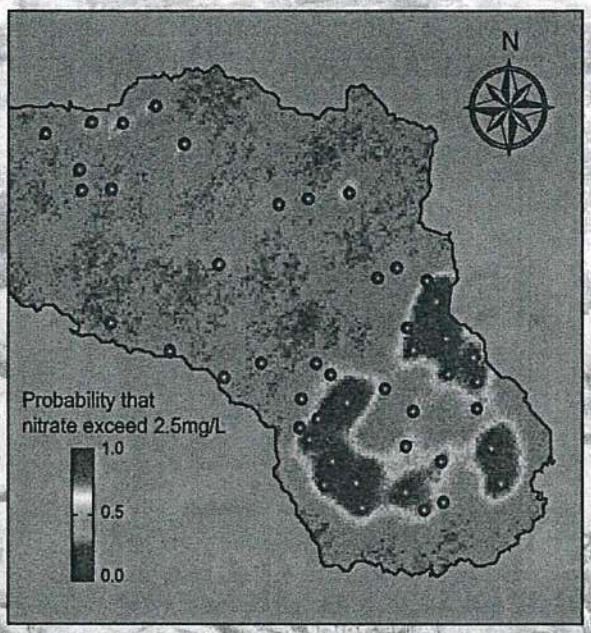
2. Pyosun Groundwater

8) Estimation of contamination susceptibility



질산염이 발생할 확률맵 (2.5 mg/L 이상일 확률, SGS 적용)

(Yun et al., in prep.)

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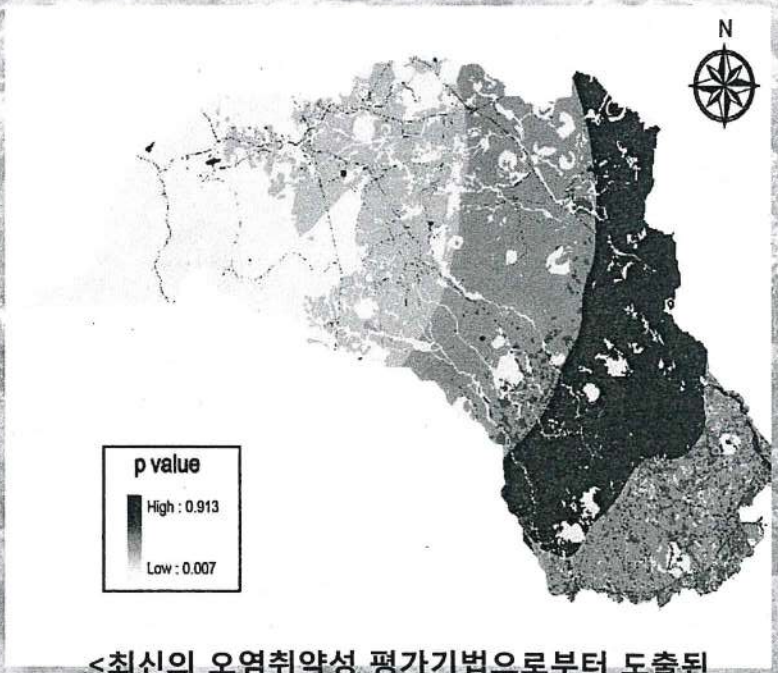
2. Pyosun Groundwater



<최신의 오염취약성 평가기법으로부터 도출된 표선유역의 지하수 오염취약성 도면>

(Yun et al., in prep.)

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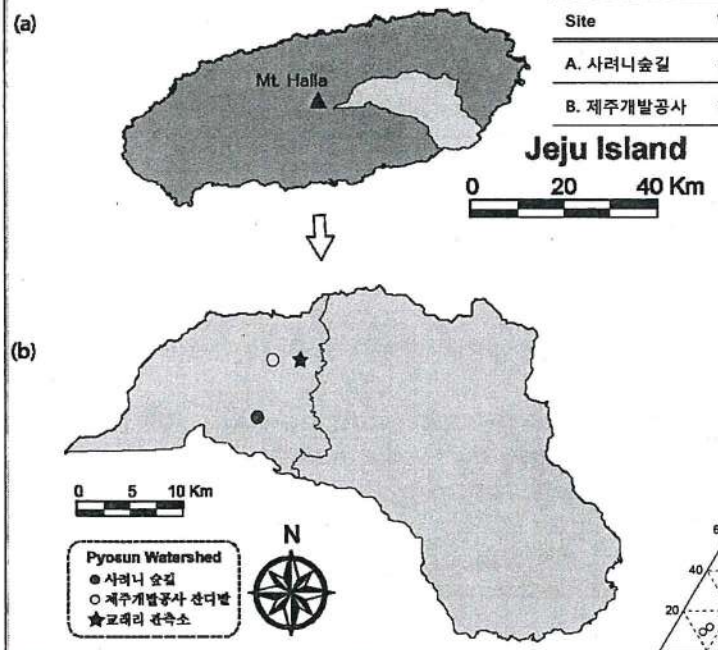
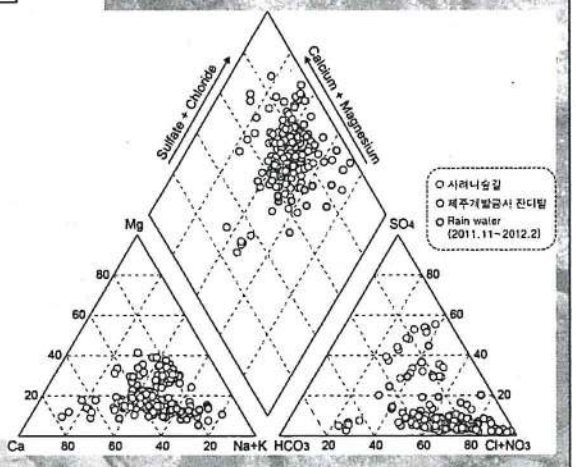
2. Pyosun Groundwater

9) Hydrogeochemical evolution & recharge-discharge characteristics of groundwater (monitoring using lysimeters)

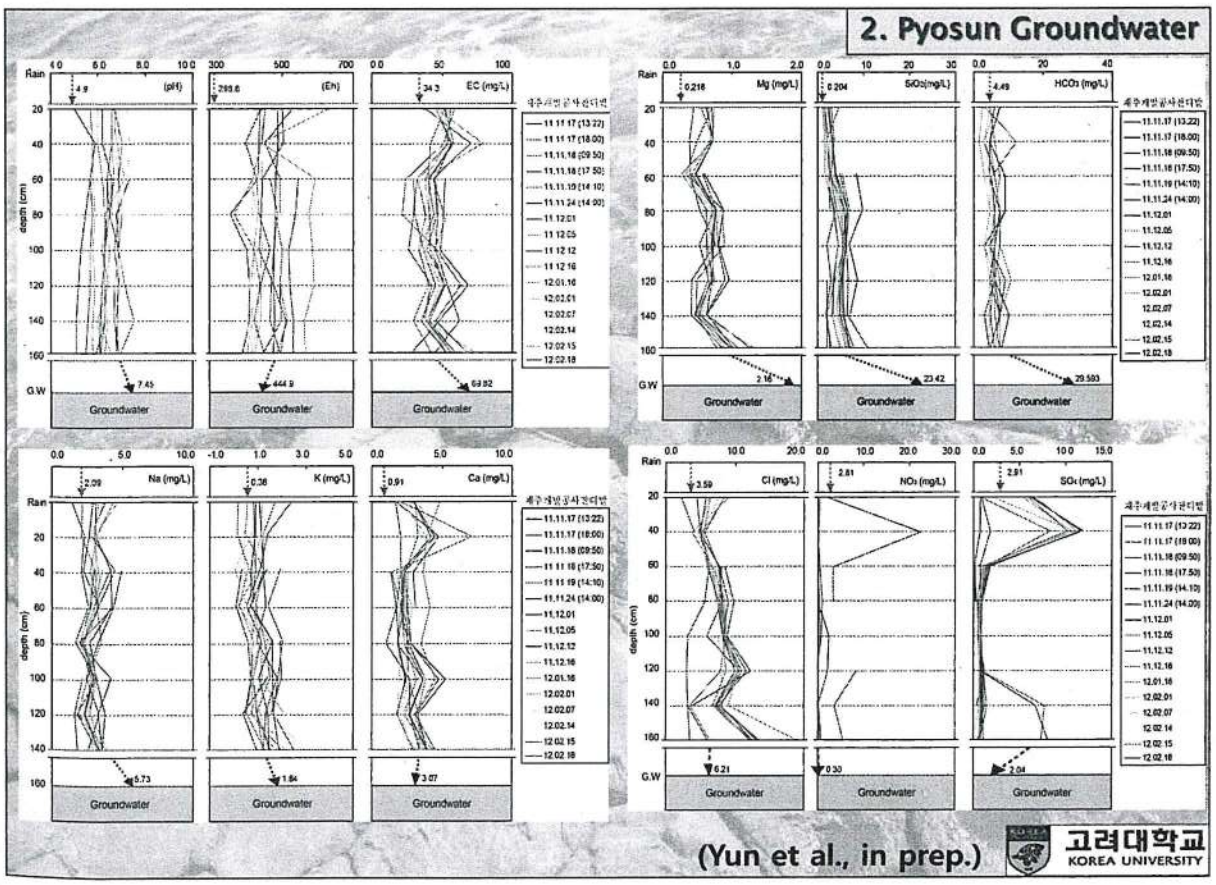
Site	Vegetation	Soil	Sample depth(cm)
A. 사려니숲길	산지대	노로통	20, 40, 60, 80, 100, 120, 140, 160
B. 제주개발공사	천연잔디밭	평대통	15, 30, 45, 60, 75, 90, 105, 120



(Yun et al., in prep.)

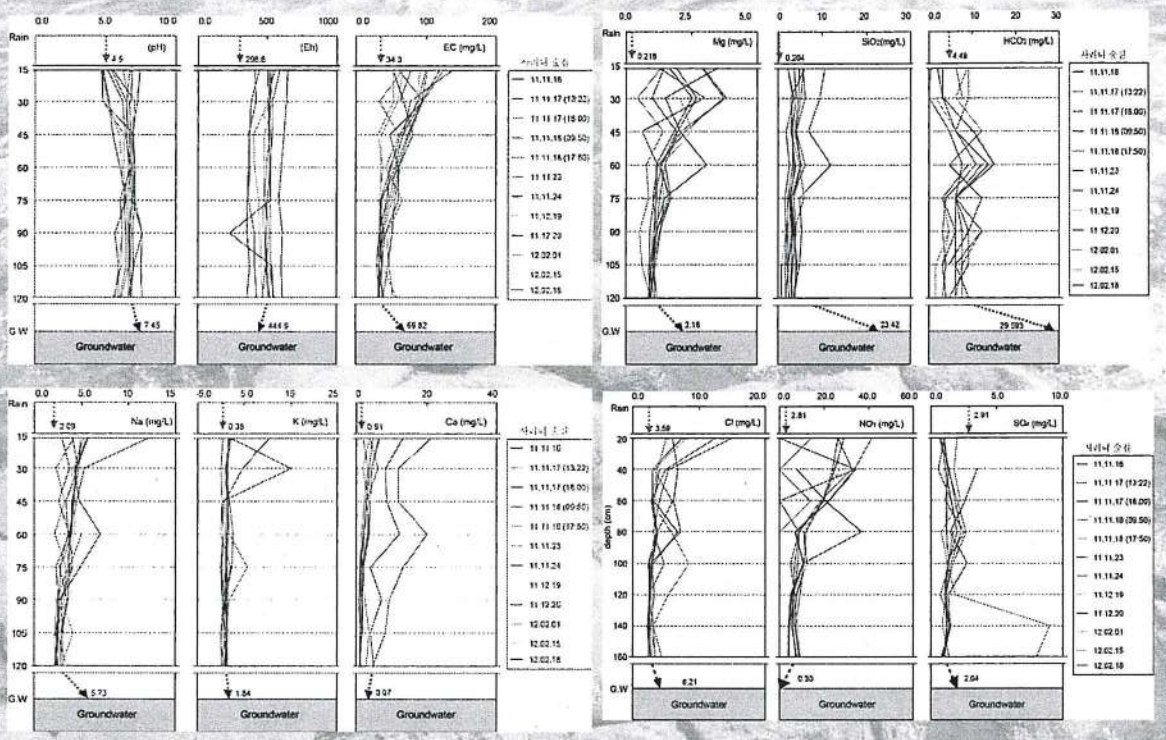


2. Pyosun Groundwater



(Yun et al., in prep.)

2. Pyosun Groundwater



(Yun et al., in prep.)

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시료 및 채수일자	심도 (cm)	산소동위원소	수소동위원소
삼 (12.1.16)	0~20	-6.42	-28.0
	20~40	-5.92	-32.5
	40~60	-5.55	-37.4
	60~80	-5.59	-39.4
	80~100	-6.44	-41.5
	100~120	-6.03	-37.9
	120~140	-6.03	-40.2
	140~160	-6.50	-43.3
삼 (12.2.1)	0~20	-6.65	-29.5
	20~40	-5.73	-29.9
	40~60	-5.70	-37.0
	60~80	-5.49	-38.8
	80~100	-6.41	-40.4
	100~120	-5.95	-39.2
	120~140	-6.47	-40.1
	140~160	-7.03	-47.4
숲 (12.1.19)	15~30	-6.10	-30.4
	30~45	-6.16	-32.3
	45~60	-6.29	-37.5
	60~75	-6.44	-38.3
	75~90	-6.54	-40.1
	90~105	-6.58	-37.5
숲 (12.1.1)	0~15	-6.41	-24.0
	30~45	-6.01	-30.6
	60~75	-6.25	-35.8
	75~90	-6.51	-38.1
	90~105	-6.71	-37.9
삼다수 1호정		-7.44	-44.4
삼다수 2호정		-7.50	-45.5
삼다수 3호정-1		-7.41	-44.0
3호정-2		-7.42	-45.8
3호정-3		-7.51	-44.7
강우 (12.1.19-20)		-6.50	-36.9
강우 (12.2.14)		-5.83	-28.7
강우 (12.2.15)		-6.11	-31.2

2. Pyosun Groundwater

Monitoring of O and H isotopes of diverse water samples

Preliminary interpretation

1) **Groundwater of Samdasoo is significantly lower in O and H isotope compositions, compared with soil water and rainwater. This may indicate that groundwater recharge occurs mainly at higher altitude areas that are far away from the study area.**
2) **This reflects that Samdasoo water is still devoid of contamination. However, extension of agricultural fields to the upstream areas should be carefully controlled.**

(Yun et al., in prep.)

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2. Pyosun Groundwater

9) Summary and suggestions

1) Soil water and groundwater in the Pyosun area, Jeju, were collected and examined to elucidate both the origin of solutes and hydrogeochemical processes controlling the water quality in a trachybasaltic volcanic terrain with steep slopes and variable land use pattern.

2) The hydrochemistry data showed a distinct land use (and land cover in relation to topography) control.
   - There was an obvious trend of progressive and remarkable increases of Cl and NO_3 toward downstream sites, due to larger degrees of anthropogenic contamination (esp., from agrochemicals and domestic sewages).

3) The PCA analysis showed an excellent grouping of both hydrochemical parameters and samples. PC1 represents the effect of anthropogenic pollution and is characteristic in groundwater and soil water samples collected at downstream sites, whereas PC2 records the effect of a natural process (i.e., W/R interaction) which is distinct in groundwater.

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2. Pyosun Groundwater

4) To estimate the relative contribution of some solutes (esp., SiO_2, HCO_3, Na, K, Ca and Mg) in groundwater, a mass balance inverse modeling was performed. The results show major roles of water-rock interaction, especially for SiO_2 and HCO_3. However, K and Na ions are partly of anthropogenic origin. Calcium and Mg ions are mostly of natural origin with minor contribution from agrochemicals.

5) The threshold (background) value of nitrate in groundwater was estimated to be about 2.5 mg/L NO_3. This value can be used as a groundwater quality guideline to be effectively used to estimate the degree of groundwater contamination.

6) This study implies that strategic groundwater management is needed in the Pyosun Watershed. In particular, agricultural activities should be better managed, focussing on better management of fertilization.

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3. Suggestion

제주 지하수의 지속가능한 관리 및 이용을 위한 제언

1) 국제시장 개척을 위한 차별적 특성 지속 발굴 및 홍보 강화
(Marketing on the Excellency of Jeju Water)

2) 지속적인 연구개발 – 수화학 특성과 기능성, 용기 등
(Continued R&D)

3) 과학적 자료에 기반한 최적 지하수 수질보전 대책 마련 및 시행
(Management of groundwater quantity and quality to sustainably exploit groundwater)

고려대학교 KOREA UNIVERSITY

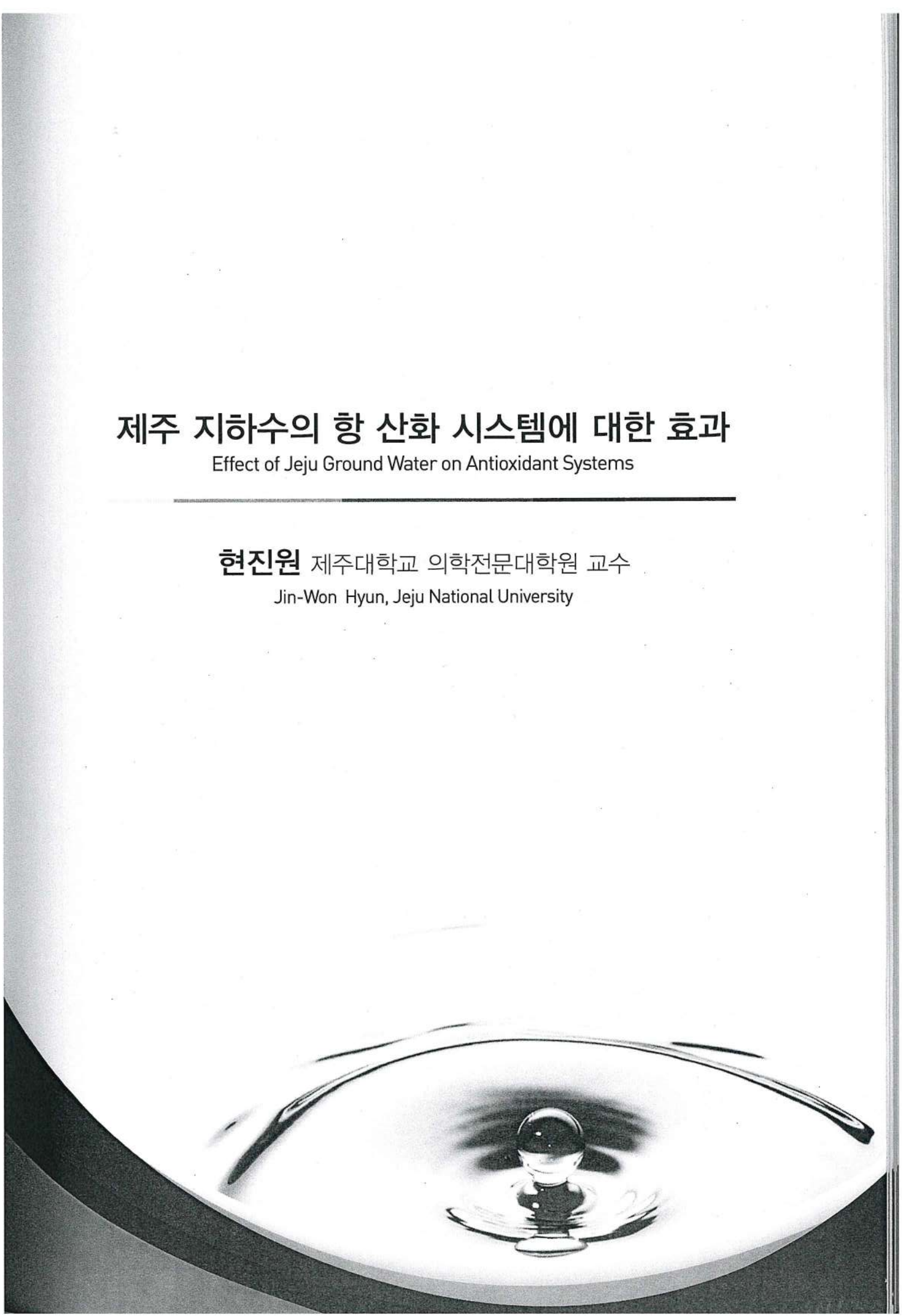
MEMO

제주 지하수의 항 산화 시스템에 대한 효과

Effect of Jeju Ground Water on Antioxidant Systems

현진원 제주대학교 의학전문대학원 교수

Jin-Won Hyun, Jeju National University



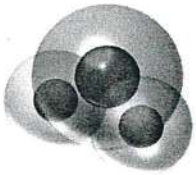
제주 지하수의 항 산화 시스템에 대한 효과

Effect of Jeju Ground Water on Antioxidant Systems

제주대학교 의학전문 대학원

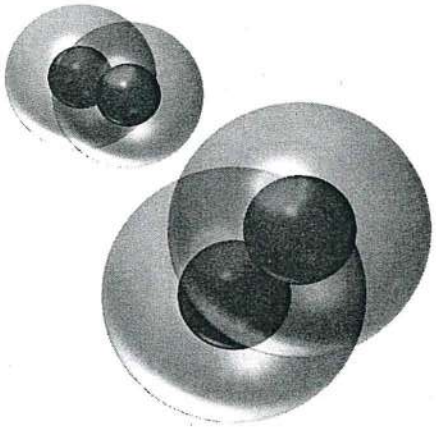
현 진 원


활성 산소종



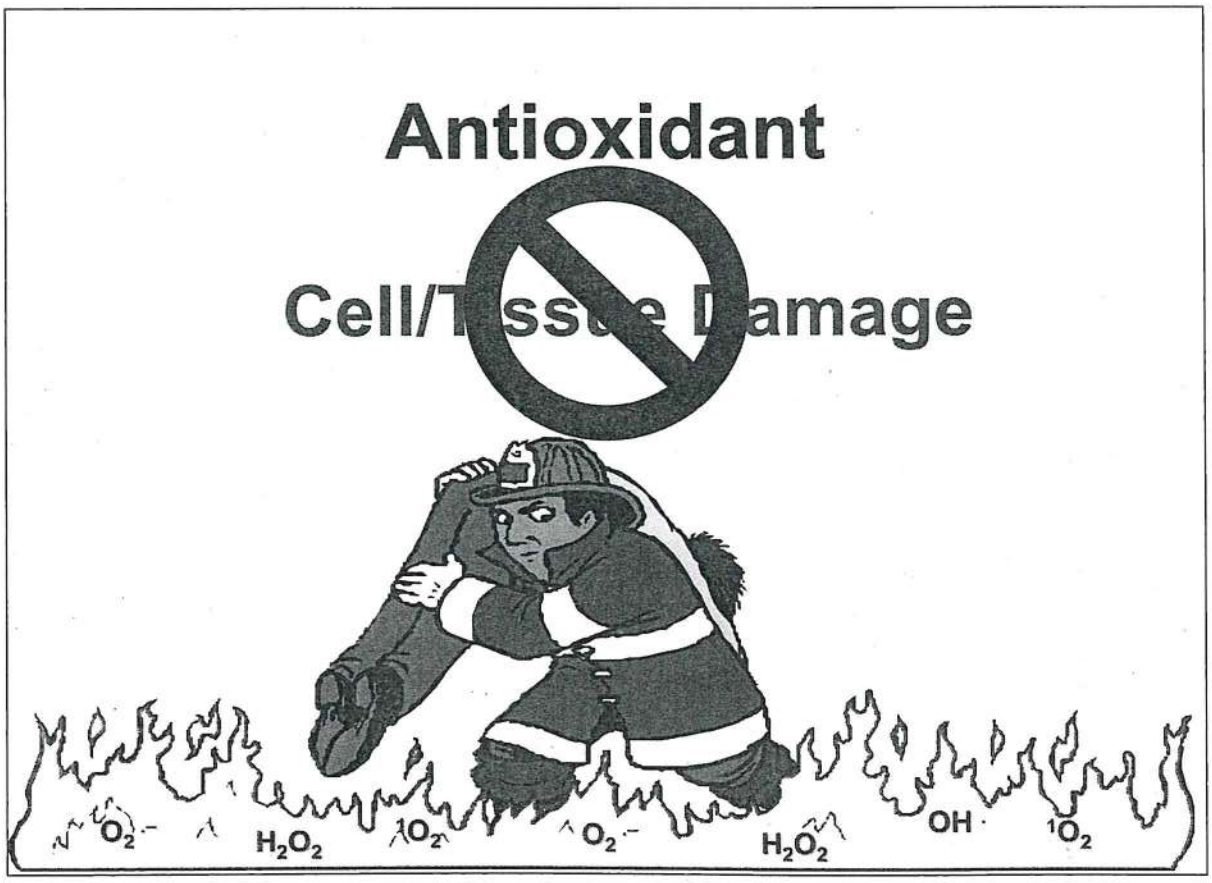
Reactive Oxygen Species (ROS)

Ö::Ö	·Ö::Ö	·Ö::Ö·
Oxygen	Superoxide anion	Peroxide
O_2	$\cdot O_2^-$	$\cdot O_2^{-2}$
H:Ö::Ö:H	·Ö:H	:Ö:H
Hydrogen Peroxide	Hydroxyl radical	Hydroxyl ion
H_2O_2	$\cdot OH$	OH^-



Oxidative Stress
(산화적 스트레스, 산화적 손상)

활성 산소종이 너무 많이 생성되거나 항 산화 시스템의 기능이 저하되는 상황에서 활성 산소종에 의해 세포가 유해 작용을 받는 상태



Defense System against Oxygen Radicals

Antioxidants

A. 효소계

1. Superoxide Dismutase $O_2^- + O_2^- \rightarrow 2H + H_2O_2$
2. Catalase $2H_2O_2 \rightarrow 2H_2O + O_2$
3. Glutathionine Peroxidase $H_2O_2 + 2GSH \rightarrow GSSG + 2H_2O$
4. Glutathionine Reductase $GSSG + NADPH + H^+ \rightarrow 2GSH + NADP^+$
5. Reduced Glutathione (GSH)
6. Heme Oxygenase (HO-1) Heme → Bilirubin + CO + Fe^{2+}

B. 비효소계 (ROS scavenging)

Vitamin C, E, Uric acid, Bilirubin etc.

Jeju Ground Water

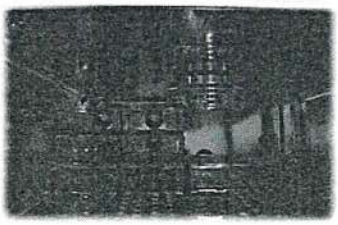
ROS ?

Antioxidants ?

Jeju 제주특별자치도개발공사
Jeju Special Self-Governing Province Development Corp.

S1

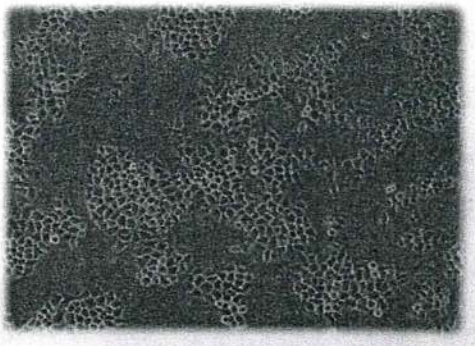
S3



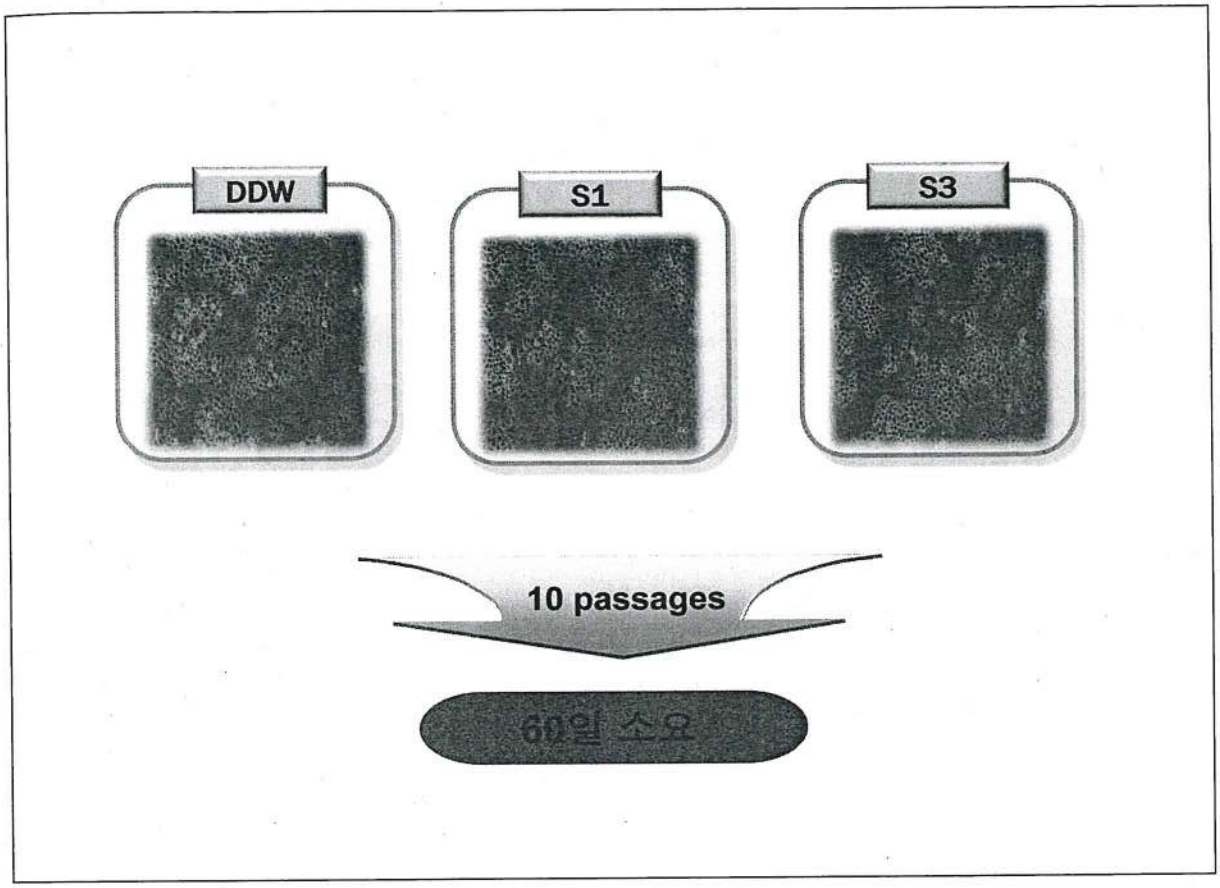
Cell Culture

Human hepatocyte-derived cell line

Chang liver cells



Media : RPMI -1640 with 10% FBS



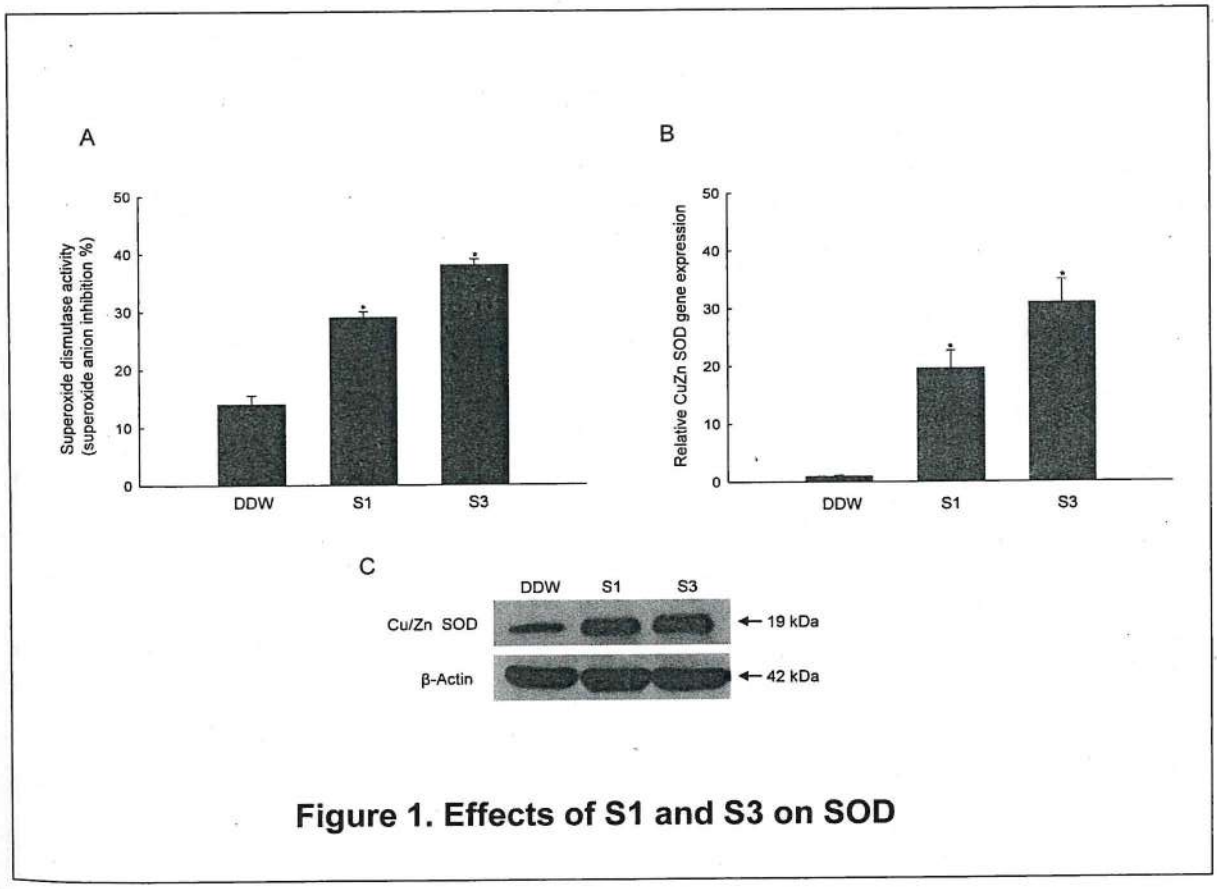


Figure 1. Effects of S1 and S3 on SOD

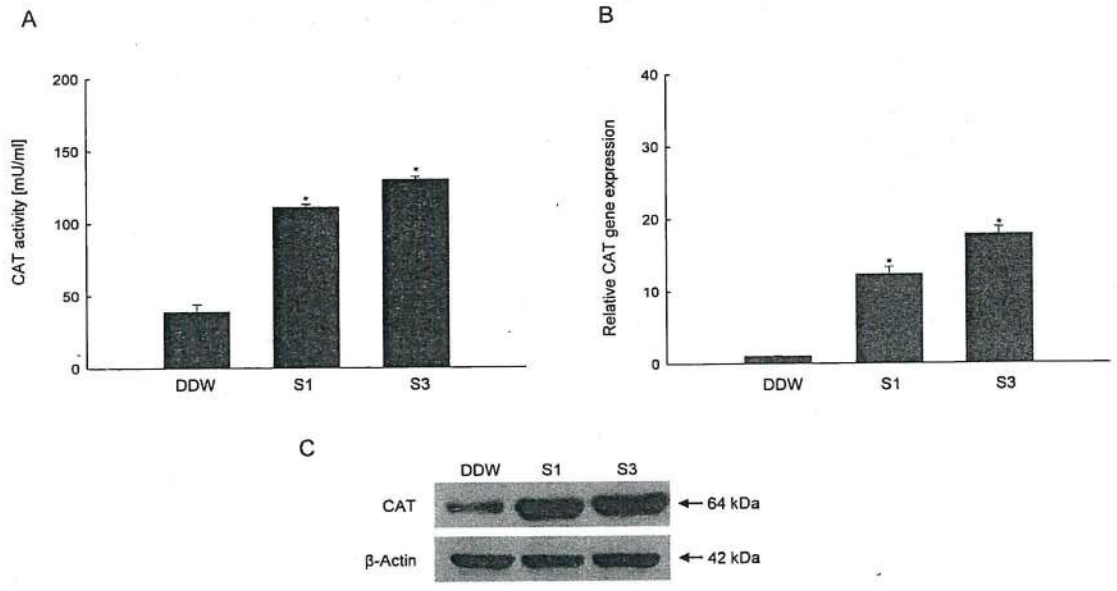


Figure 2. Effects of S1 and S3 on CAT

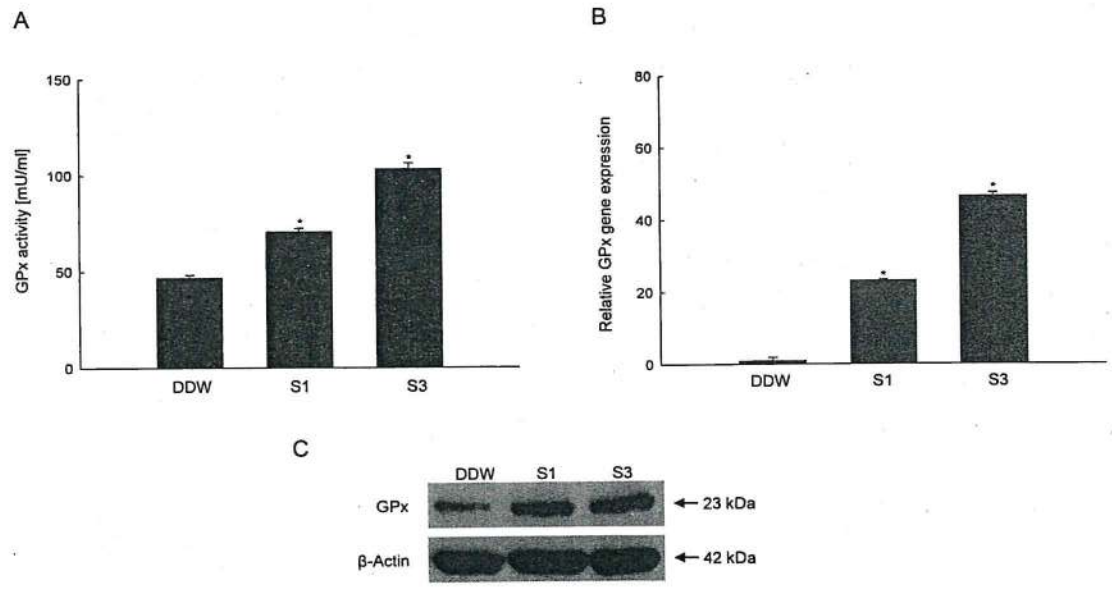


Figure 3. Effects of S1 and S3 on GPx

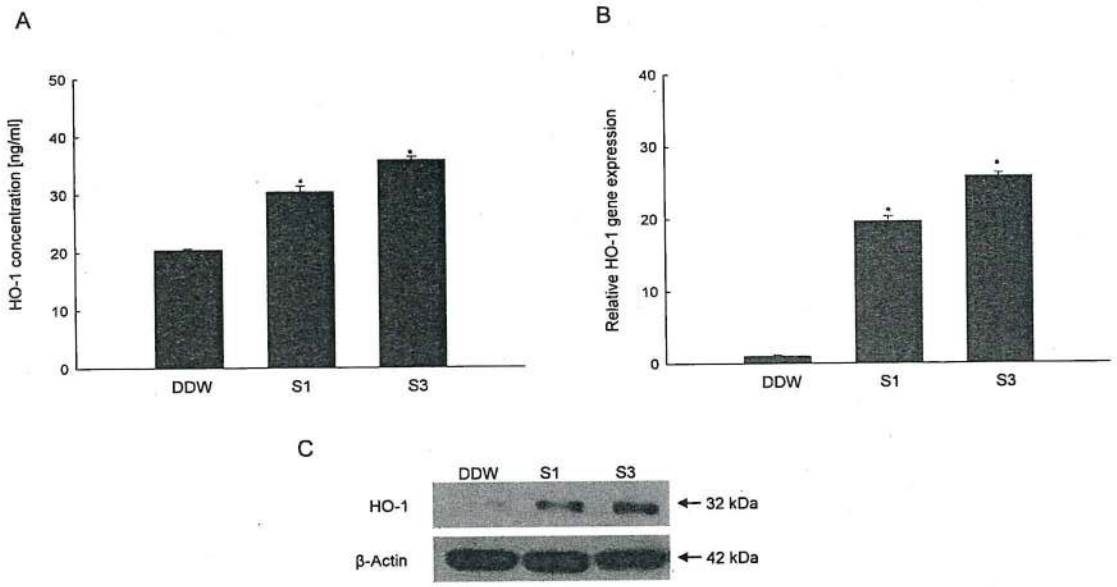
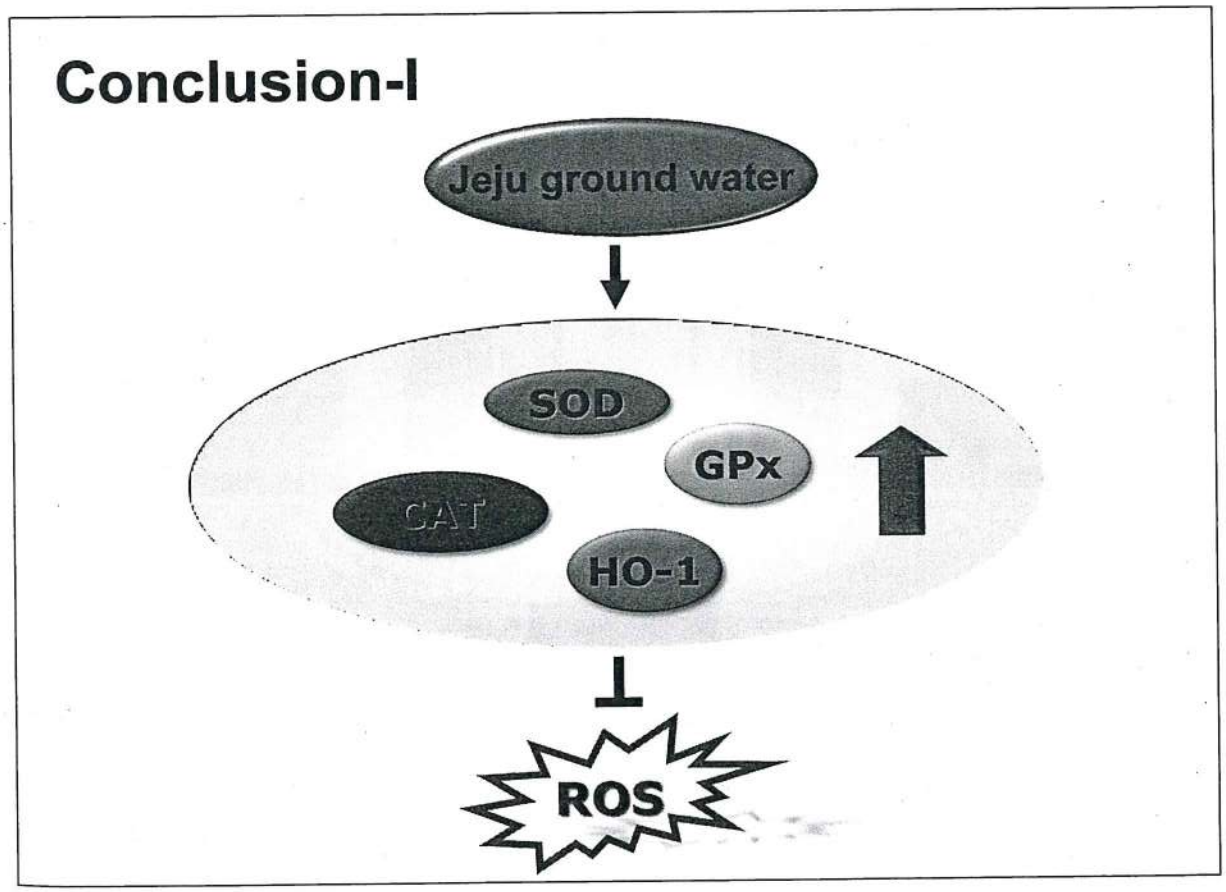


Figure 4. Effects of S1 and S3 on HO-1



Vanadium ion

Antioxidants ?

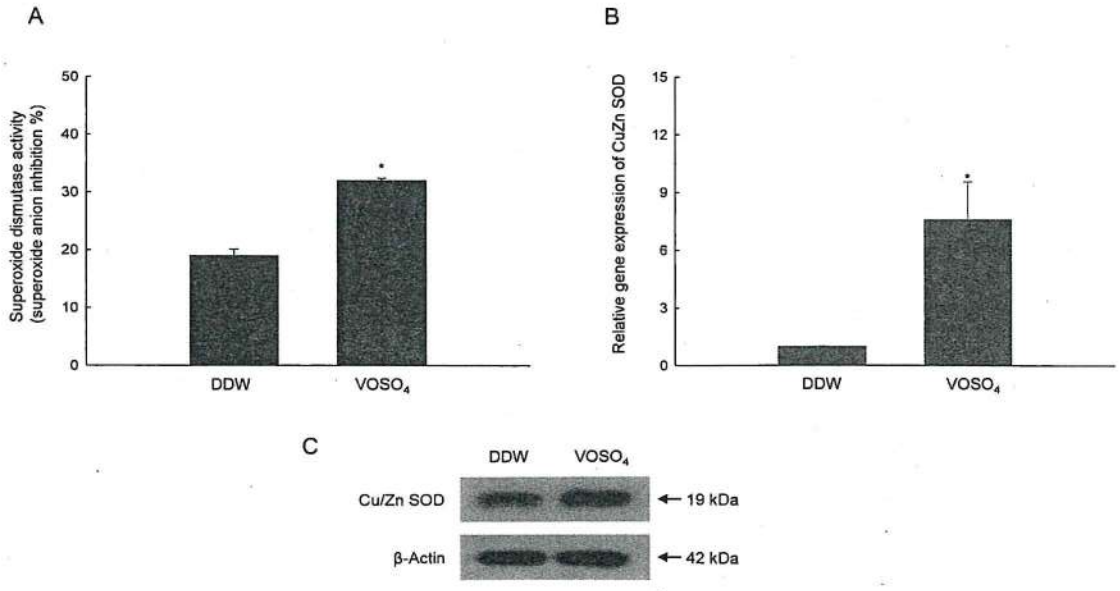


Figure 5. Effect of $VOSO_4$ on SOD

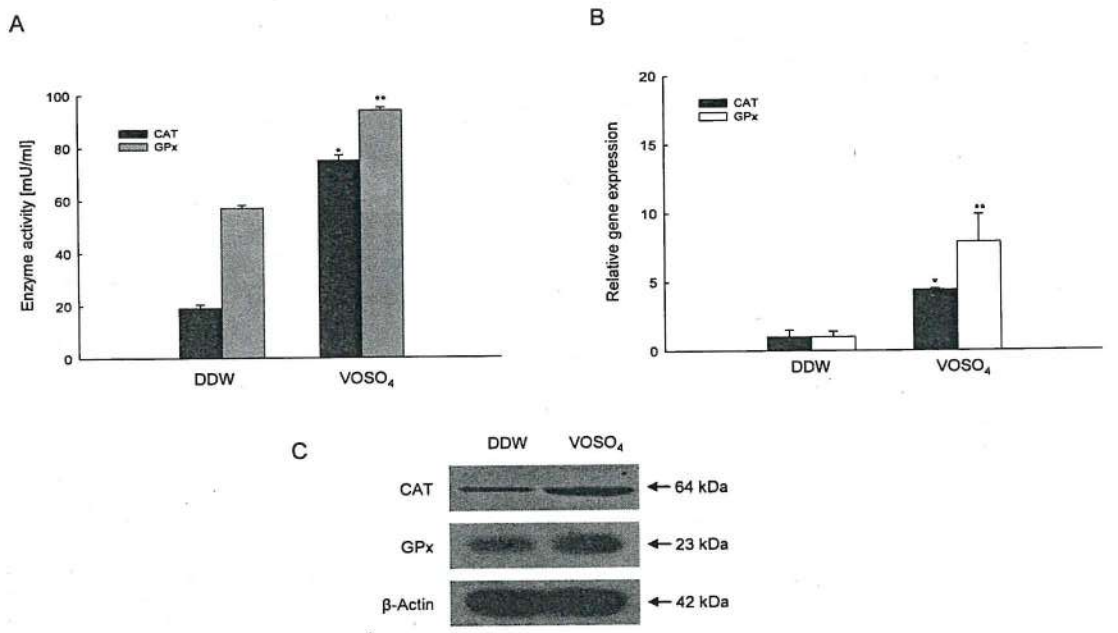


Figure 6. Effect of $VOSO_4$ on CAT and GPx activities

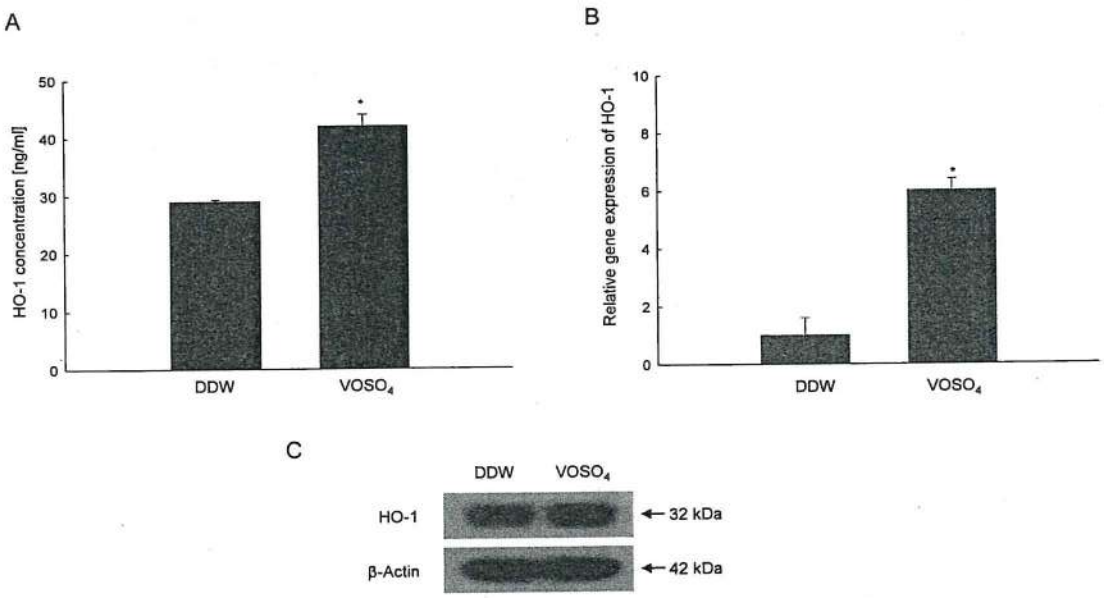
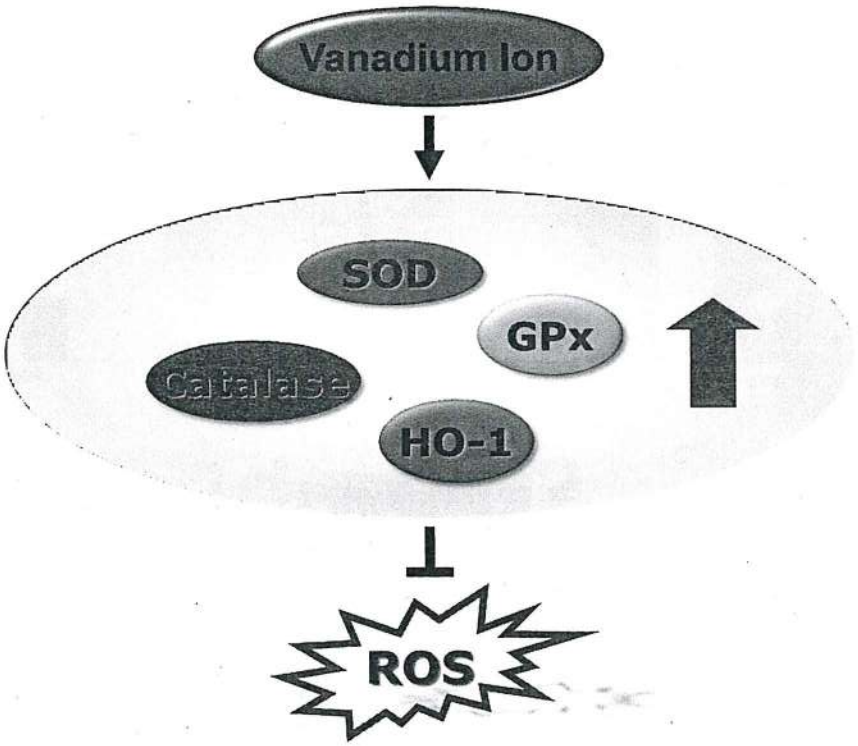


Figure 7. Effect of $VOSO_4$ on HO-1

Conclusion -II



Biol Trace Elem Res
DOI 10.1007/s12011-011-9277-5

Jeju Ground Water Containing Vanadium Enhances Antioxidant Systems in Human Liver Cells

Areum Daseul Kim · Rui Zhang · Kyoung Ah Kang · Ho Jin You · Kyung Goo Kang · Jin Won Hyun

(2012 *in press*)

Defense System

1. Superoxide Dismutase (SOD)

$$O_2^{\bullet-} + O_2^{\bullet-} + 2H^+ \longrightarrow H_2O_2$$

2. Catalase (CAT)

$$2H_2O_2 \longrightarrow 2H_2O + O_2$$

3. Glutathione Peroxidase (GPx)

$$H_2O_2 + 2GSH \longrightarrow GS\text{-}GS + 2H_2O$$

$$L\text{-}OOH + 2GSH \longrightarrow GS\text{-}GS + L\text{-}OH + H_2O$$

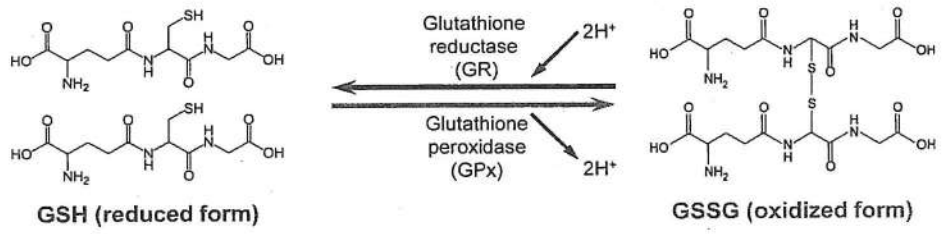
4. Reduced Glutathione (GSH)

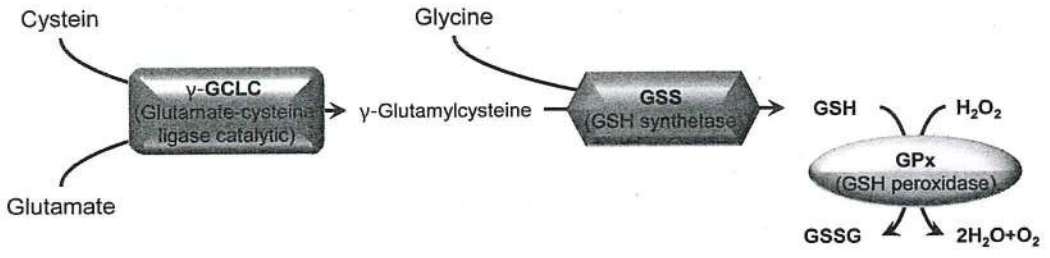
5. Heme Oxygenase (HO-1)

Heme ⟶ Bilirubin + CO + Fe^{2+}

Glutathione (GSH)

- Glutamate-Cystein-Glycine
- **Major endogenous antioxidant**
- Regulation of the nitric oxide cycle





11/50

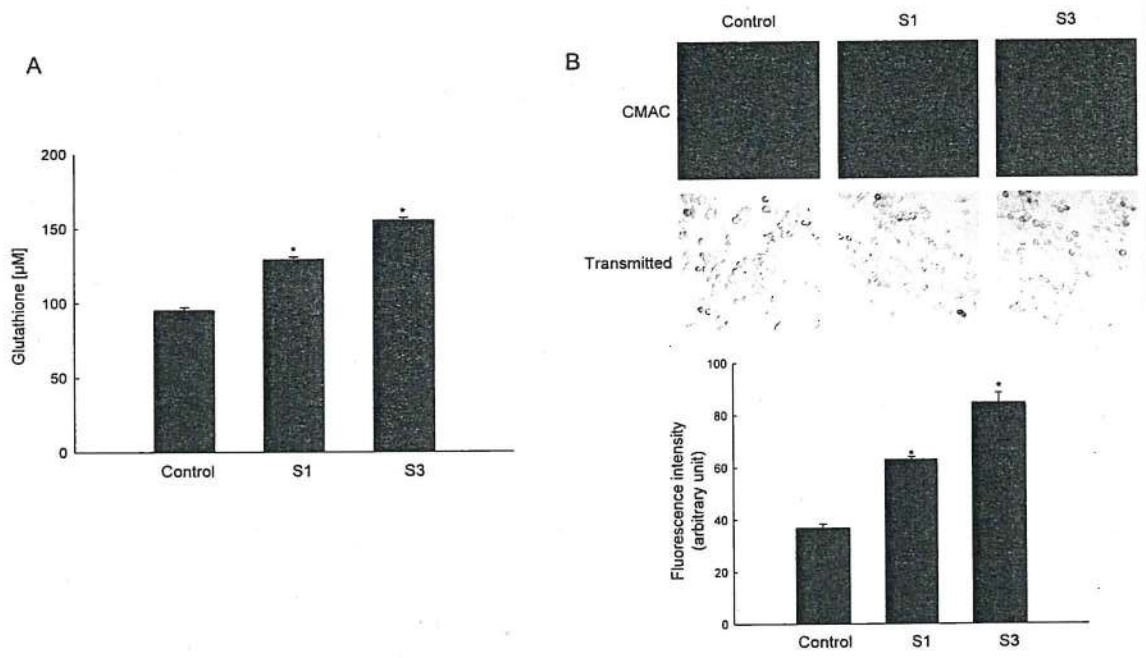
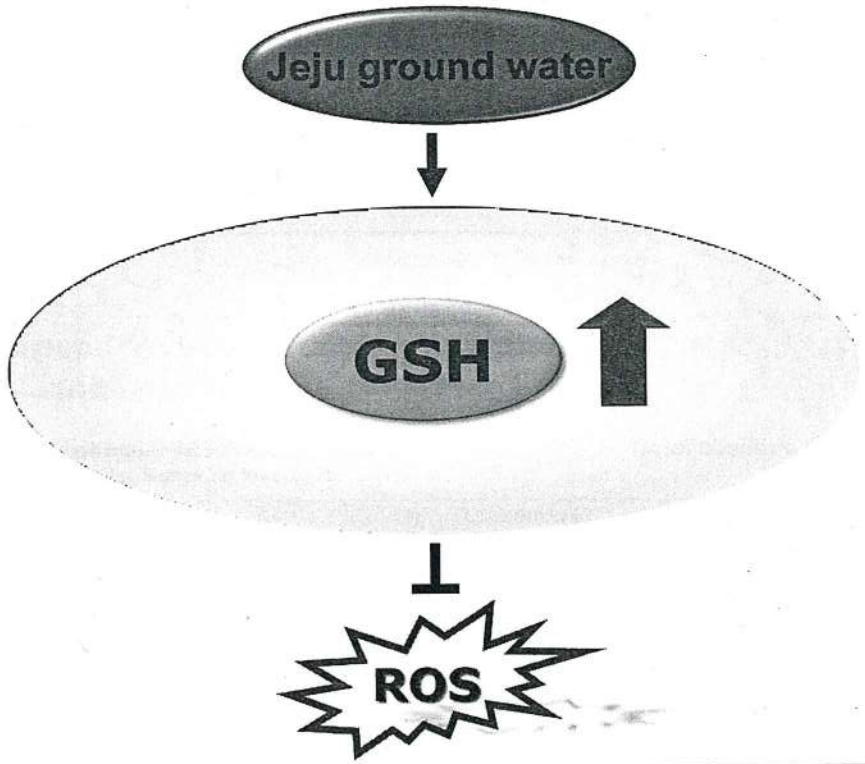


Figure 1. Jeju ground water increases cellular GSH level

Conclusion-I



Vanadium ion

GSH ?

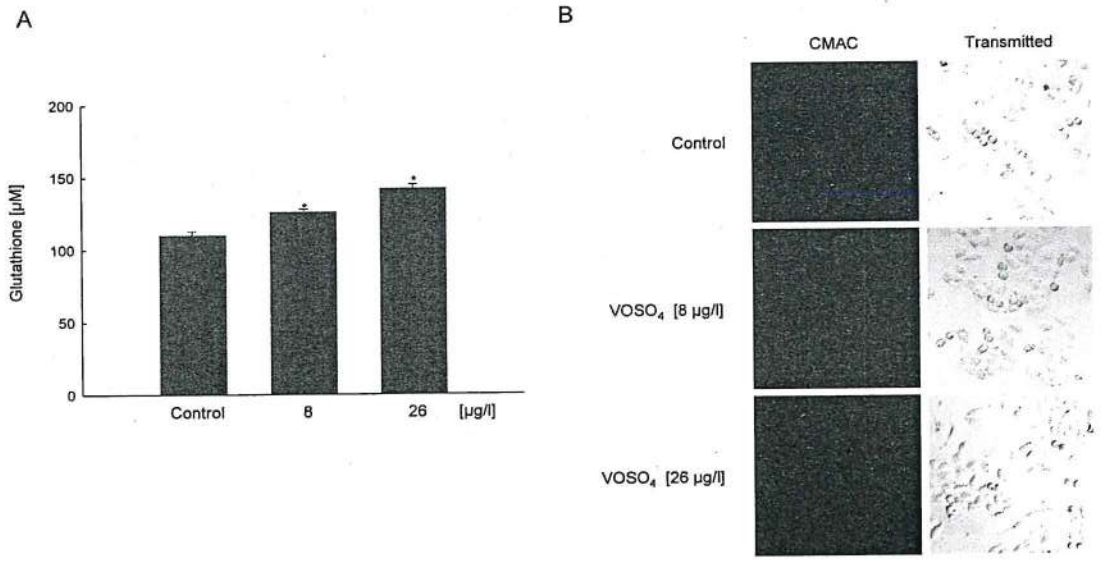


Figure 2. Vanadyl sulfate increases cellular GSH level and induces GCLC expression

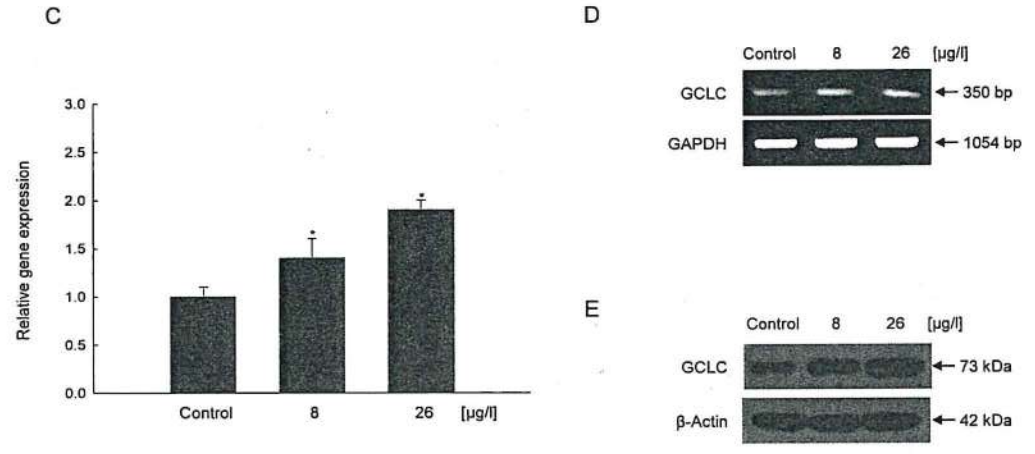


Figure 3. Vanadyl sulfate increases cellular GSH level and induces GCLC expression

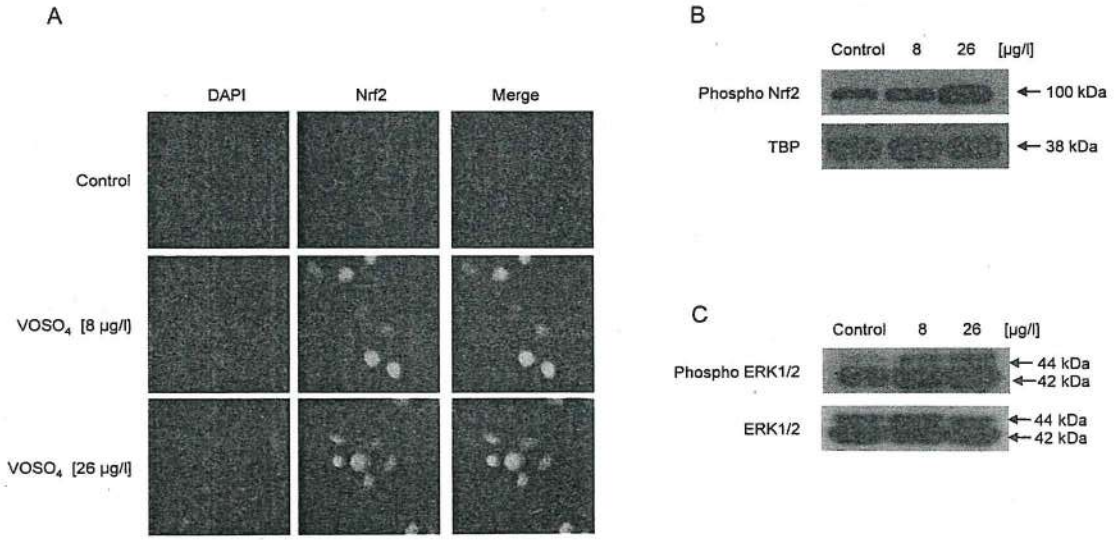
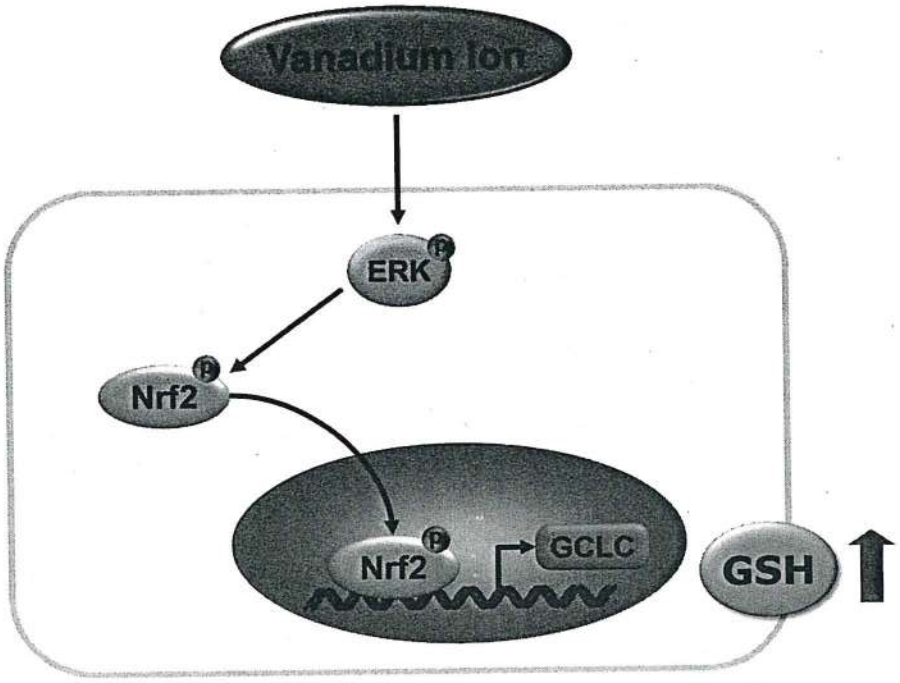


Figure 4. Vanadyl sulfate induces the activation of Nrf2 and ERK

Conclusion-II



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Article

Increased Glutathione Synthesis Following Nrf2 Activation by Vanadyl Sulfate in Human Chang Liver Cells

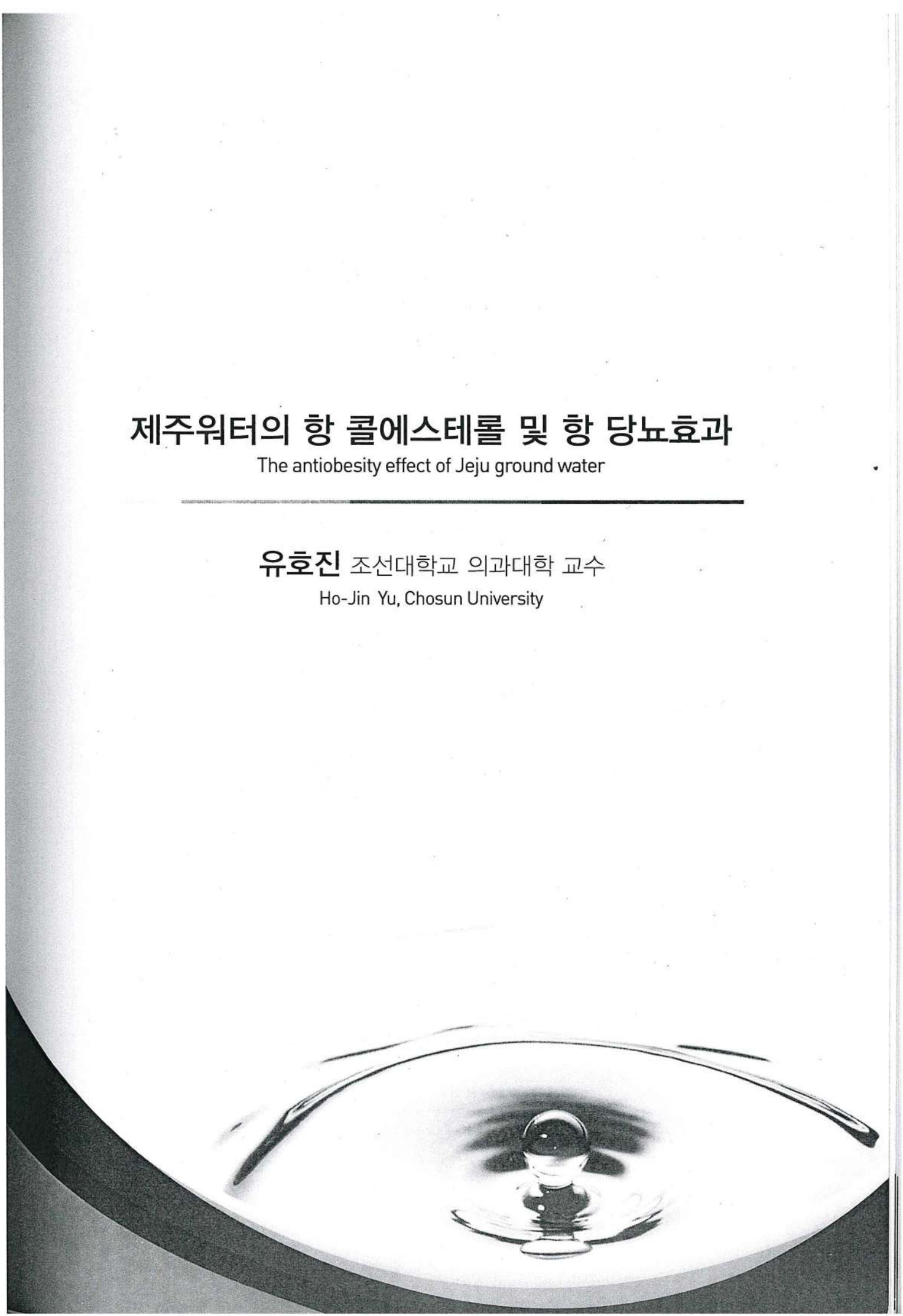
Areum Daseul Kim [1], Rui Zhang [1], Kyoung Ah Kang [2], Ho Jin You [3] and Jin Won Hyun [1,*]

제주워터의 항 콜에스테롤 및 항 당뇨효과

The antiobesity effect of Jeju ground water

유호진 조선대학교 의과대학 교수

Ho-Jin Yu, Chosun University



제주워터의 항 콜에스테롤 및 항 당뇨효과

조선대학교 의과대학 유호진

"Obesity"

Energy Intake >> Energy Expenditure

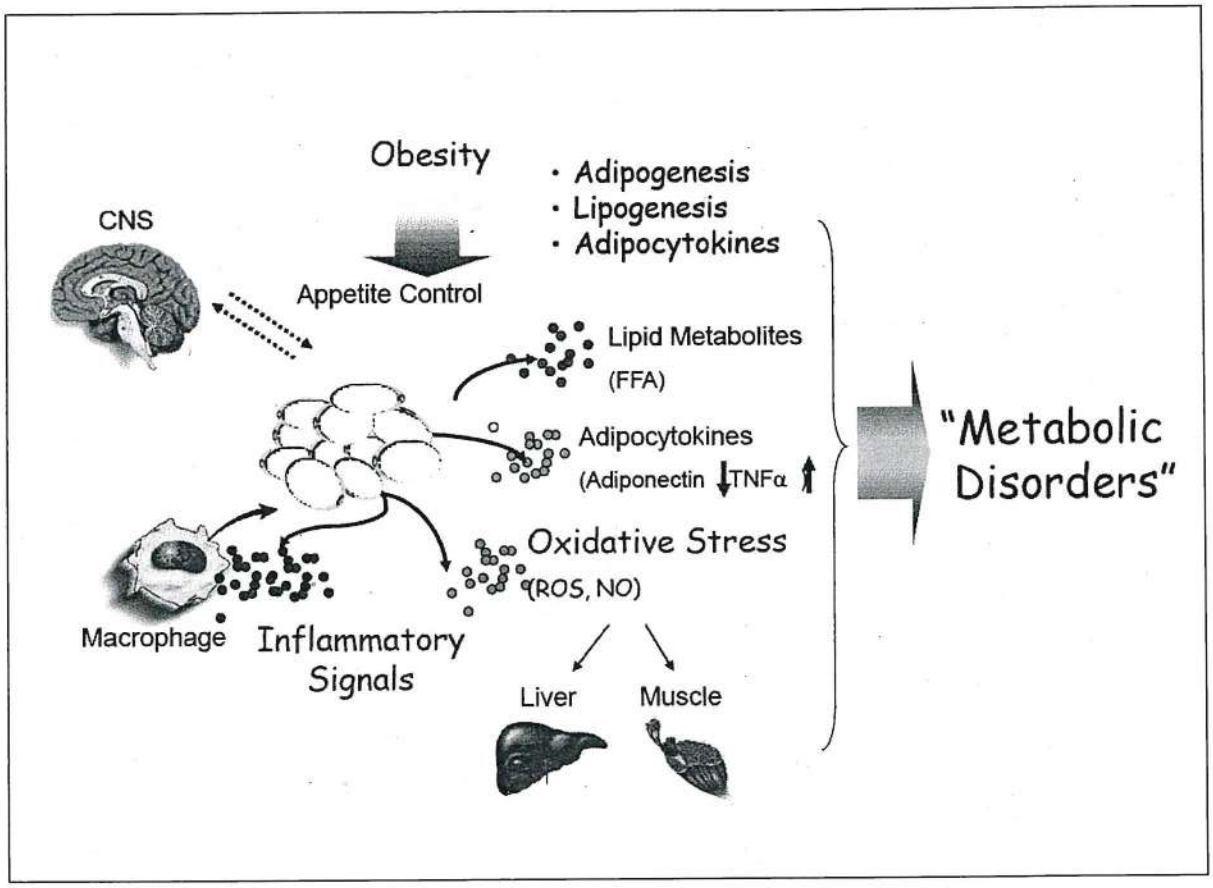
Modified from National Geographic (2004)

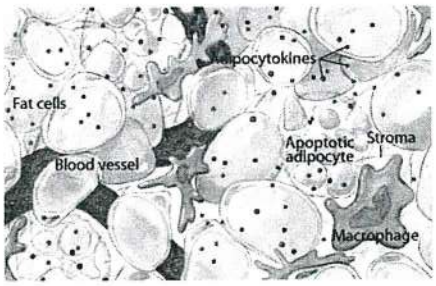
"Adipocyte Differentiation"

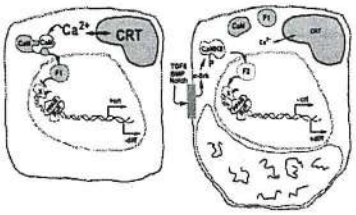
Increased Adipose Cell Number
Increased Adipose Cell Size
Increased Lipid Metabolism

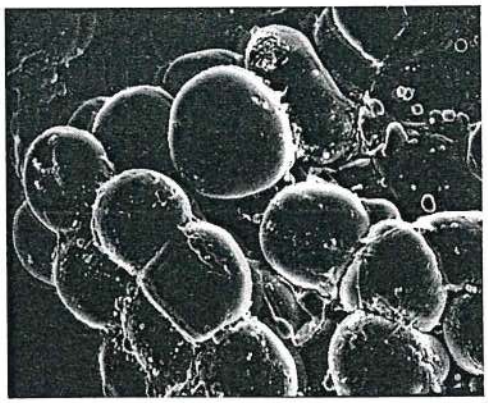
"Metabolic Disorders"

- Hyperlipidemia
- Hypercholesterolemia
- Hypertension
- Cardiovascular Diseases
- Cancer (Breast and Colon etc)
- Type II Diabetes & Insulin Resis.

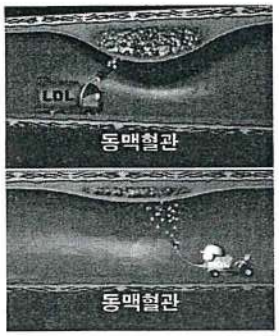

Obesity
• Adipogenesis
• Lipogenesis
• Adipocytokines
CNS
Appetite Control
Lipid Metabolites
(FFA)
Adipocytokines
(Adiponectin ↓TNFα ↑)
Oxidative Stress
(ROS, NO)
Macrophage
Inflammatory Signals
Liver
Muscle
"Metabolic Disorders"

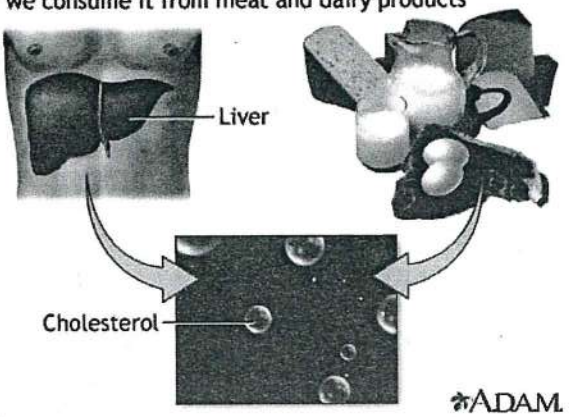

Adipocytokines
Fat cells
Blood vessel
Apoptotic adipocyte
Stroma
Macrophage


Ca2+
CRT

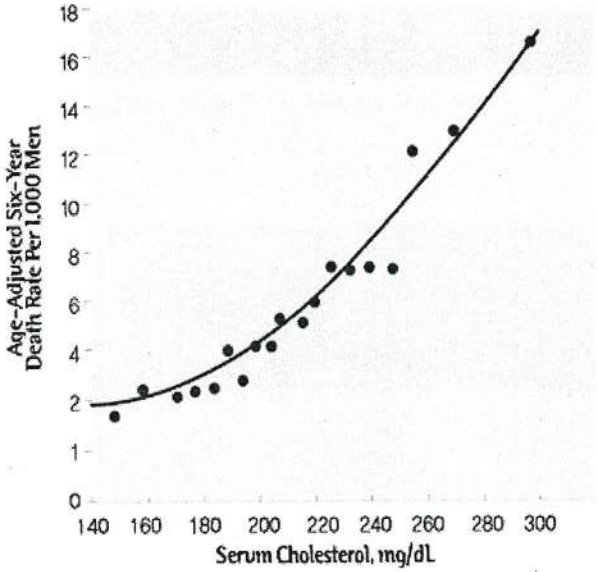


고지혈증

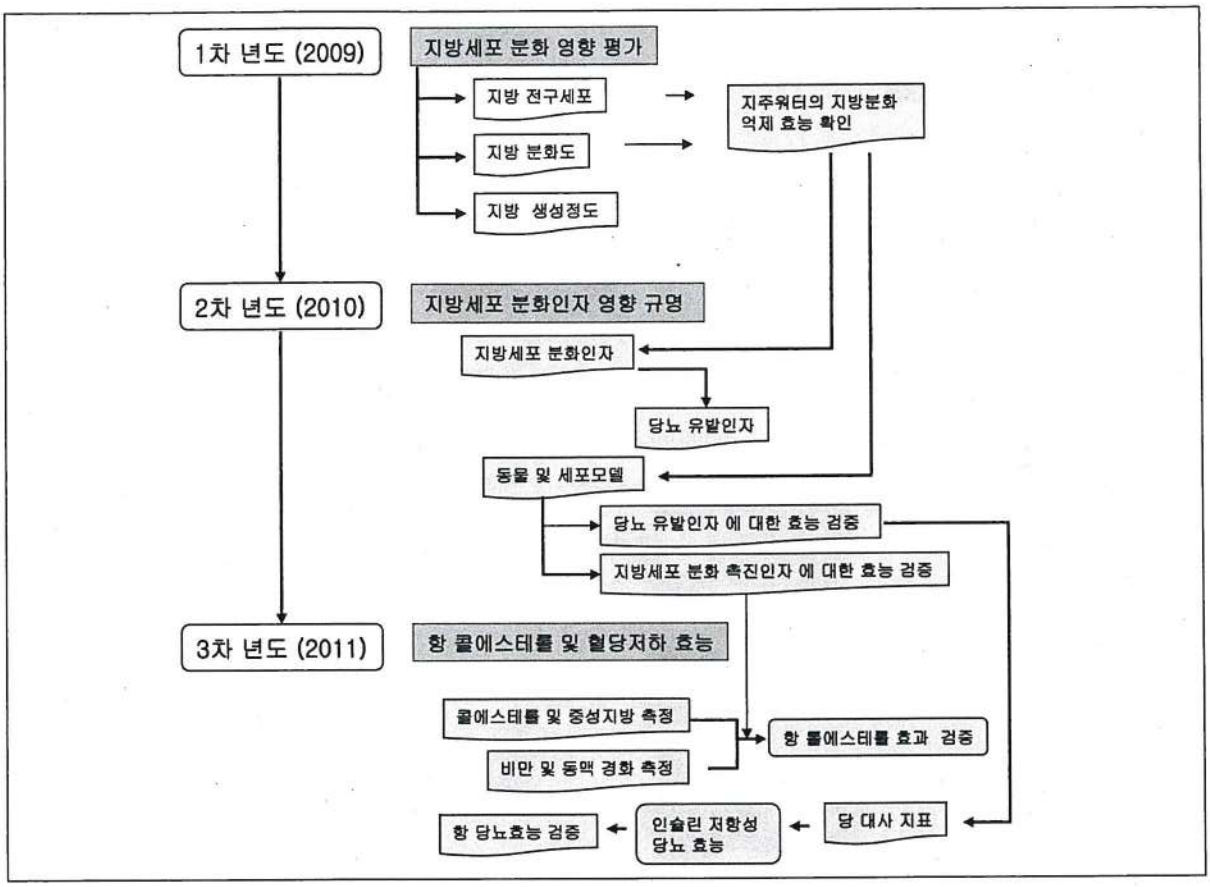




361,662명의 환자를 평균 6년간 추적연구한 결과
혈중 콜레스테롤과 관상동맥으로 인한 사망의 관계



Stamler J et al : JAMA 256 : 2823, 1986


1차 년도 (2009)
지방세포 분화 영향 평가
지방 전구세포
지방 분화도
지방 생성정도
지주워터의 지방분화 억제 효능 확인
2차 년도 (2010)
지방세포 분화인자 영향 규명
지방세포 분화인자
당뇨 유발인자
동물 및 세포모델
당뇨 유발인자 에 대한 효능 검증
지방세포 분화 촉진인자 에 대한 효능 검증
3차 년도 (2011)
항 콜에스테롤 및 혈당저하 효능
콜에스테롤 및 중성지방 측정
비만 및 동맥 경화 측정
항 콜에스테롤 효과 검증
항 당뇨효능 검증
인슐린 저항성 당뇨 효능
당 대사 지표

연구 결과

지방세포 분화에 미치는 영향 평가

preadipocytes (지방전구세포)

↓ Differentiation (분화)

adipocytes (지방세포)

1. 지방세포수 증가
2. 지방세포 크기증가
3. 지방 대사 증가

평가 시료

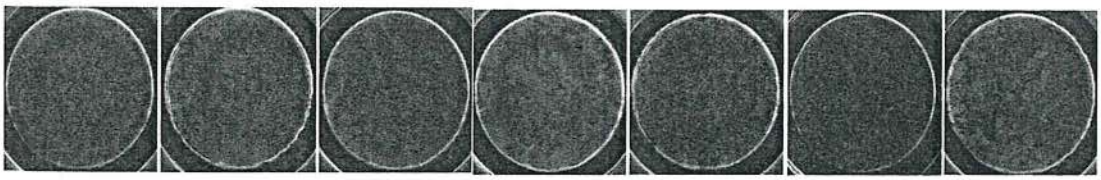
- 증류수
- S1
- S2
- S3
- 서울 수돗물
- 에비앙
- 롯데 아이리스

지방세포분화 및 지방 생성에 미치는 영향

Oil Red O staining (저배율)

- differentiation for 2 weeks (48 well)

증류수 S-1 S-2 S-3 서울 수돗물 외국생수 (E사) 국내생수 (I 사)

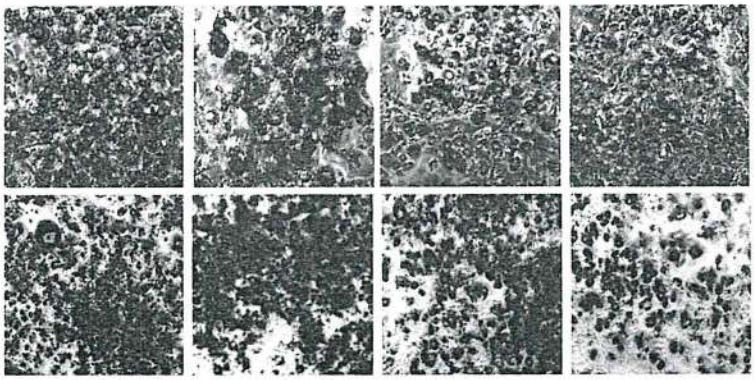


지방세포분화 및 지방 생성에 미치는 영향

Oil Red O staining (고배율)

- differentiation for 2 weeks (48 well)

증류수 S-1 S-2 S-3



지방세포분화 및 지방 생성에 미치는 영향

Oil Red O staining (고배율)

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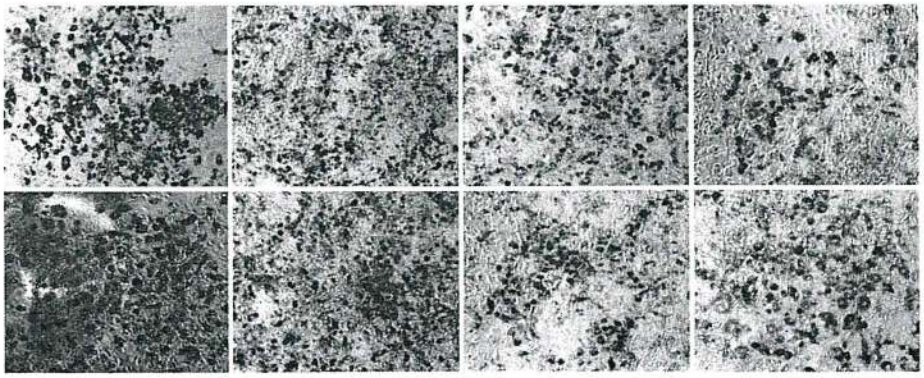
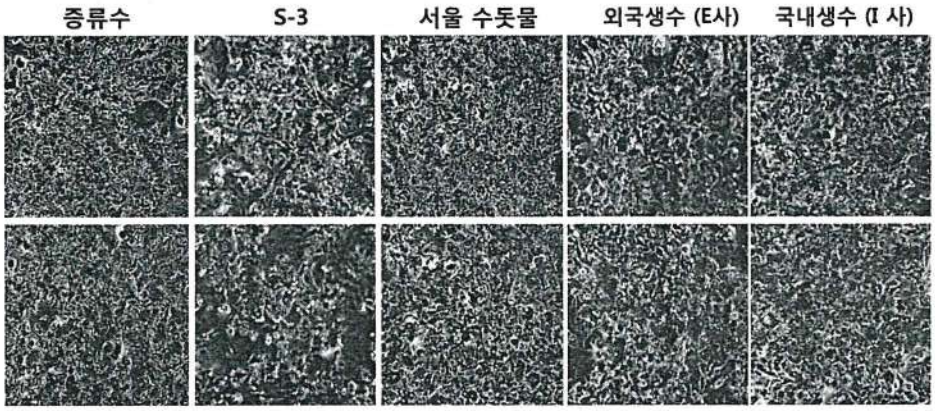


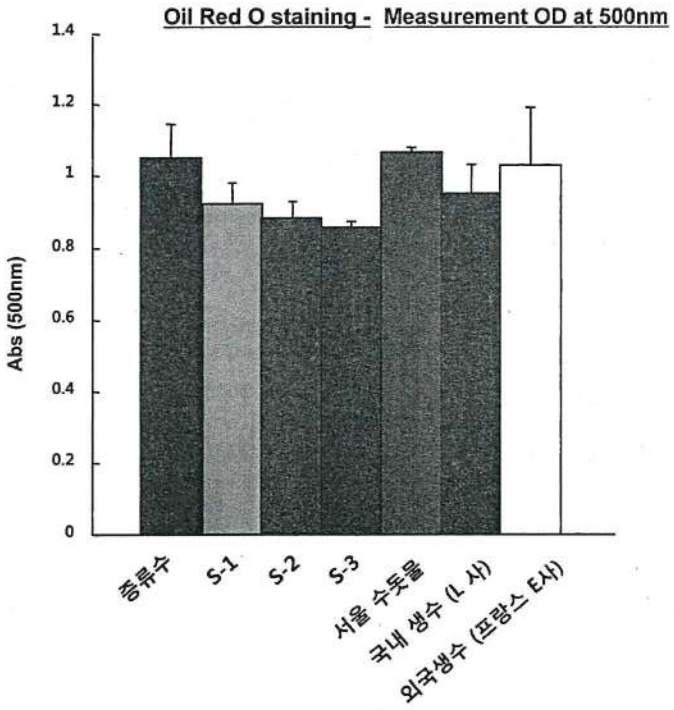
지방세포분화 및 지방 생성에 미치는 영향

Oil Red O staining (고배율)

- differentiation for 2 weeks (48 well)



지방세포분화 및 지방 생성에 미치는 영향



2 차년도 내용

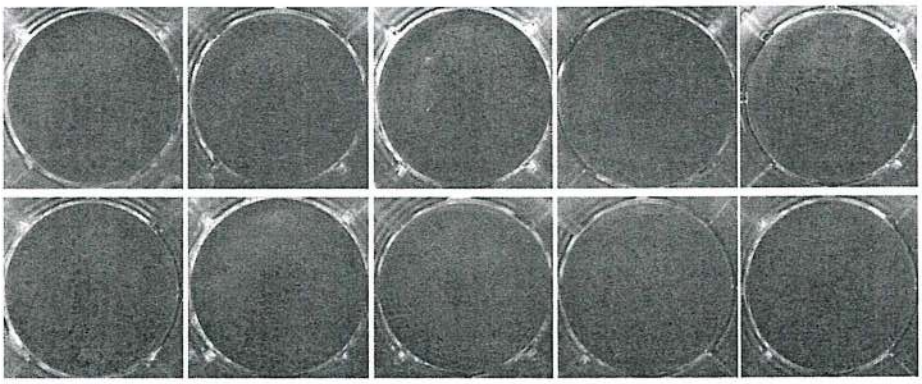
지방세포분화 및 지방 생성에 미치는 영향

Oil Red O staining (저배율)

- differentiation for 10 days (48 well)

정수기
(청호나이스)

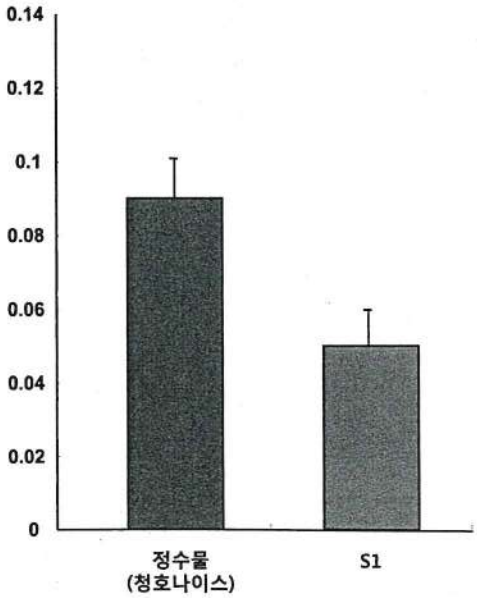
S1



2 차년도 내용

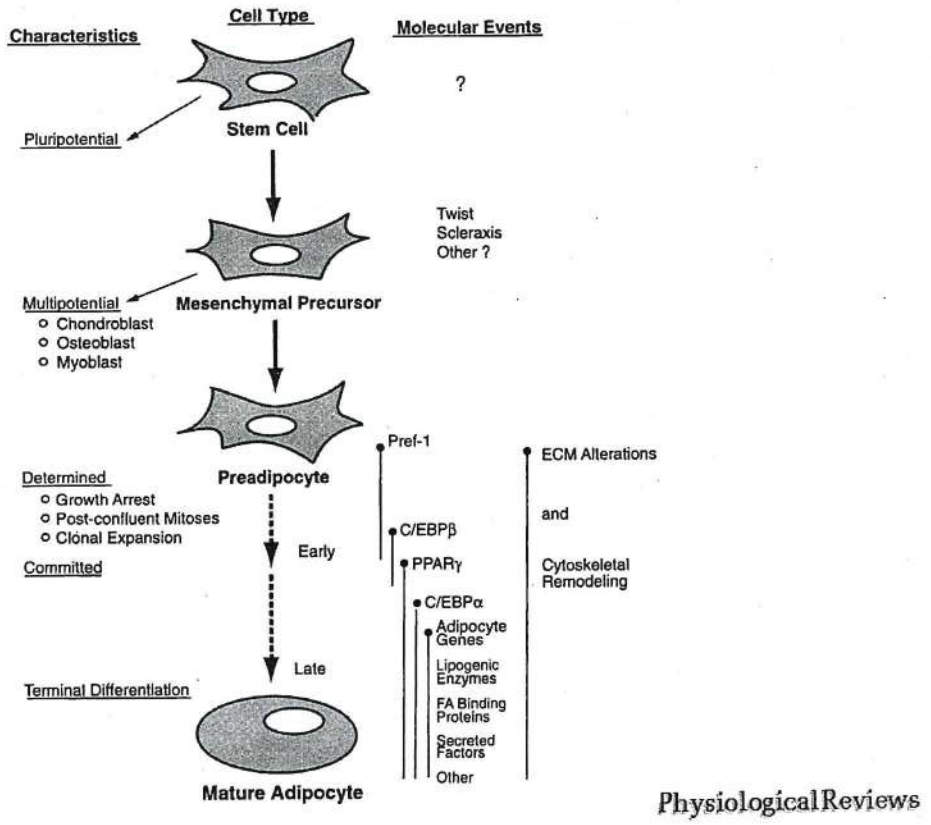
지방세포분화 및 지방 생성에 미치는 영향

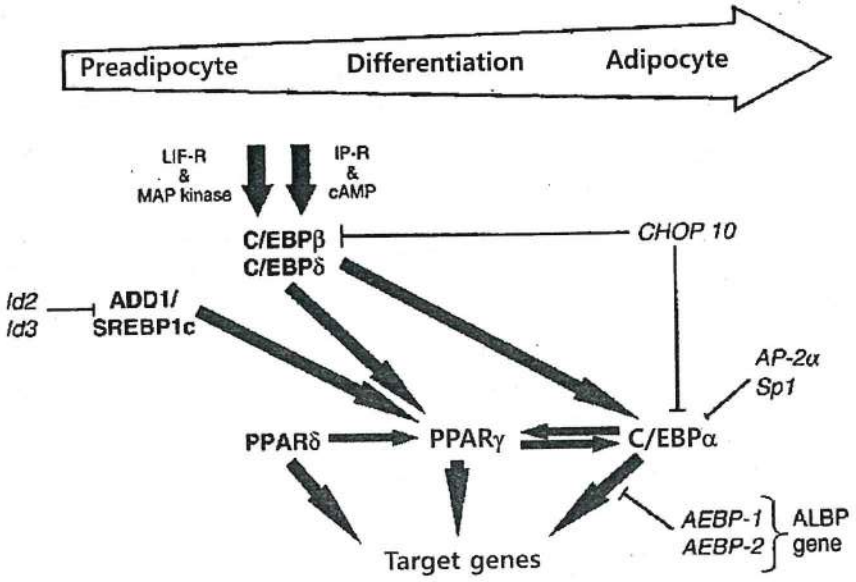
Oil Red O staining - Measurement OD at 500nm



지방 분화 조절 인자에 미치는 영향 평가

1. PPARγ
2. C/EBPα
3. aP2 (Fatty acid-binding protein 2)
4. LPL (adipocyte lipoprotein lipase)
5. Leptin
6. Pref-1 (preadipocyte secreted factor-1)
7. Adiponectin





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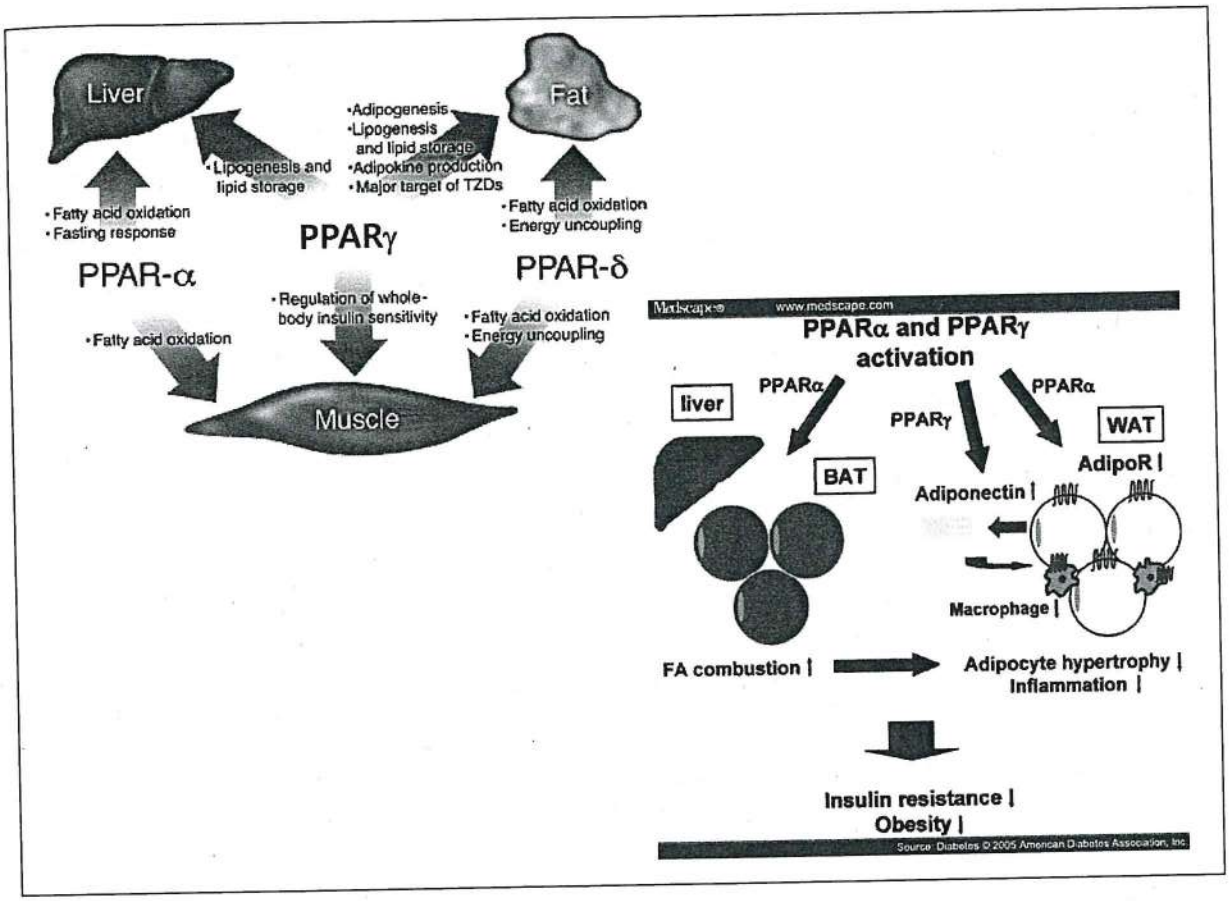
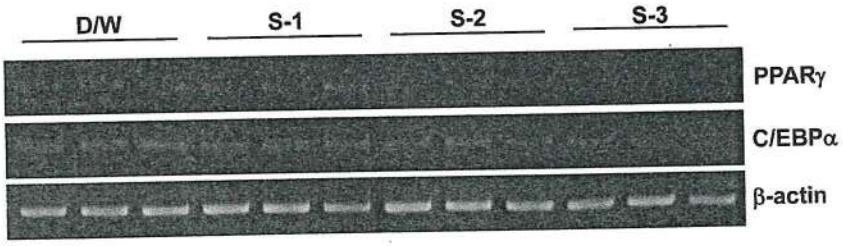
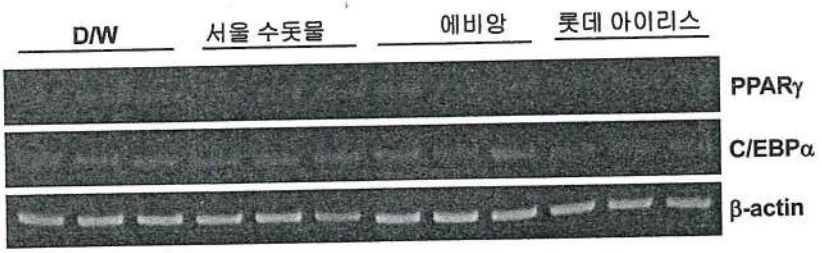
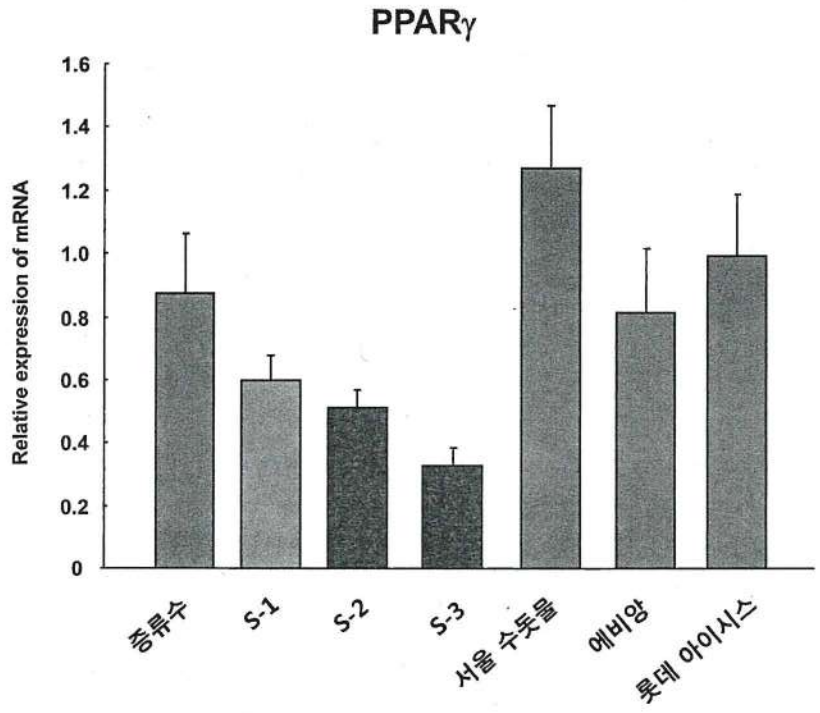
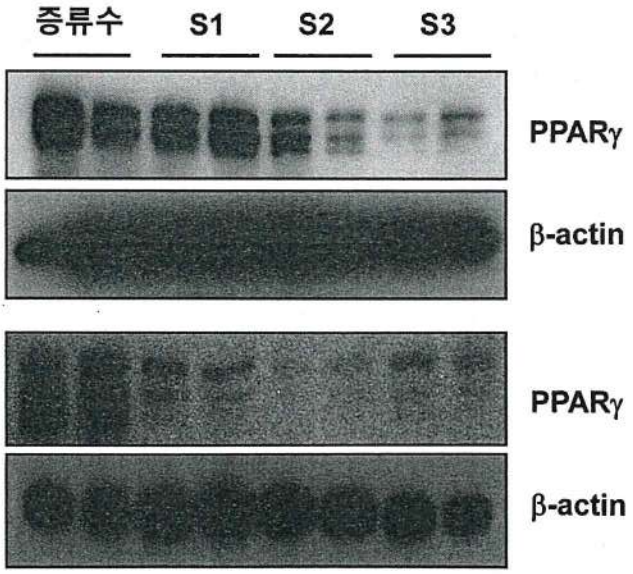


지방세포 분화인자 발현에 미치는 영향






PPARγ
Relative expression of mRNA
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0
증류수
S-1
S-2
S-3
서울 수돗물
에비앙
롯데 아이시스


증류수
S1
S2
S3
PPARγ
β-actin
PPARγ
β-actin

지방 분화 조절 인자에 미치는 영향 평가

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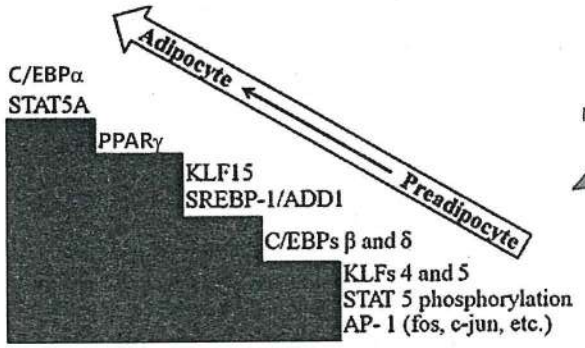
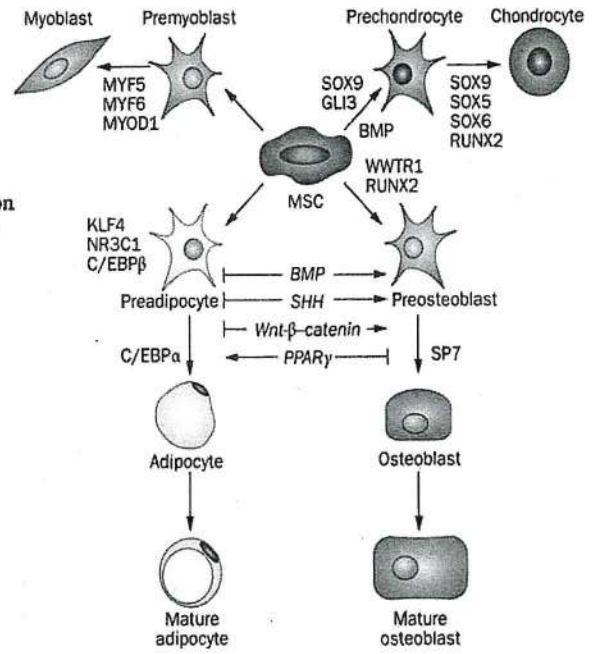
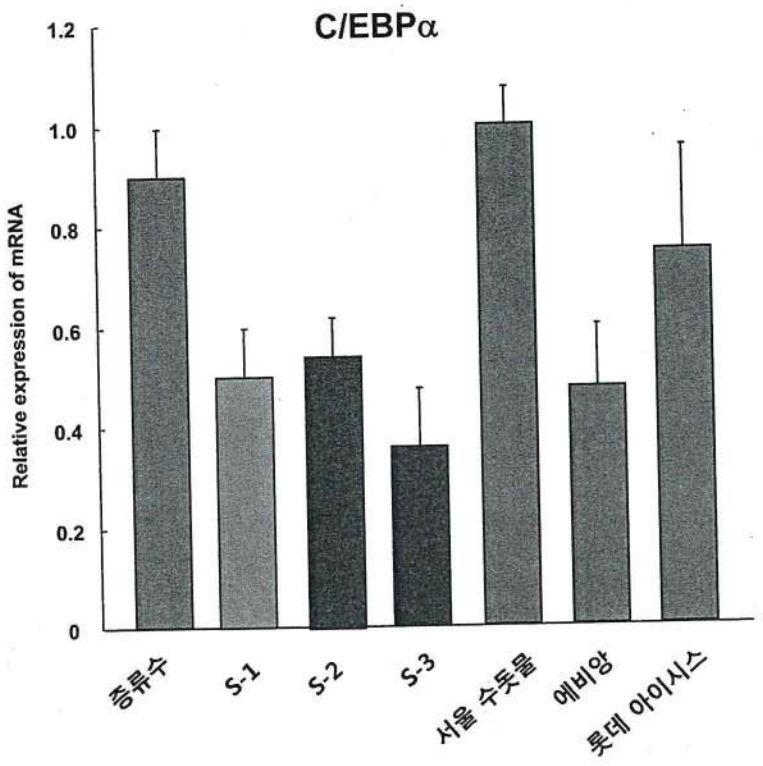
7. Adiponectin







지방 분화 조절 인자에 미치는 영향 평가

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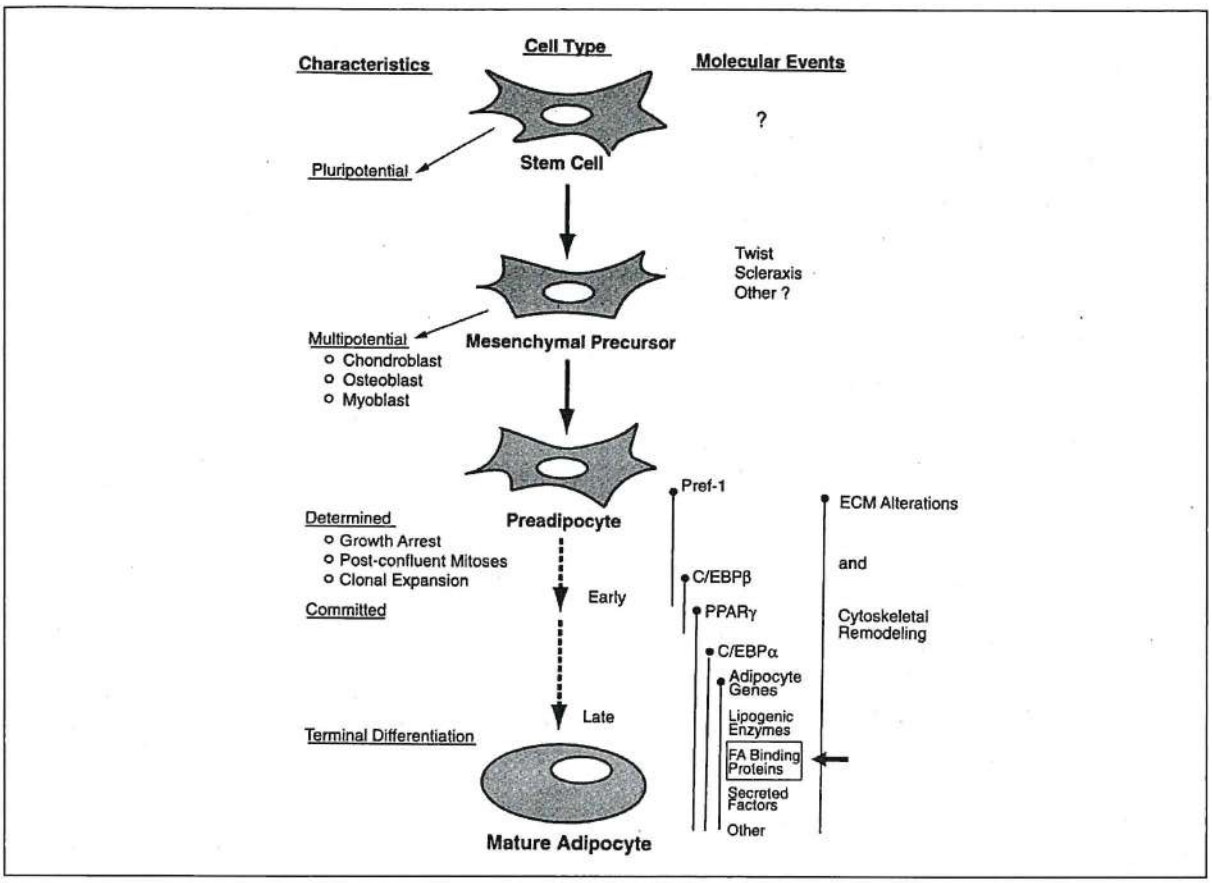
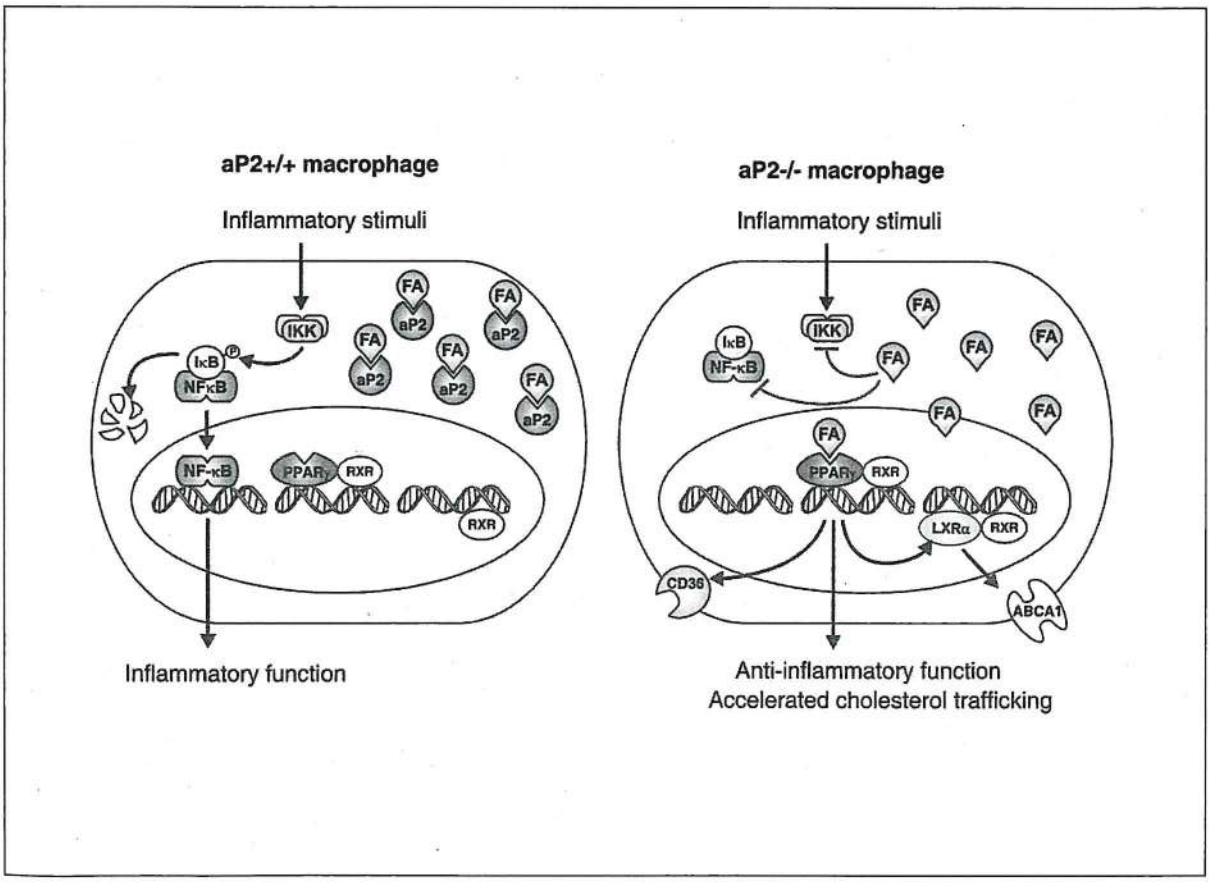
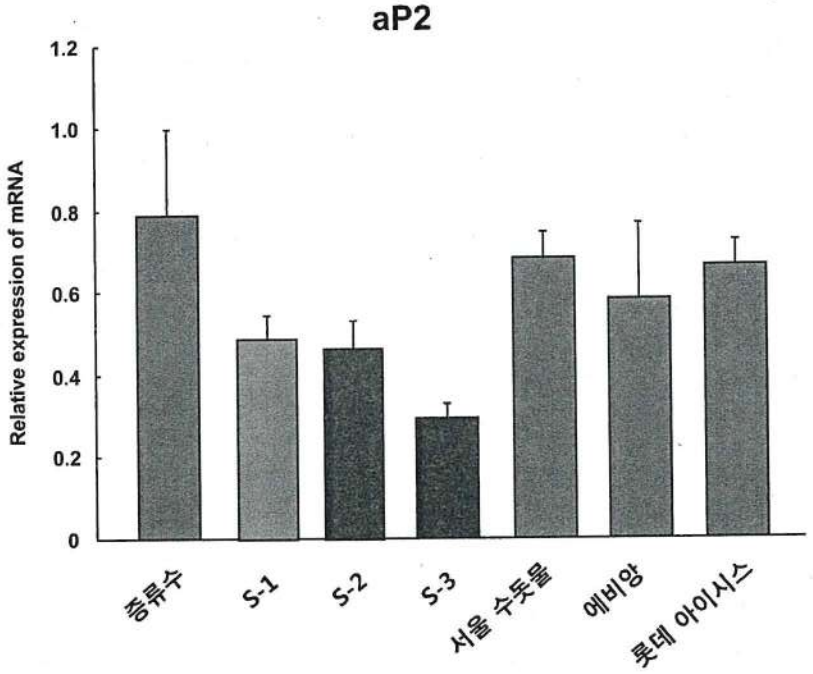

Characteristics
Cell Type
Molecular Events
?
Pluripotential
Stem Cell
Twist
Scleraxis
Other ?
Multipotential
Mesenchymal Precursor
Chondroblast
Osteoblast
Myoblast
Pref-1
ECM Alterations
Determined
Preadipocyte
Growth Arrest
Post-confluent Mitoses
Clonal Expansion
and
C/EBPβ
Early
Committed
PPARγ
Cytoskeletal Remodeling
C/EBPα
Adipocyte Genes
Late
Lipogenic Enzymes
Terminal Differentiation
FA Binding Proteins
Secreted Factors
Other
Mature Adipocyte


aP2+/+ macrophage
Inflammatory stimuli
IKK
IκB
NFκB
FA
aP2
NF-κB
PPARγ
RXR
Inflammatory function
aP2-/- macrophage
Inflammatory stimuli
IKK
IκB
NF-κB
FA
PPARγ
RXR
LXRα
CD36
ABCA1
Anti-inflammatory function
Accelerated cholesterol trafficking



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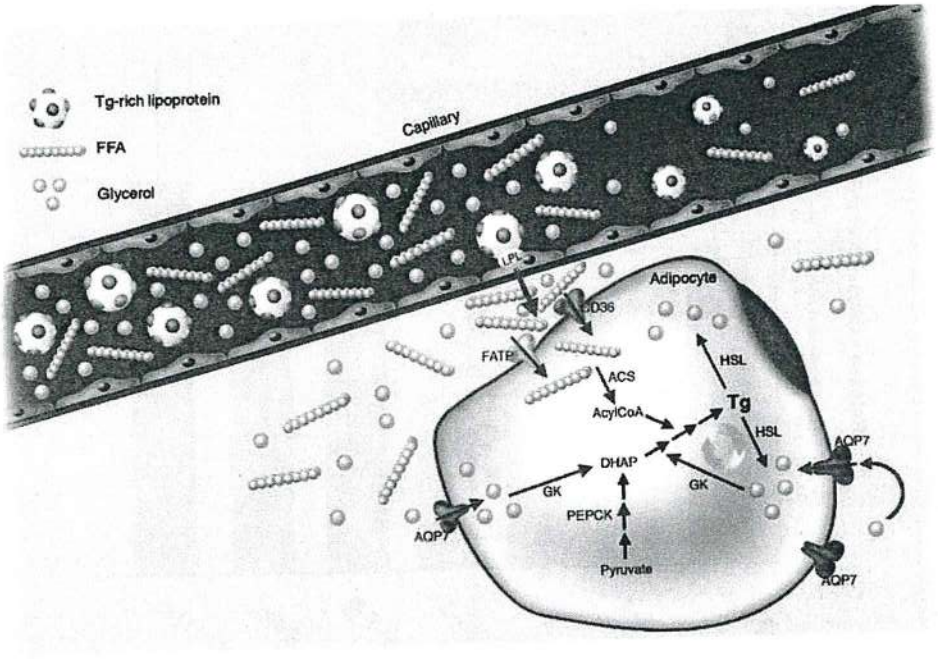
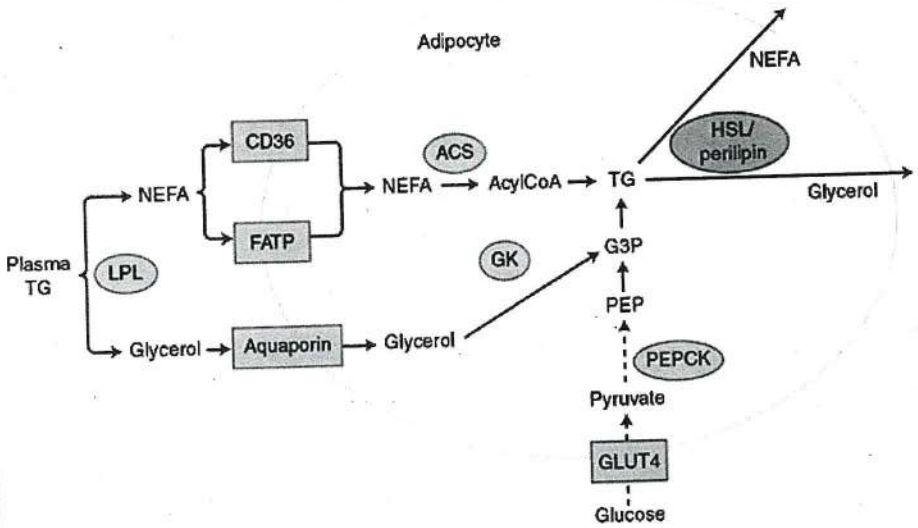
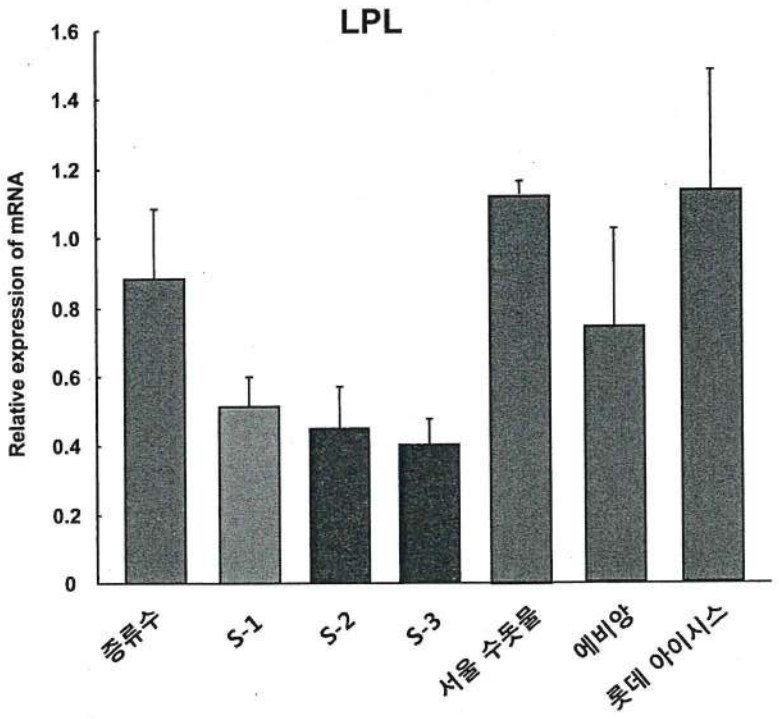




PPARγ target genes and adipocyte metabolism

Expert Reviews in Molecular Medicine ©2005 Cambridge University Press



지방 분화 조절 인자에 미치는 영향 평가

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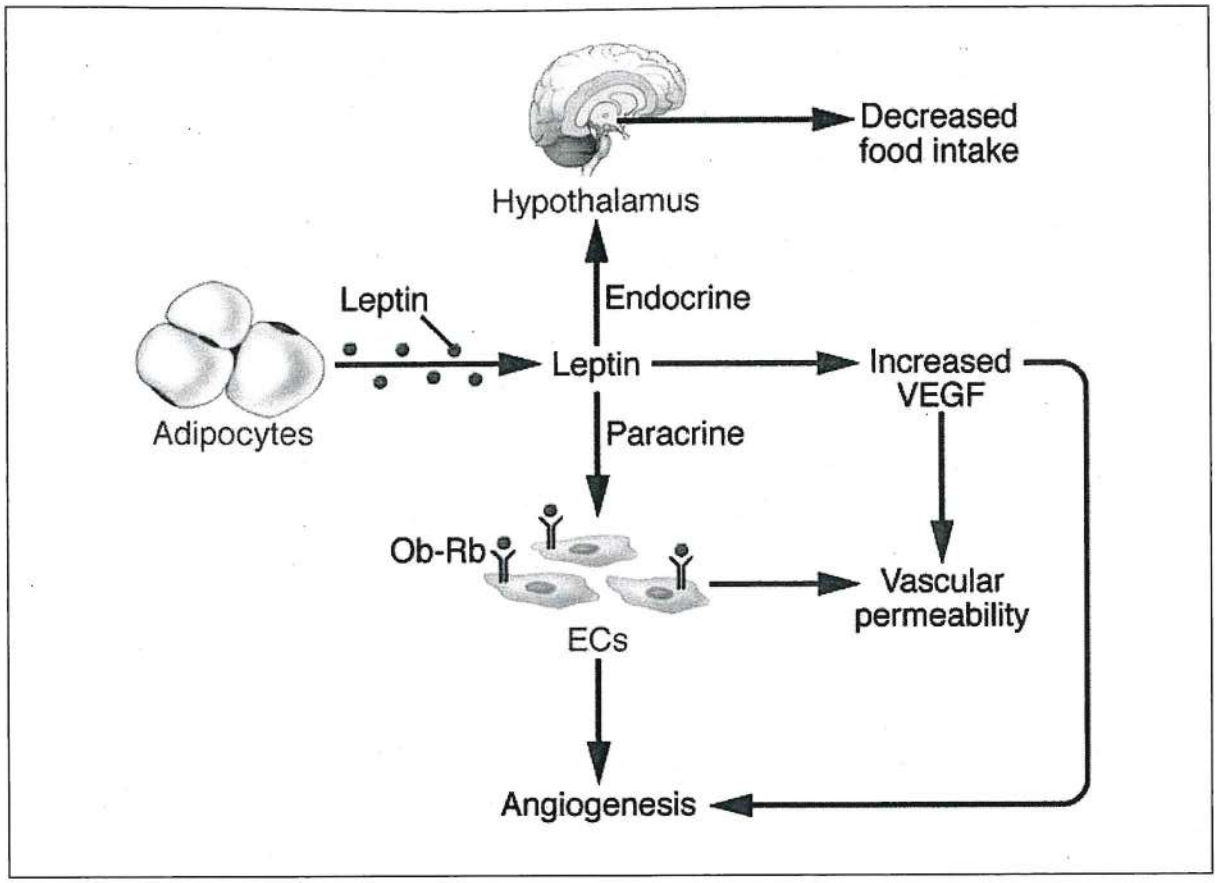
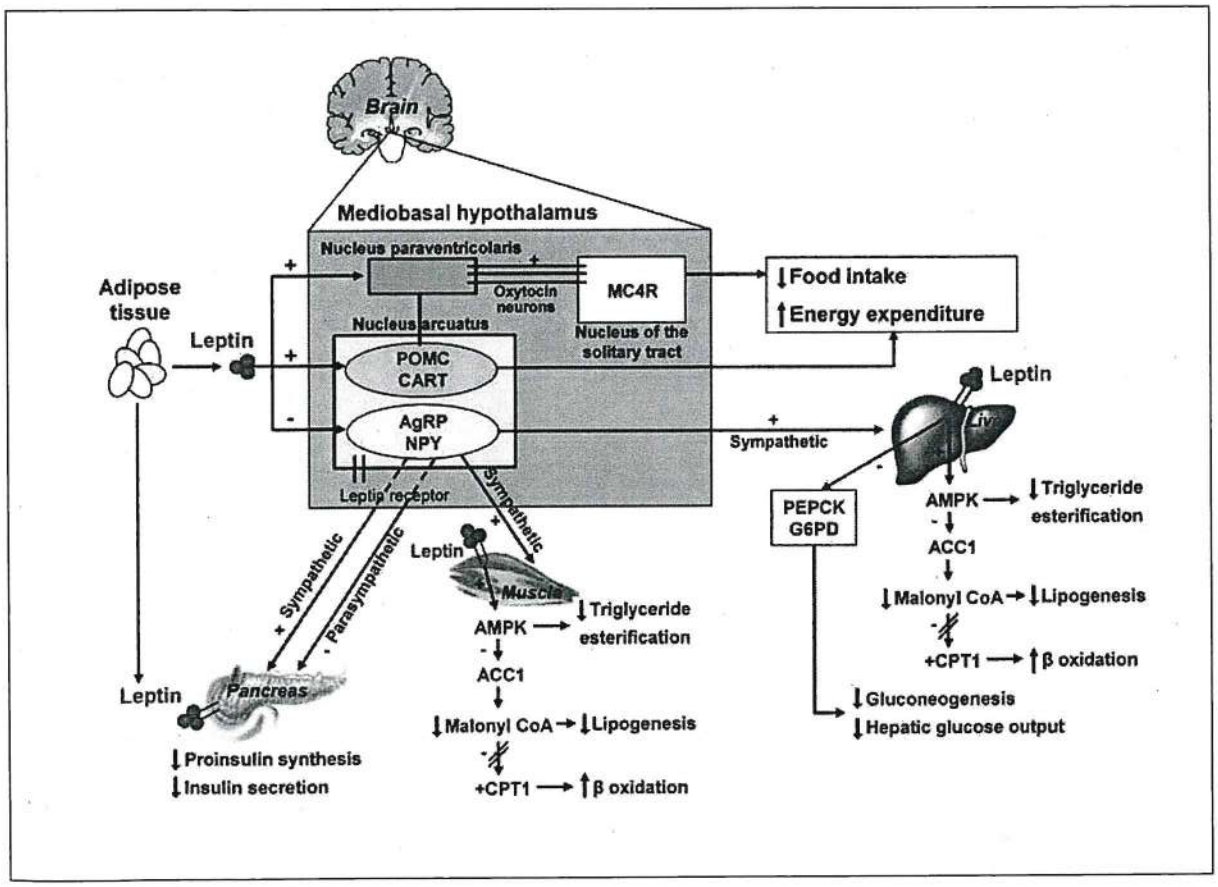
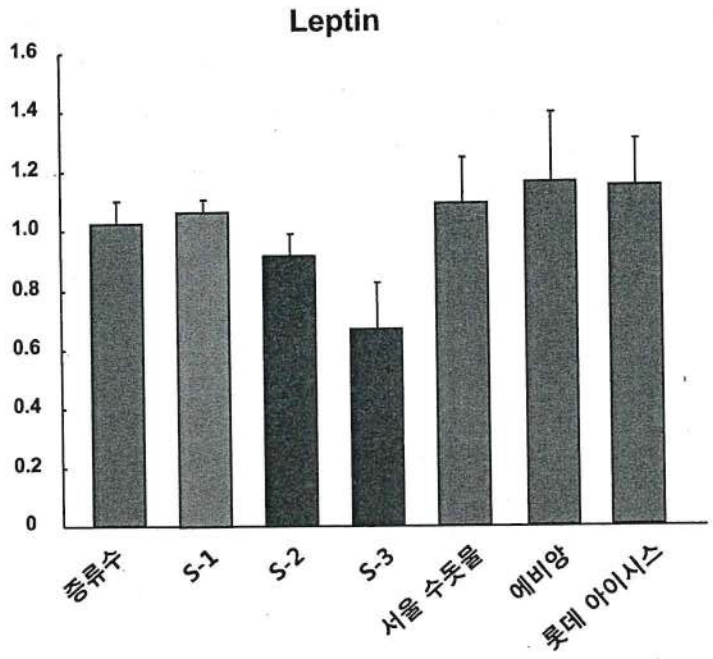

Decreased food intake
Hypothalamus
Endocrine
Leptin
Adipocytes
Leptin
Increased VEGF
Paracrine
Ob-Rb
Vascular permeability
ECs
Angiogenesis


Brain
Mediobasal hypothalamus
Nucleus paraventricolaris
Oxytocin neurons
MC4R
Nucleus of the solitary tract
Nucleus arcuatus
POMC CART
AgRP NPY
Leptin receptor
Adipose tissue
Leptin
↓Food intake
↑Energy expenditure
Sympathetic
Leptin
Liv
PEPCK G6PD
AMPK
↓Triglyceride esterification
ACC1
↓Malonyl CoA
↓Lipogenesis
+CPT1
↑β oxidation
↓Gluconeogenesis
↓Hepatic glucose output
Sympathetic
Parasympathetic
Leptin
Muscle
AMPK
↓Triglyceride esterification
ACC1
↓Malonyl CoA
↓Lipogenesis
+CPT1
↑β oxidation
Leptin
Pancreas
↓Proinsulin synthesis
↓Insulin secretion



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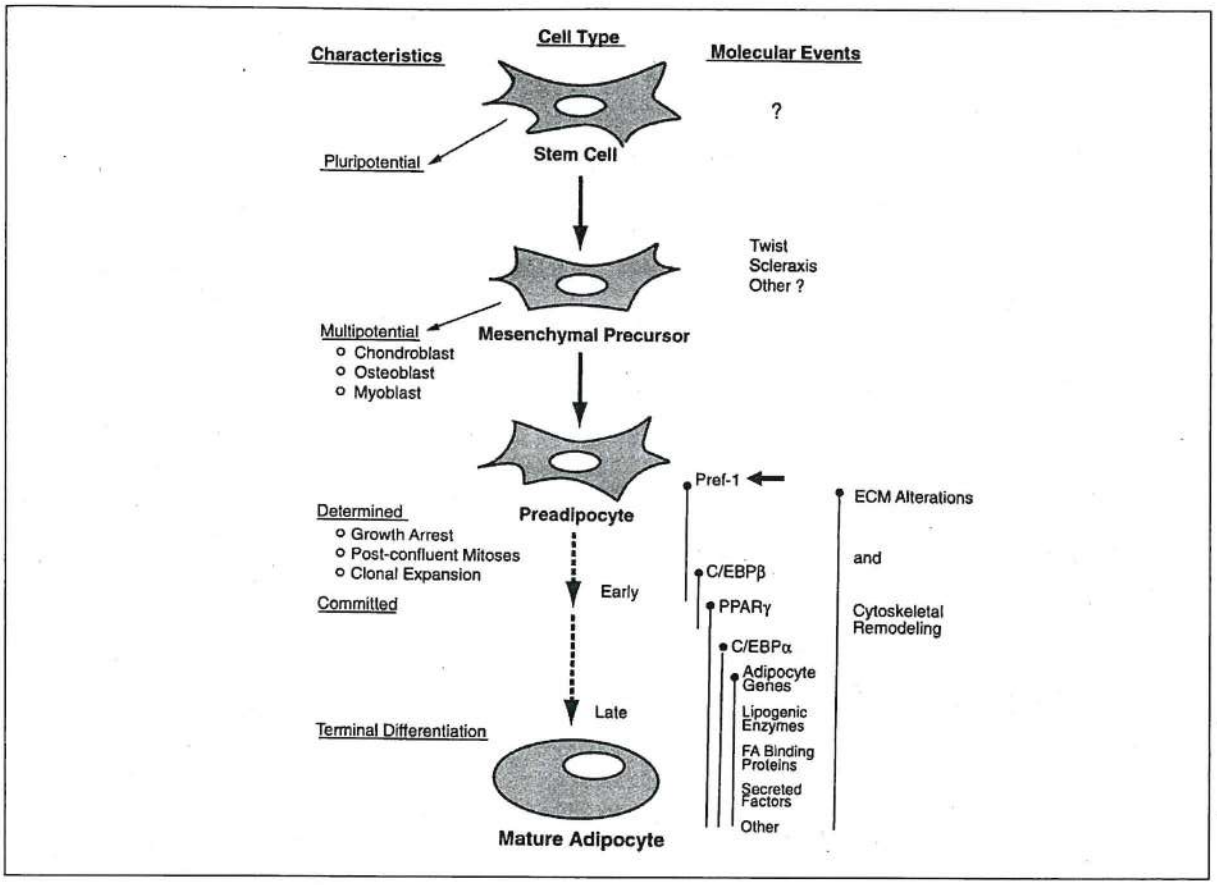
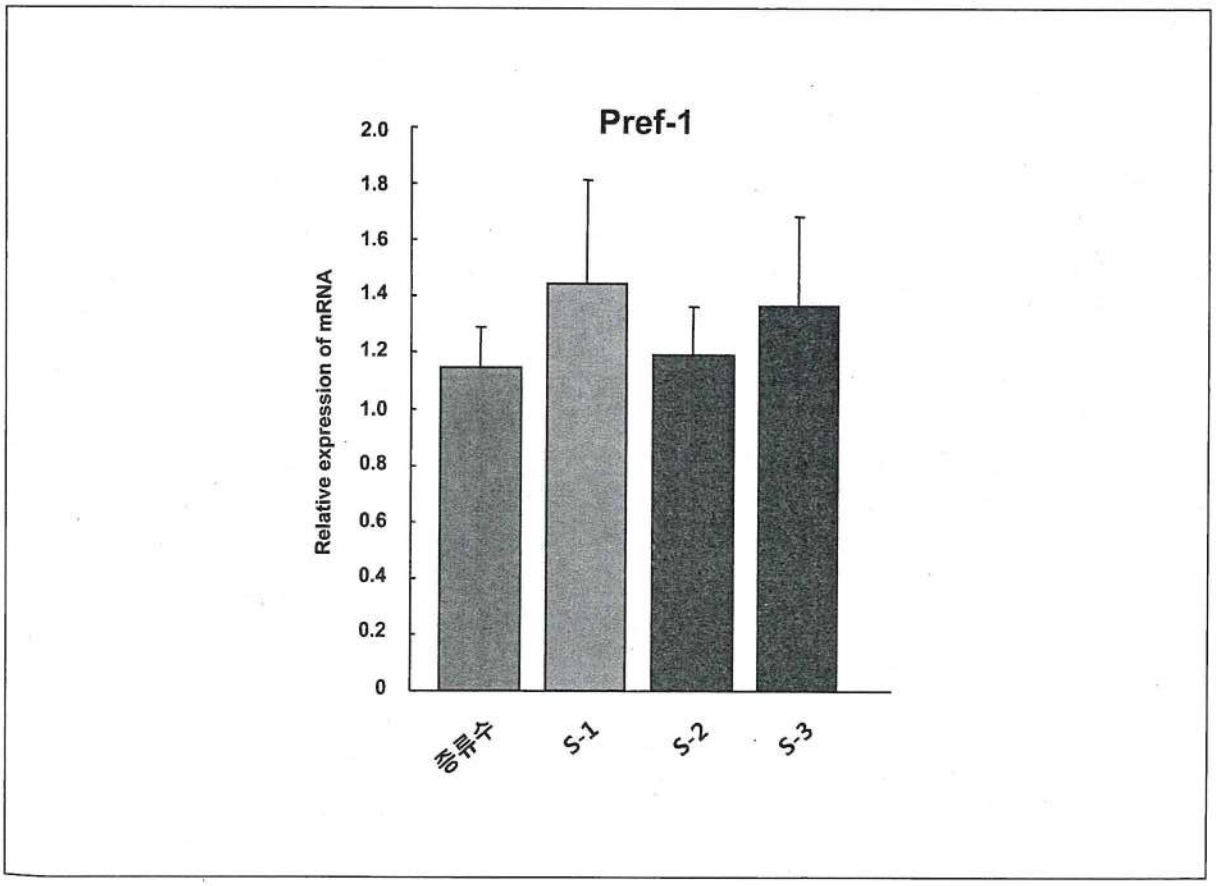

Characteristics
Cell Type
Molecular Events
?
Pluripotential
Stem Cell
Twist
Scleraxis
Other ?
Multipotential
Mesenchymal Precursor
Chondroblast
Osteoblast
Myoblast
Pref-1
ECM Alterations
Determined
Preadipocyte
Growth Arrest
Post-confluent Mitoses
Clonal Expansion
and
C/EBPβ
Early
Committed
PPARγ
Cytoskeletal
Remodeling
C/EBPα
Adipocyte Genes
Late
Lipogenic Enzymes
Terminal Differentiation
FA Binding Proteins
Secreted Factors
Other
Mature Adipocyte


Pref-1
Relative expression of mRNA
2.0
1.8
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0
종류수
S-1
S-2
S-3

지방 분화 조절 인자에 미치는 영향 평가

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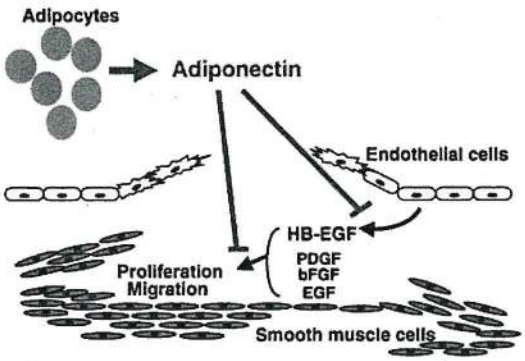
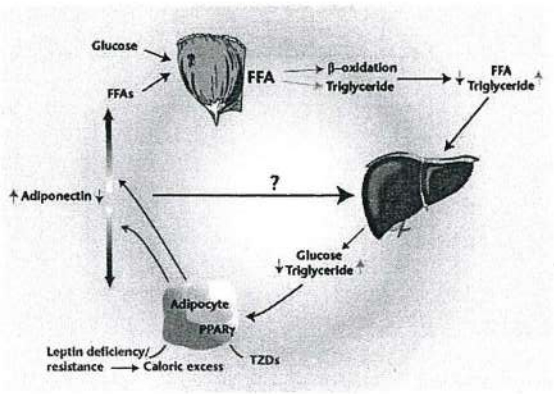
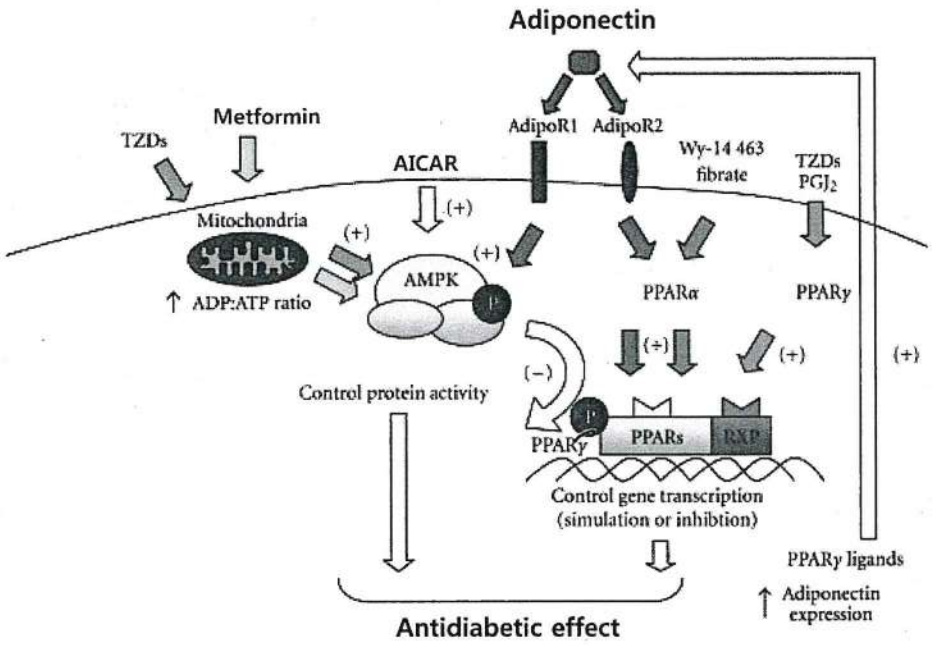
7. **Adiponectin**

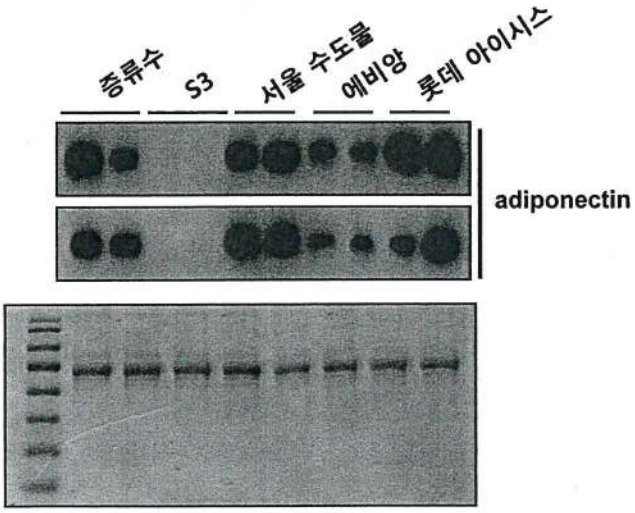






지방세포 분화인자 분비에 미치는 영향

Secreted adiponectin levels



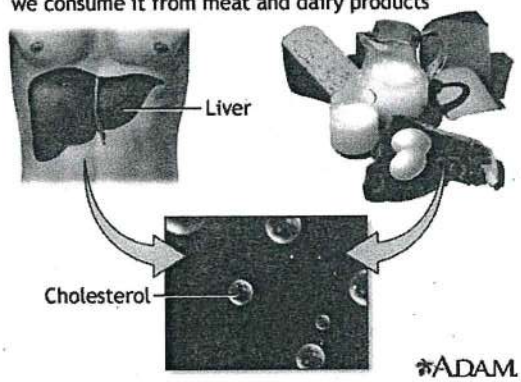
2 차년도 내용

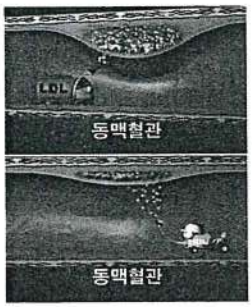
동물 실험

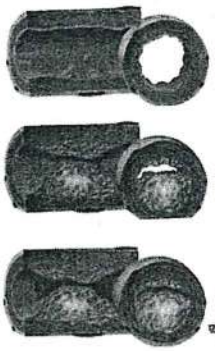
연구개발의 필요성

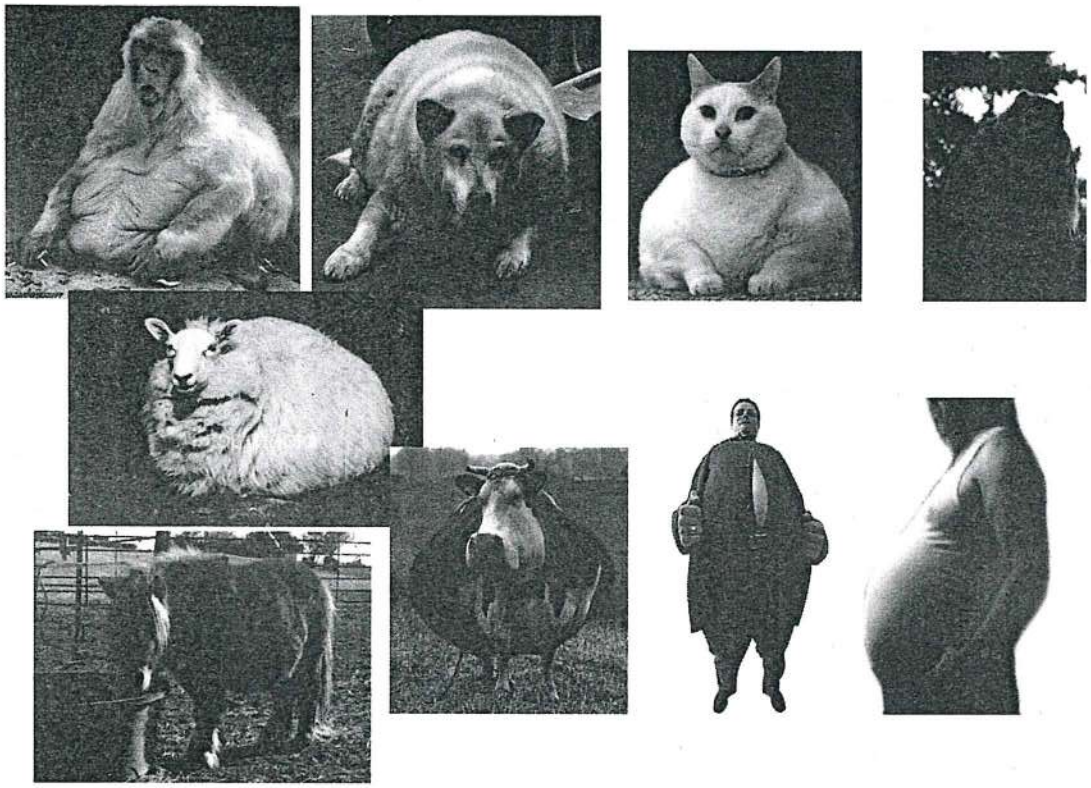
고 지혈증

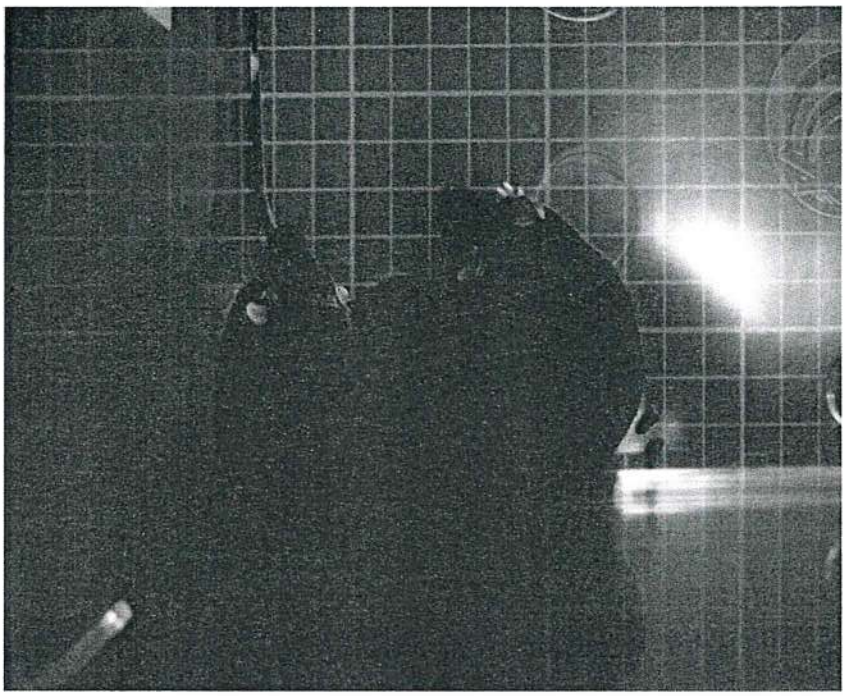
Cholesterol is produced by the liver and
we consume it from meat and dairy products



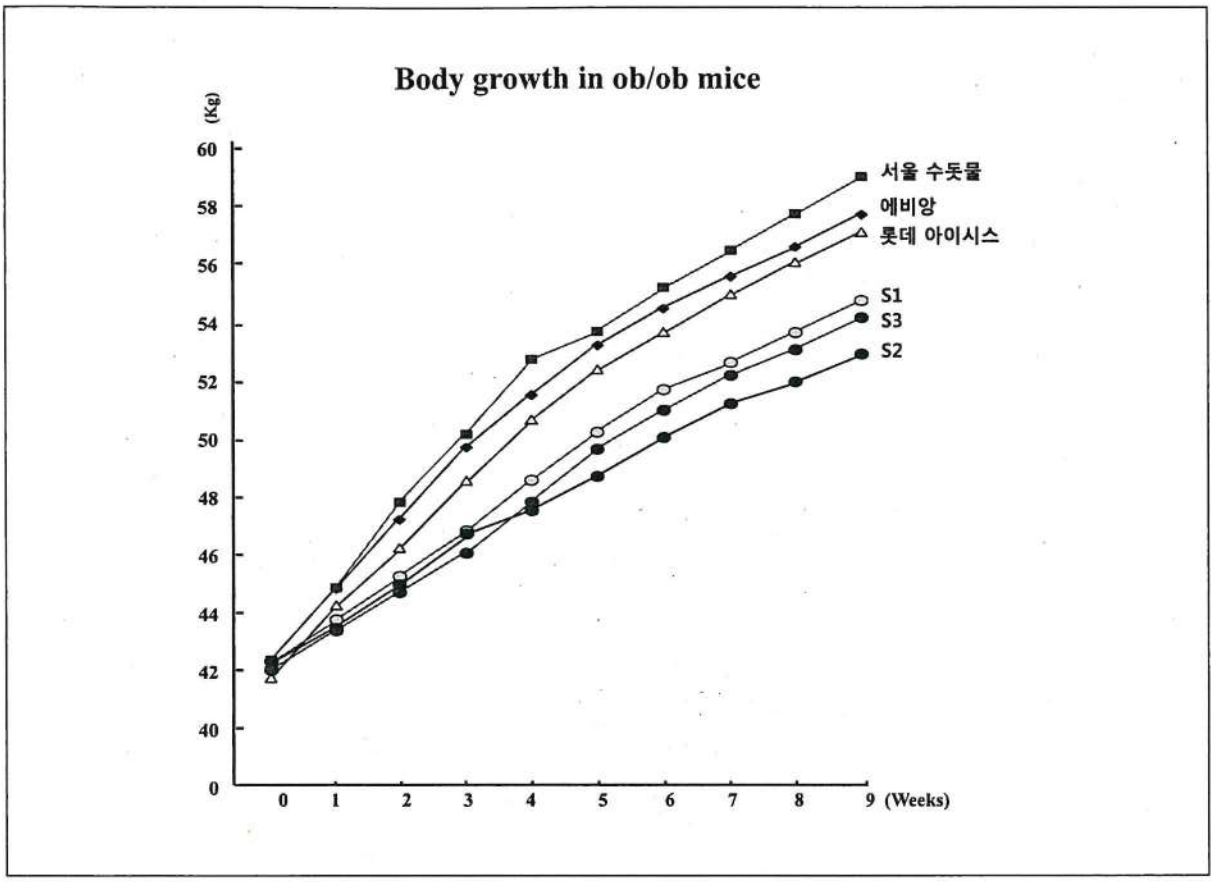


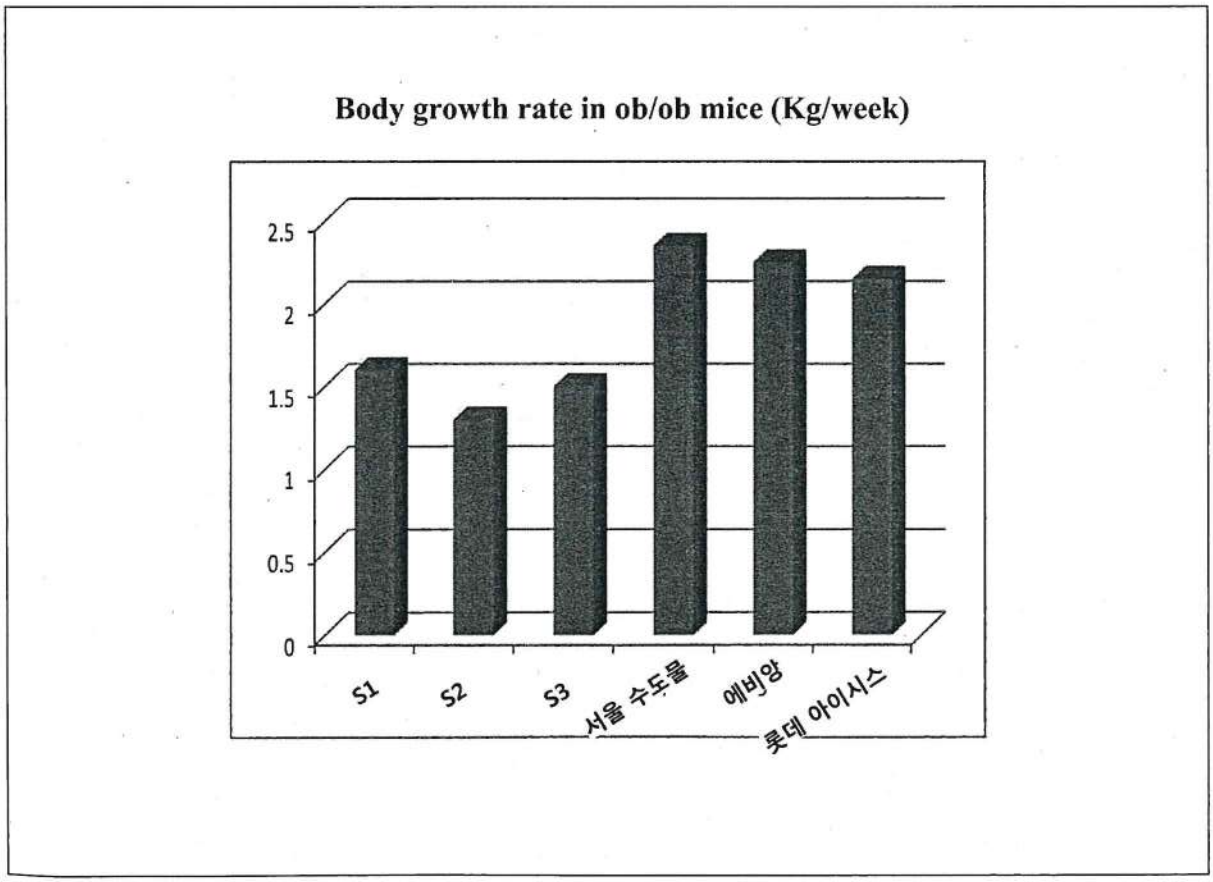


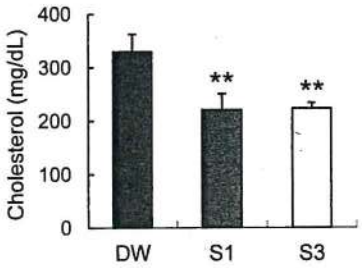


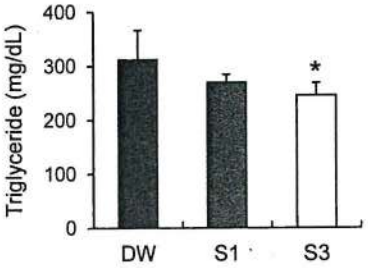


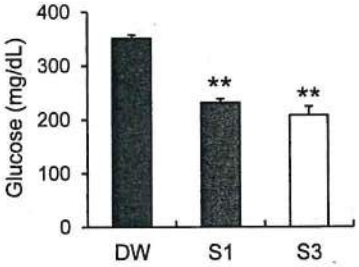
	S1	S2	S3	SS(서울수돗물)	에비앙	롯데 아이시스
2010.10.5	42.25	42.25	42	42.5	42	41.75
2010.10.12	43.75	43.5	43.5	44.75	44.75	44.25
2010.10.19	45.25	45	44.75	47.75	47.25	46.25
2010.10.26	46.75	46.75	46	50.25	49.75	48.5
2010.11.2	48.5	47.5	47.75	52.75	51.5	50.75
2010.11.9	50.25	48.75	49.75	53.75	53.25	52.5
2010.11.16	51.75	50	51	55.25	54.5	53.75
2010.11.23	52.75	51.25	52.25	56.5	55.5	55
2010.11.30	53.75	52	53.25	57.75	56.5	56
2010.12.07	54.75	53	54.25	59	57.5	57


Body growth in ob/ob mice
(Kg)
60
58
56
54
52
50
48
46
44
42
40
0
0 1 2 3 4 5 6 7 8 9 (Weeks)
서울 수돗물
에비앙
롯데 아이시스
S1
S3
S2


Body growth rate in ob/ob mice (Kg/week)
2.5
2
1.5
1
0.5
0
S1
S2
S3
서울 수도물
에비앙
롯데 아이시스


Cholesterol (mg/dL)
400
300
200
100
0
**
**
DW
S1
S3


Triglyceride (mg/dL)
400
300
200
100
0
*
DW
S1
S3


Glucose (mg/dL)
400
300
200
100
0
**
**
DW
S1
S3

HOW IT WORKS

연구 결과 요약

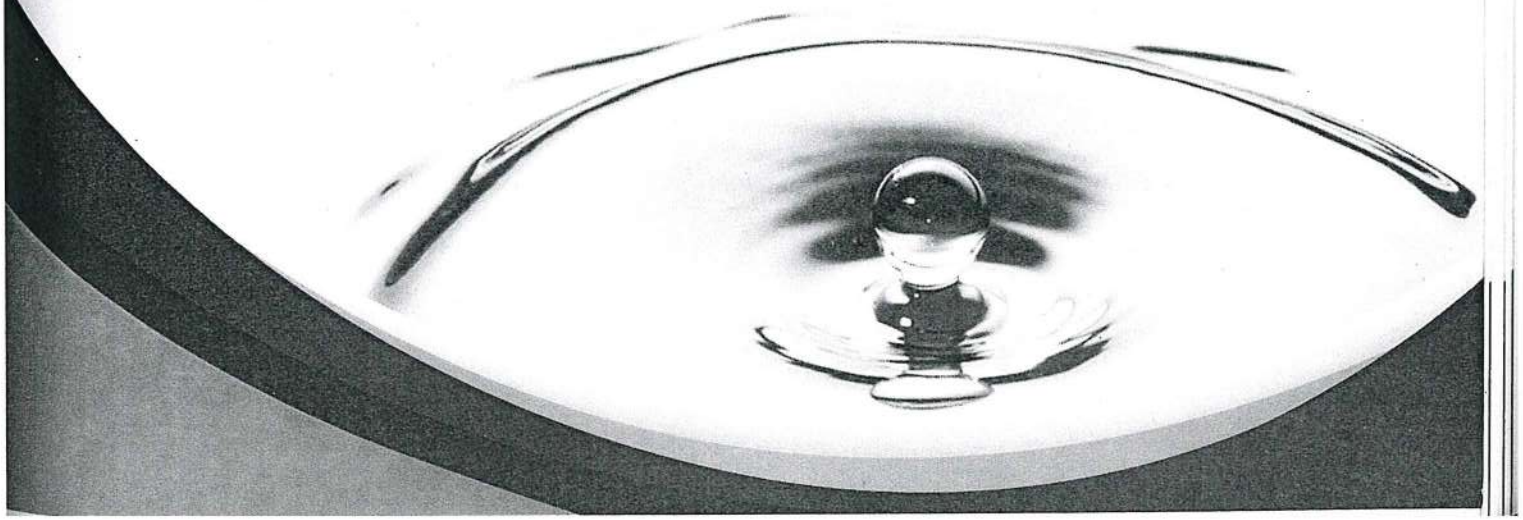
- 제주워터(S1, S2, S3) 투여 시 대조군에 비하여 지방세포 분화 및 지방세포 생성을 억제 시키는 효과를 확인하였음.
- 제주워터는 지방분화 를 유도하는 유도인자의 발현을 감소 시켰음.
- 비만 동물 (ob/ob mouse) 에서 제주워터(S1, S2, S3) 투여 시 대조군에 비하여 고지방식에 의한 체중 증가 억제 효능이 있었음.
- 비만동물 (ob/ob mouse) 에서 고지방식에 의한 혈중 콜에스테롤, 중성지방, 및 혈당 저하 효능이 있었음.

제주워터가 당뇨병환자의 혈당에 미치는 효과

Effect of natural Jeju ground water on blood glucose in diabetes patients

고관표 제주대학교병원 내분비대사내과 교수

Gyan-Pyo Ko, Jeju National University Hospital

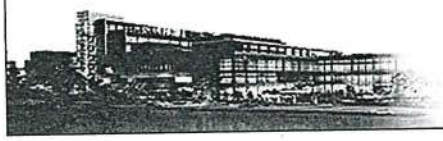


제주워터가 당뇨병환자의 혈당에 미치는 효과

-이중맹검 무작위배정 임상시험-

고 관 표

제주대학교병원 내분비대사내과



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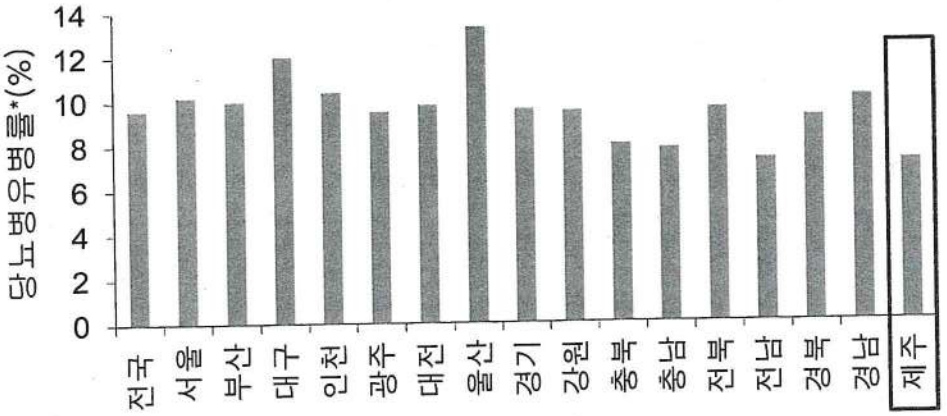
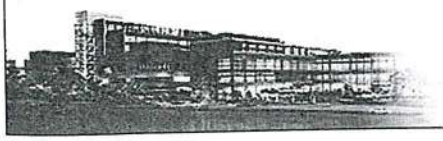
시도별 당뇨병 유병률
2007-2009, 제4기 국민건강영양조사



* 만30세 이상, 2005년 추계인구로 연령표준화



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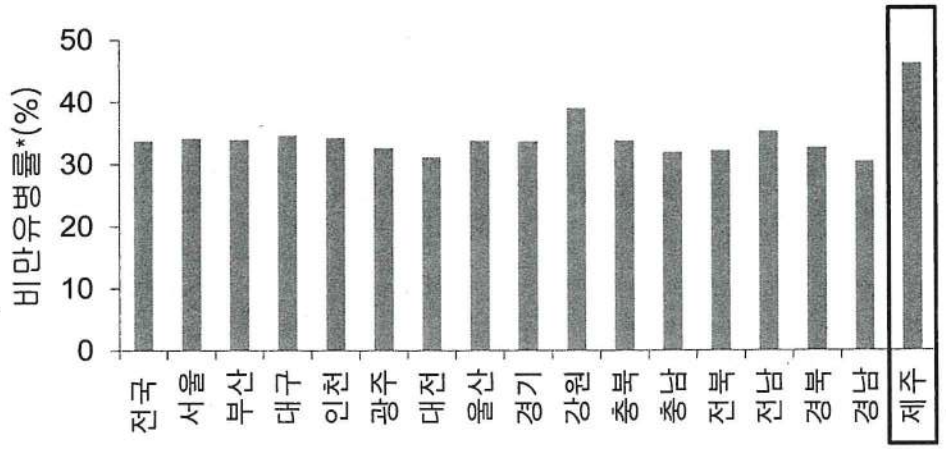

* 만30세 이상, 2005년 추계인구로 연령표준화

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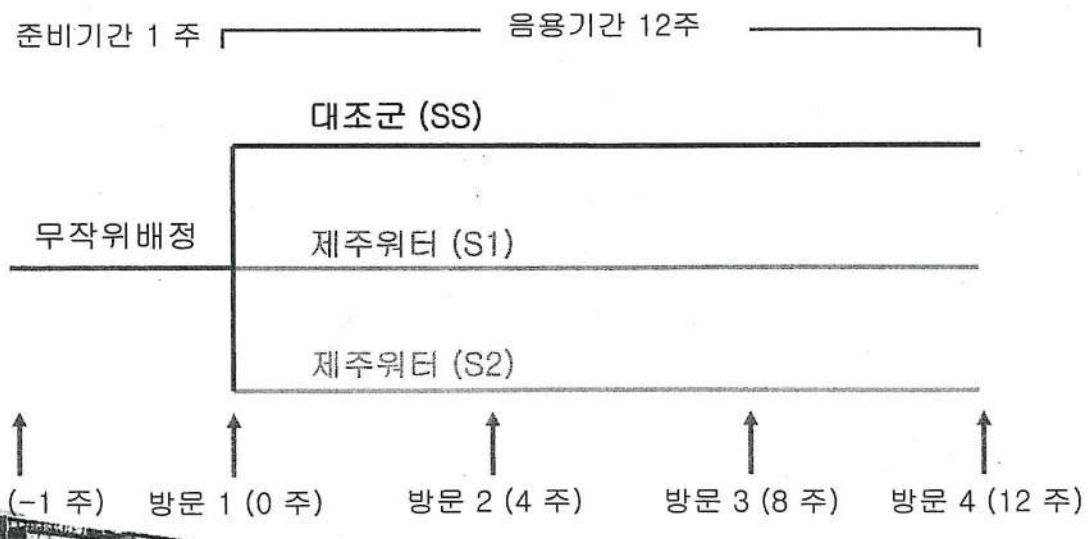
임상시험 디자인
이중맹검 무작위배정 대조군비교 임상시험



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피험자의 선정기준과 제외기준

- 선정기준
  - 당뇨병으로 진단 받은 환자
  - 가장 최근 당화혈색소가 9% 이하인 환자
  - 최근 12주 이내 당뇨병과 고지혈증 약제의 종류와 용량을 변경하지 않은 환자
  - 20세 이상 80세 미만의 환자
  - 임상시험의 목적, 방법, 효과 등에 대한 설명을 듣고 동의서에 서명한 환자
- 제외기준
  - 수분섭취로 악화될 수 있는 질환
    - ✓심한 고혈압
    - ✓울혈성 심부전
    - ✓신증후군
    - ✓말기신질환
    - ✓복수를 동반한 간경화
    - ✓심한 부종
  - 악성종양 환자
  - 임산부

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시험수의 특성 비교

		대조군	제주워터	
약어		SS	S1	S2
수원지		서울수돗물	교래관정	대포관정
0.2 μm 필터여과		+	+	+
이화학 성분	pH	7.4	7.7	8.2
	EC (μs/cm)	130.1	74.4	105.5
	경도 (mg/L)	40.5	17.5	23.1
음이온	F (mg/L)	0.1	0	0.1
	Cl (mg/L)	12.4	6	5.3
	NO3 (mg/L)	9.7	1.5	1.2
	SO4 (mg/L)	8.6	1.7	1.8
주요 미네랄	Ca (mg/L)	11.6	3.4	2.7
	K (mg/L)	2.4	2.1	4.2
	Mg (mg/L)	2.5	2.6	3.5
	Na (mg/L)	6.3	5.9	9.7
	SiO2 (mg/L)	8	27.2	27.4
미량원소	V (μg/L)	1.5	7.5	19.4
	Al (μg/L)	24.3	2.3	6.7
	B (μg/L)	8.2	5.2	7.6
	Fe (μg/L)	64.2	15	17.3
	Cr (μg/L)	0.3	0.2	0.3
	Zn (μg/L)	12.7	0.5	8.3
	Mn (μg/L)	1.7	0.1	0

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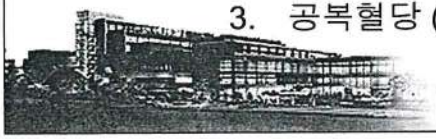
연구목적

1. 일차 목적
   - 각각의 제주워터와 대조군 간 시험수 음용 12주 후 당화혈색소 (HbA1c)가 7% 미만인 대상의 비율의 차이 - PP분석

2. 이차 목적
   - 각각의 제주워터와 대조군 간 시험수 음용 4, 8, & 12 주 후 혈당조절지표들의 차이
     1. 당화혈색소 (HbA1c)
        - 2-3개월 간 혈당수준 반영
     2. Fructosamine
        - 2-4주 간 혈당수준 반영
     3. 공복혈당 (FPG)



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피험자 수 산정근거

- 검정력 (1-β) 80%, 유의수준 0.05
- 예비연구 (제2형 당뇨병환자에서 제주지역 바나듐 함유 지하수의 혈당개선 효과)
  - 당화혈색소 7% 미만의 비율: 대조군 50%, 제주워터군 74.1%
  - 탈락률 23.5%
- 계산공식
  - nc=nt=((Zα√(2×Ψ×(1-Ψ))+(Zβ√(Pc(1-Pc)+Pt(1-Pt))))/(Pt-Pc)2
    - ✓((1.96√(2×0.62×(1-0.62))+(0.842√(0.5(1-0.5)+0.741(1-0.741))))/(0.741-0.5)2=62.6
- **각 군당 77.3명, 총 232명 필요**
  - 예상탈락률 23.5%를 감안하면 n=62.6+(62.6×0.235)=77.3
  - N=77.3+(2×77.3)=232

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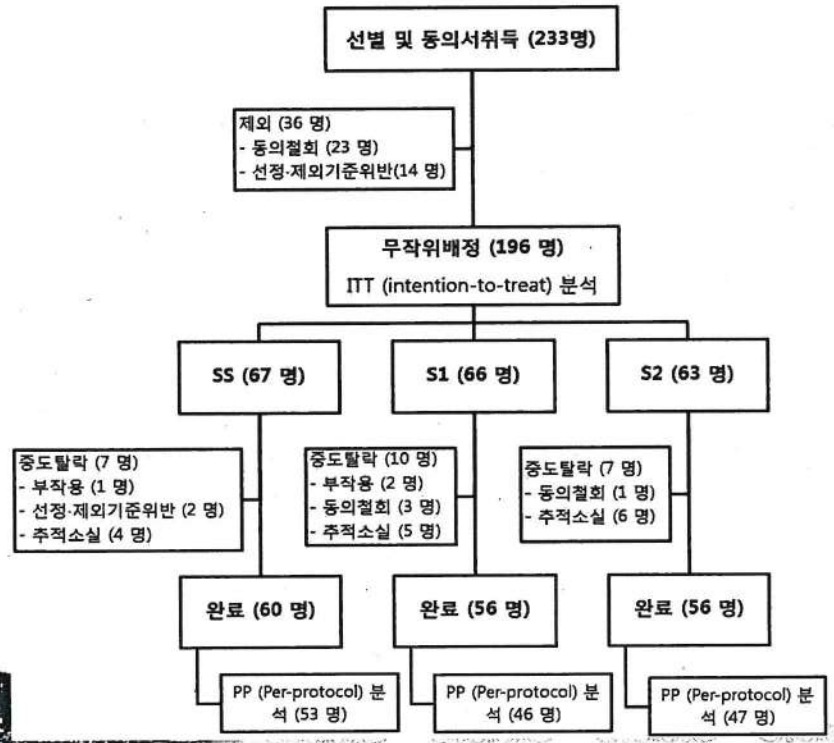
피험자 분포



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피험자의 기저특징 (ITT 분석)

	SS	S1	S2	*P**
인원	67	66	63	
성별 (남/녀)	55/12	42/24	46/17	0.057
나이 (year-old)	58.1±1.2	58.9±1.1	59.7±1.0	0.574
체질량지수 (kg/cm^2)	26.0±0.4	26.0±0.4	25.8±0.5	0.898
허리둘레 (cm)	90.5±0.8	89.5±0.9	90.4±1.1	0.702
허리-엉덩이 비	0.95±0.01	0.94±0.01	0.95±0.01	0.227
수축기혈압 (mmHg)	141.2±1.9	140.3±2.1	142.8±2.3	0.711
이완기혈압 (mmHg)	82.3±1.4	84.6±1.3	83.9±1.4	0.454
당화혈색소 (%)	7.42±0.14	7.43±0.13	7.26±0.12	0.575
당뇨병 유병기간 (years)	9.5±0.9	8.1±1.0	8.0±0.8	0.418
흡연 (%)	22.4	18.5	23.8	0.709
고혈압 (%)	50.7	48.5	50.0	0.965
고지혈증 (%)	49.3	51.5	46.8	0.866

*ANOVA or Chi-square test

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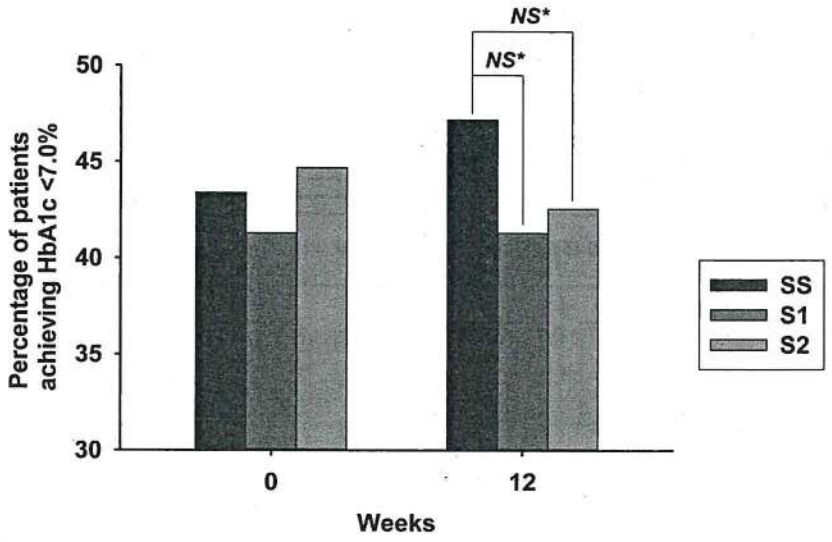
일차 목적- 당화혈색소 7% 미만의 빈도 (PP 분석)



* No siginificance (Logistic regression analysis).

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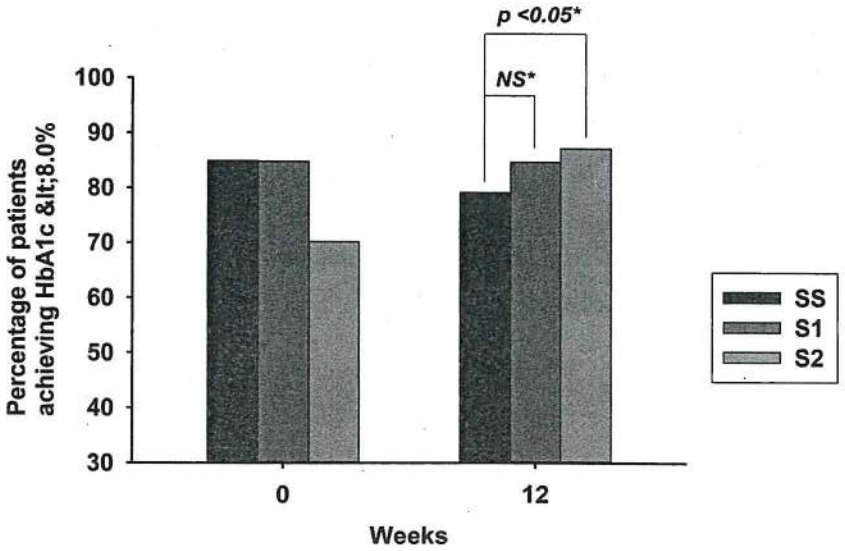
당화혈색소 8% 미만의 빈도 (PP 분석)



* Logistic regression analysis.

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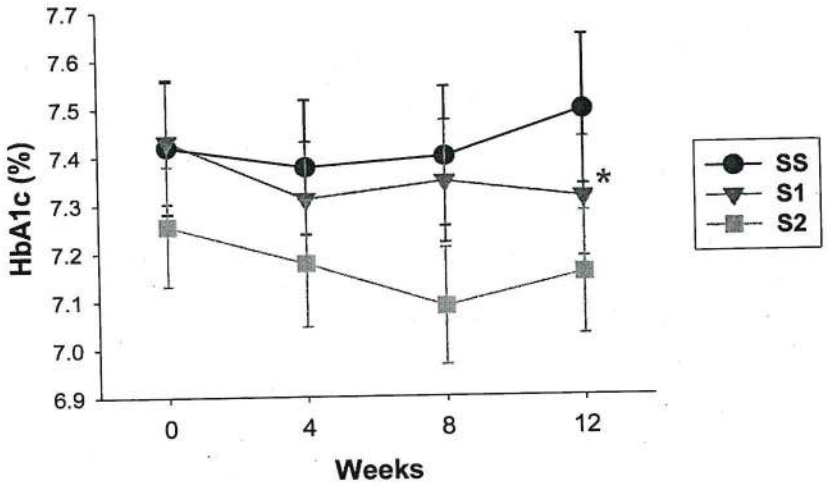
당화혈색소의 변화 (ITT 분석)



* P <0.05 vs SS (Linear regression analysis).

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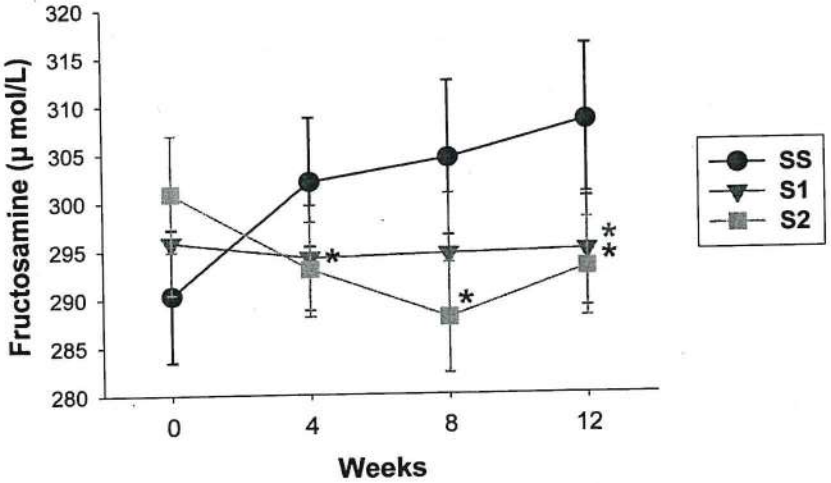
Fructosamine의 변화 (ITT 분석)



* P <0.05 vs SS (Linear regression analysis).

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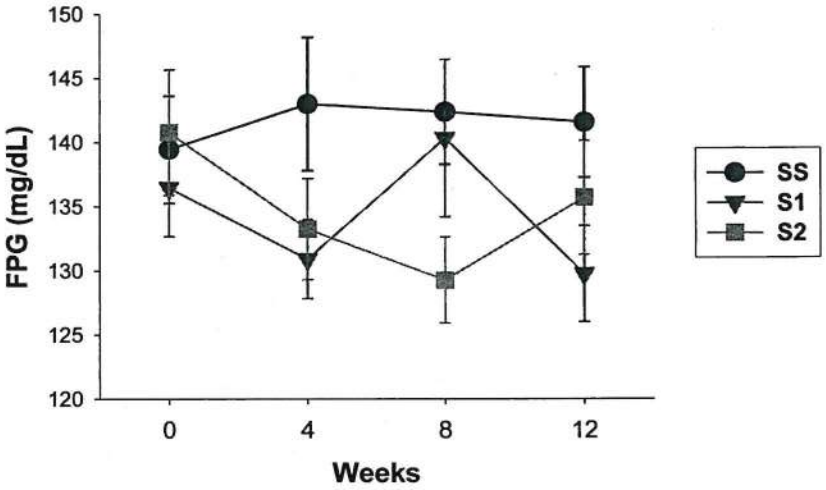
공복혈당의 변화 (ITT 분석)



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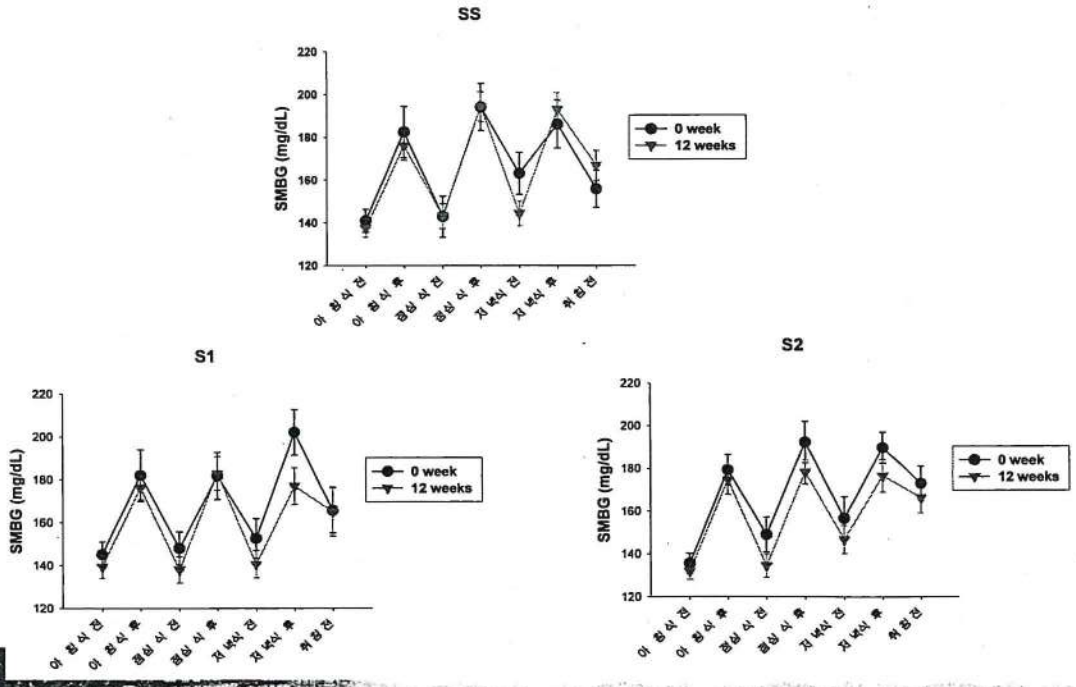
각 군에서 자가혈당측정치의 변화 (ITT 분석)



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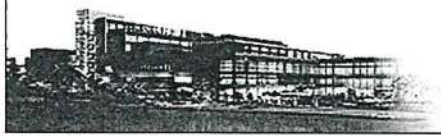
요약

- 당화혈색소 7% 미만의 대상 빈도- 일차목적
  - 제주워터군과 서울수돗물군 간 차이가 없었음
  - 당화혈색소 8% 미만의 대상 빈도는 제주워터 (S2)에서 서울수돗물군보다 높았음
- 당화혈색소
  - 12주 후 제주워터 (S1)군이 서울수돗물군보다 낮았음
- Fructosamine
  - 12주 후 제주워터군 (S1)이 fructosamine보다 낮았음
  - 4, 8, & 12주 후 제주워터군 (S2)이 fructosamine보다 낮았음
- 혈당조절지표들은 대체적으로 제주워터군 (S1, S2)이 서울수돗물군보다 낮은 경향을 보임



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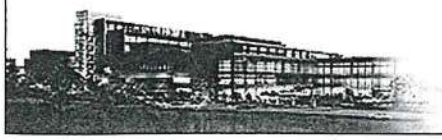
결론

- 제주워터가 서울수돗물보다 당뇨병환자의 혈당을 개선시킬 가능성이 있음
- 향후 일차 평가지표를 변경한 임상시험이 시행된다면 제주워터의 혈당개선효과를 명확히 증명할 수 있음



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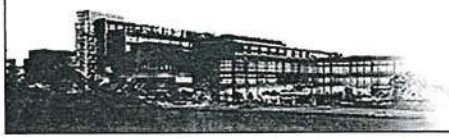
고려사항

- 역삼투압정수기의 유해성 ?
  - 대조군과 실험군을 모두 제균필터로 여과했음
- 다른 미네랄워터와의 차별성 ?
  - 추후 타 지역 지하수를 대조군으로 하는 임상시험이 필요함



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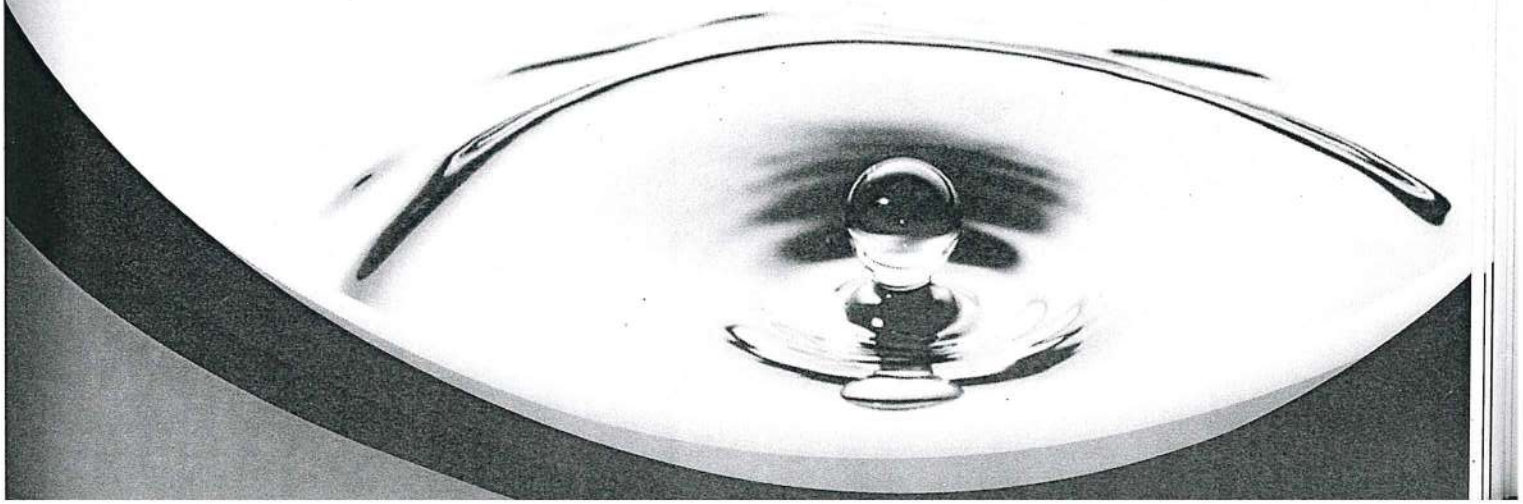
MEMO

제주 지하수의 면역활성 효능 및 그 메커니즘

Immune activation of Jeju water and its possible mechanism

지영흔 제주대학교 수의과대학 교수

Young-Heun Jee, Jeju National University



College of Veterinary Medicine

제주 지하수의 면역활성 효능 및 그 메커니즘

(Immune activation of Jeju water and its possible mechanism)

Youngheun Jee
Jeju National University

Lab of Neuroimmunology

College of Veterinary Medicine

발 표 개 요

서론	● 면역활성이란? ● 연구의 필요성
연구 목표 및 결과	● 연구 개발 최종목표 ● 면역기능억제 및 만성스트레스 동물모델 구축법 및 평가법 ● 결과
결론	● 결론

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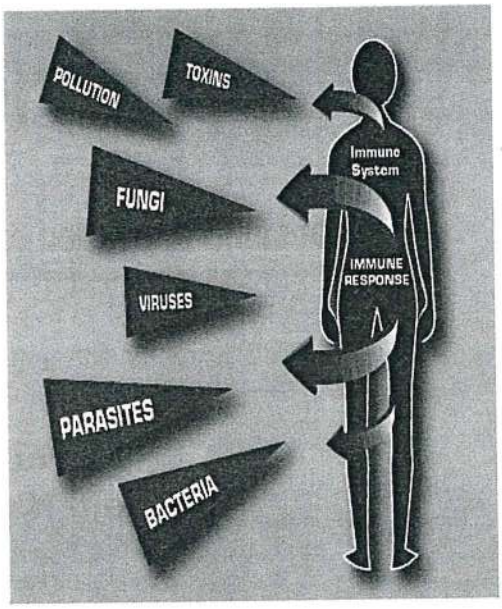
Properties of Immune response



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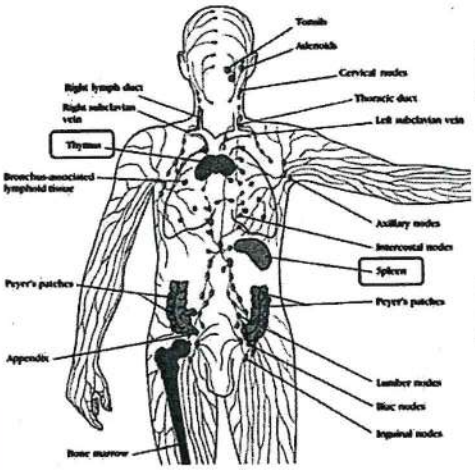
Immune System: Magic doctor

생체 방어 수단 - 면역계



세포매개성면역
(cellular immunity)

T-Lymphocyte

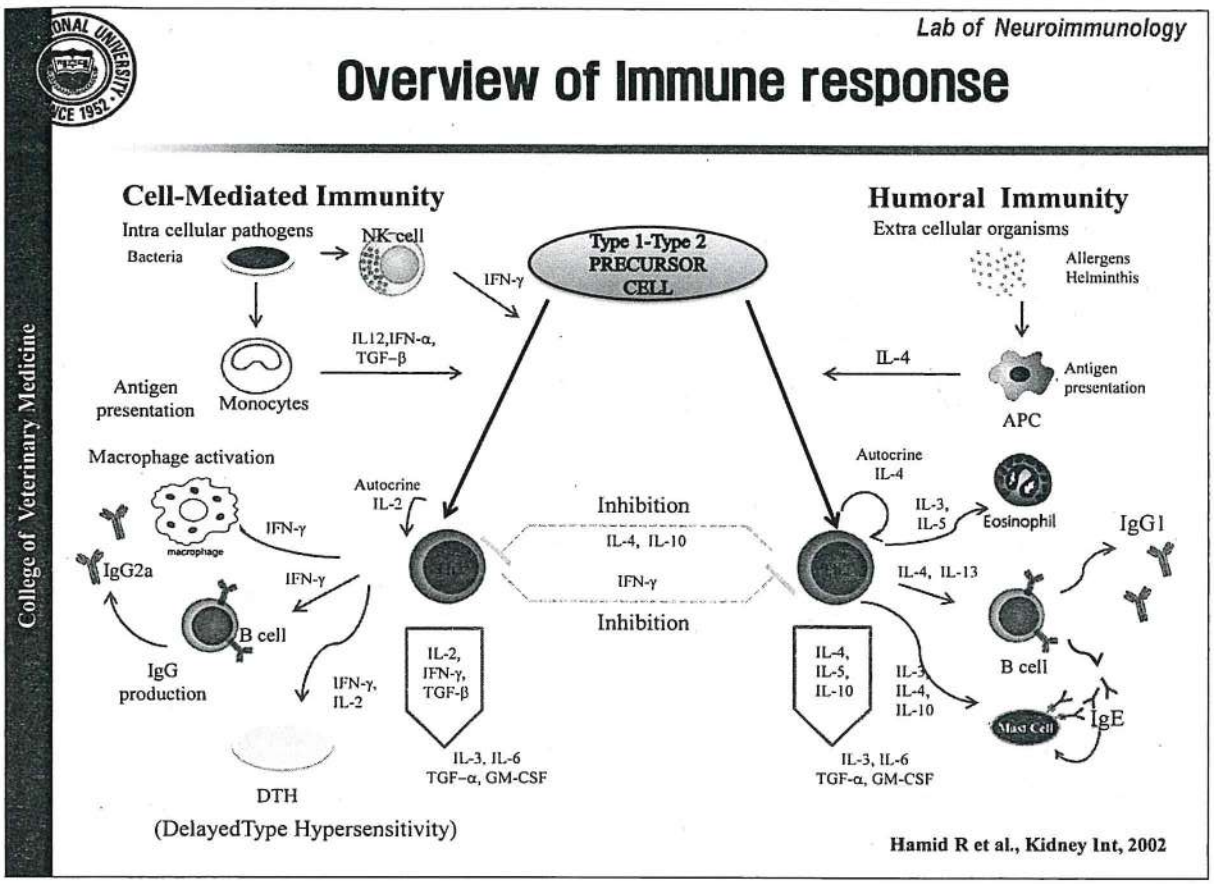
사이토카인
(cytokine : IL-2, IL-4, IFN-γ 등)

체액성면역
(humoral immunity)

B-Lymphocyte

항체 (antibody : IgM, IgG, IgG1, IG2a 등)

Yoshimura A et al., Nat Rev Immunol, 2007
Waldmann Herman et al., Science, 2004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Overview of Immune response
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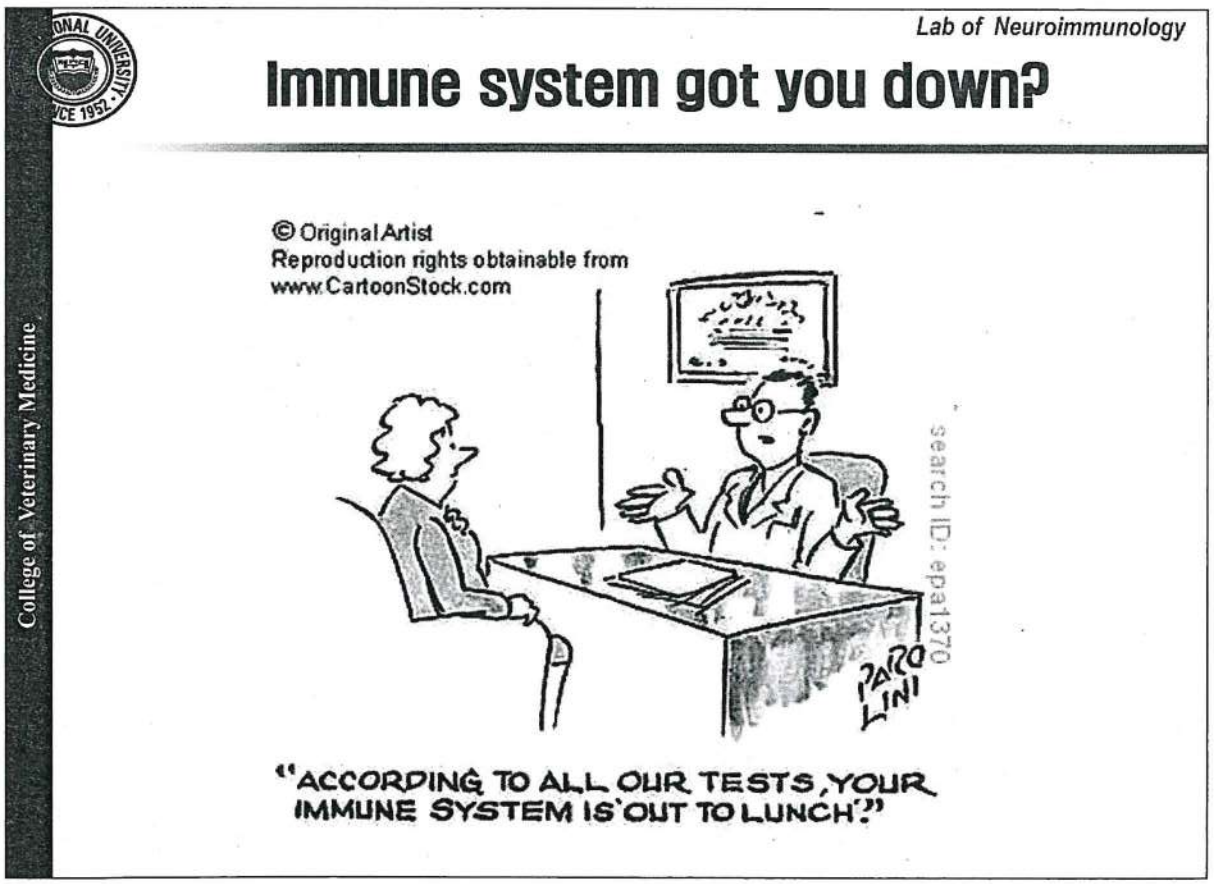
Cell-Mediated Immunity
Intra cellular pathogens
Bacteria
NK cell
IFN-γ
Type 1-Type 2 PRECURSOR CELL
Humoral Immunity
Extra cellular organisms
Allergens Helminthis
IL12,IFN-α, TGF-β
IL-4
Antigen presentation
Monocytes
Antigen presentation
APC
Macrophage activation
Autocrine IL-2
Autocrine IL-4
Inhibition
IL-4, IL-10
IFN-γ
Inhibition
IL-3, IL-5
Eosinophil
IgG1
IgG2a
macrophage
IFN-γ
IFN-γ
IL-4, IL-13
B cell
IgG production
IFN-γ, IL-2
IL-2, IFN-γ, TGF-β
IL-4, IL-5, IL-10
IL-3, IL-4, IL-10
B cell
Mast Cell
IgE
IL-3, IL-6 TGF-α, GM-CSF
IL-3, IL-6 TGF-α, GM-CSF
DTH
(DelayedType Hypersensitivity)
Hamid R et al., Kidney Int, 2002


Lab of Neuroimmunology
Immune system got you down?
College of Veterinary Medicine
© Original Artist
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search ID: epa1370
PARO LINI
"ACCORDING TO ALL OUR TESTS, YOUR IMMUNE SYSTEM IS 'OUT TO LUNCH'."

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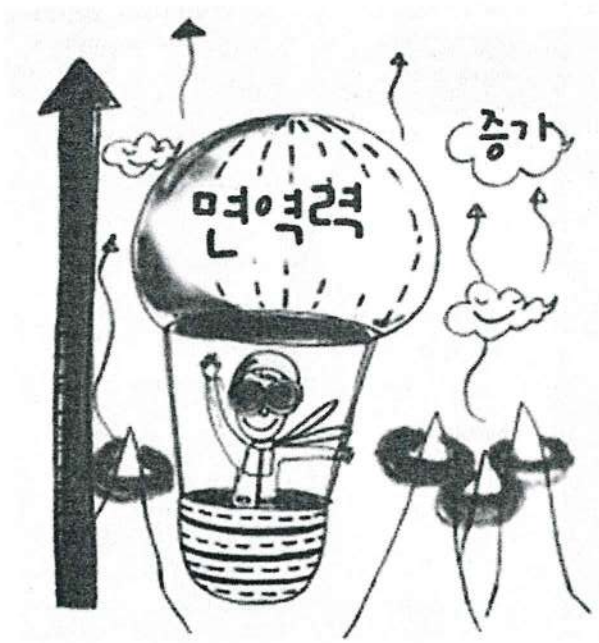
Immune Boosting foods to the rescue



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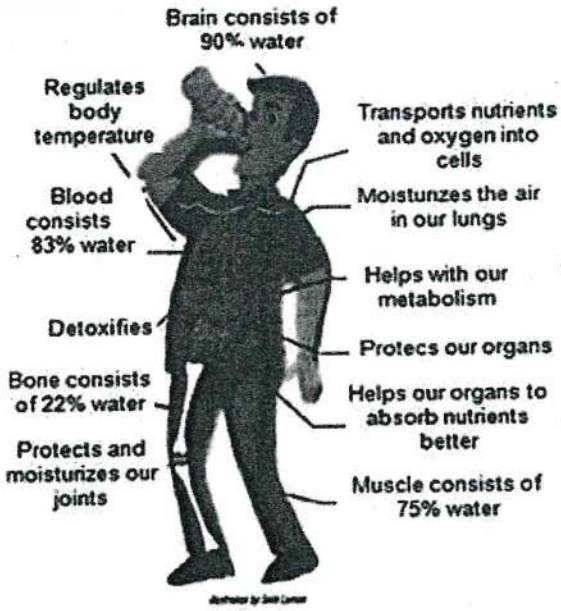
Functions of Water in The Body



The human body is anywhere from 55% to 78% water depending on body size. It is the main component of human body.

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물에 관한 생리활성 연구 사례 (1)

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음용수의 생리활성 효능에 대한 국내, 외 연구사례

- Xanthine oxidase가 유발한 활성산소로 인한 DNA 손상에 알칼리수가 미치는 효과 연구 [Biochem Bioph Res Co, 1997]
- 과산화 수소로 인해 유발된 활성산소로 인한 DNA 손상에 알칼리수가 미치는 보호효능 연구 [Appl Biochem Biotech, 2006]
- 중탄산나트륨 (HCO3-)이 다량 함유된 미네랄 워터를 28일간 음수시킨 임상실험에서 혈중 칼슘 농도의 상승 및 뼈의 소실 억제 효과 연구 [J Nutr Heath Aging, 2004]
- 칼슘 및 중탄산나트륨의 함량이 높은 미네랄 워터의 음수가 골밀도에 미치는 영향에 관한 임상실험 [Bone, 2009]

화산암반수에 대한 생리활성 효능 연구사례

- 인슐린 비의존형 당뇨병 자연유발 마우스를 이용한 바나듐 함유 천연 화산암반수의 혈당저하 효능(일본 동경의과대학)
- 바나듐 함유 천연 화산암반수의혈당저하 효능에 대한 임상시험 (Biomed Res Trace Elements, 17(1),11-16)
- 바나듐 함유 천연 암반수의 혈당저하 효능에 대한 동물시험 (아사히음료, 일본약학대학, 동경의학대학,79th Annual Meeting of the Japanese Pharmacological Society,2009)

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물에 관한 생리활성 연구 사례 (2)

College of Veterinary Medicine

음용수의 활성산소군 생성 및 DNA 손상 억제 효과 연구사례

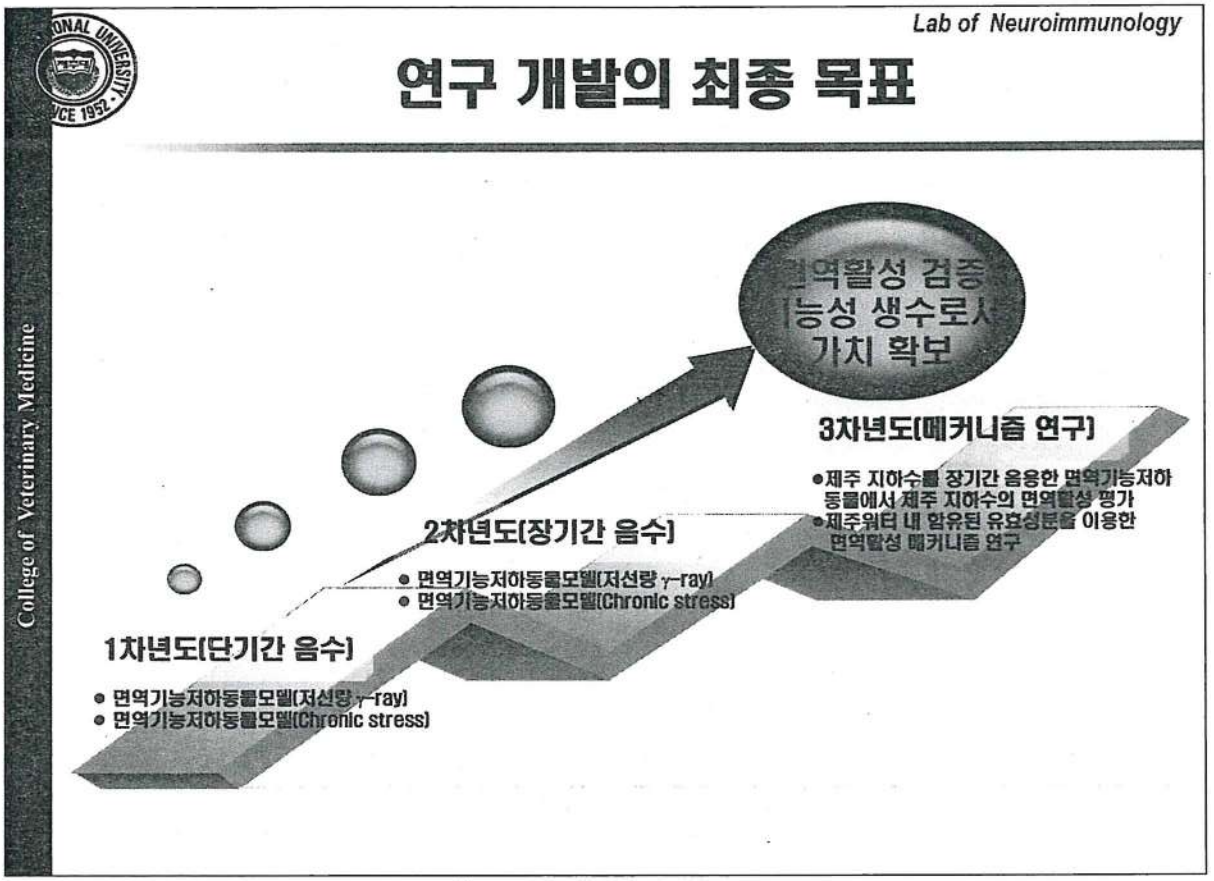
- Xanthine oxidase가 유발한 활성산소로 인한 DNA 손상에 알칼리수가 미치는 효과 연구 [Biochem Bioph Res Co, 1997]
- 당뇨병 모델 마우스에서 활성산소군 생성 감소에 알칼리수가 미치는 영향 연구 [Cytotechnology, 2002]
- 과산화 수소로 인해 유발된 활성산소로 인한 DNA 손상에 알칼리수가 미치는 보호효능 연구 [Appl Biochem Biotech, 2006]

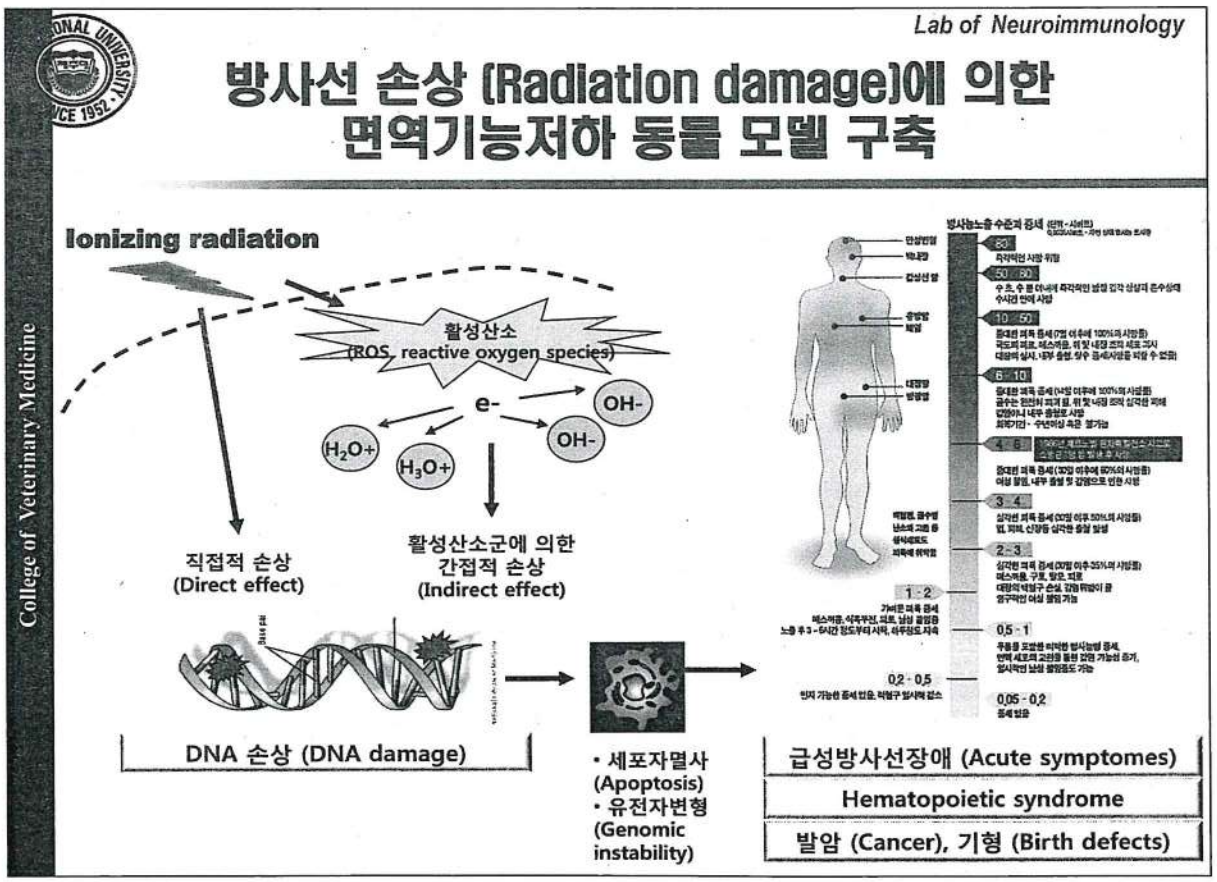
음용수의 종양세포 억제 효능 연구사례

- 종양세포 전이에 영향을 미치는 혈관 생성인자들에 대한 알칼리수의 억제 효과 연구 [Bio Pham Bull, 2006]
- 유해 화학물질에 의한 세포 변성의 억제에 알칼리수가 미치는 효능 연구 [Cytotechnology, 2005]
- 알칼리수가 마우스의 피부암세포 성장과 변이에 미치는 억제 효과 연구 [J Kor Sci Jung Sci, 2003]

음용수의 당뇨병 억제 효능 연구사례

- Streptozotocin에 의한 췌장베타세포의 파괴로 유도된 제 1형 당뇨병 동물 모델의 혈당 수치 조절에 대한 알칼리수 효능 연구 [Life Sci, 2006]
- 성인병과 관련하여 발생하는 제 2형 당뇨의 동물모델에서 알칼리수가 미치는 혈당 저하, 인슐린 수치 상승 작용 연구 [Bio Pham Bull, 2007]


Lab of Neuroimmunology
연구 개발의 최종 목표
College of Veterinary Medicine
면역활성 검증
기능성 생수로서
가치 확보
3차년도(메커니즘 연구)
●제주 지하수를 장기간 음용한 면역기능저하 동물에서 제주 지하수의 면역활성 평가
●제주워터 내 함유된 유효성분을 이용한 면역활성 메커니즘 연구
2차년도(장기간 음수)
● 면역기능저하동물모델(저선량 γ-ray)
● 면역기능저하동물모델(Chronic stress)
1차년도(단기간 음수)
● 면역기능저하동물모델(저선량 γ-ray)
● 면역기능저하동물모델(Chronic stress)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방사선 손상 (Radiation damage)에 의한
면역기능저하 동물 모델 구축
College of Veterinary Medicine
Ionizing radiation
활성산소
(ROS, reactive oxygen species)
e-
OH-
OH-
H2O+
H3O+
직접적 손상
(Direct effect)
활성산소군에 의한
간접적 손상
(Indirect effect)
DNA 손상 (DNA damage)
• 세포자멸사
(Apoptosis)
• 유전자변형
(Genomic
instability)
급성방사선장애 (Acute symptomes)
Hematopoietic syndrome
발암 (Cancer), 기형 (Birth defects)

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방사선에 의한 면역세포 손상 (Radiation damage of immune cells)

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Radio sensitivity (RS) cell type

= Probability of a cell, tissue or organ of suffering an effect per unit of dose

Bergonie and Tribondeau (1906): "RS and Rate of Cell Division Law"
RS will be greater if the cell:

Is rapidly dividing, poorly differentiation & long mitotic period

Very high Sensitivity:	High Sensitivity:	Low Sensitivity:
Primitive blood cells Splenocytes Lymphocytes Intestinal epithelium Bone marrow cells	Mature red blood cells Muscle cells Ganglion cells Mature connective tissues	Gastric mucosa Mucous membranes Esophageal epithelium Urinary bladder epithelium

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방사선에 의한 면역세포 손상에 따른 면역기능 저하에 대해 제주지하수는 영향을 미치는가?

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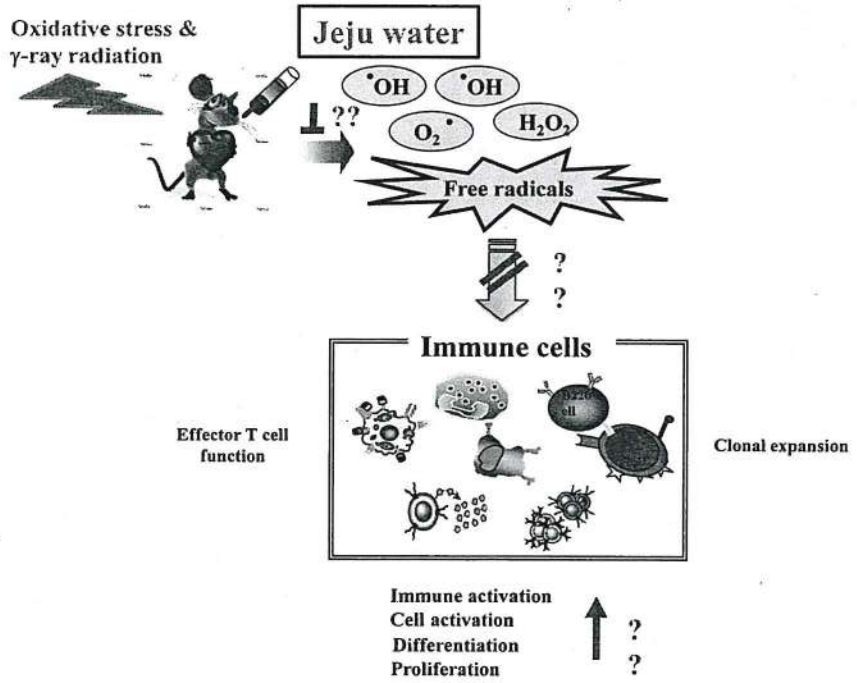

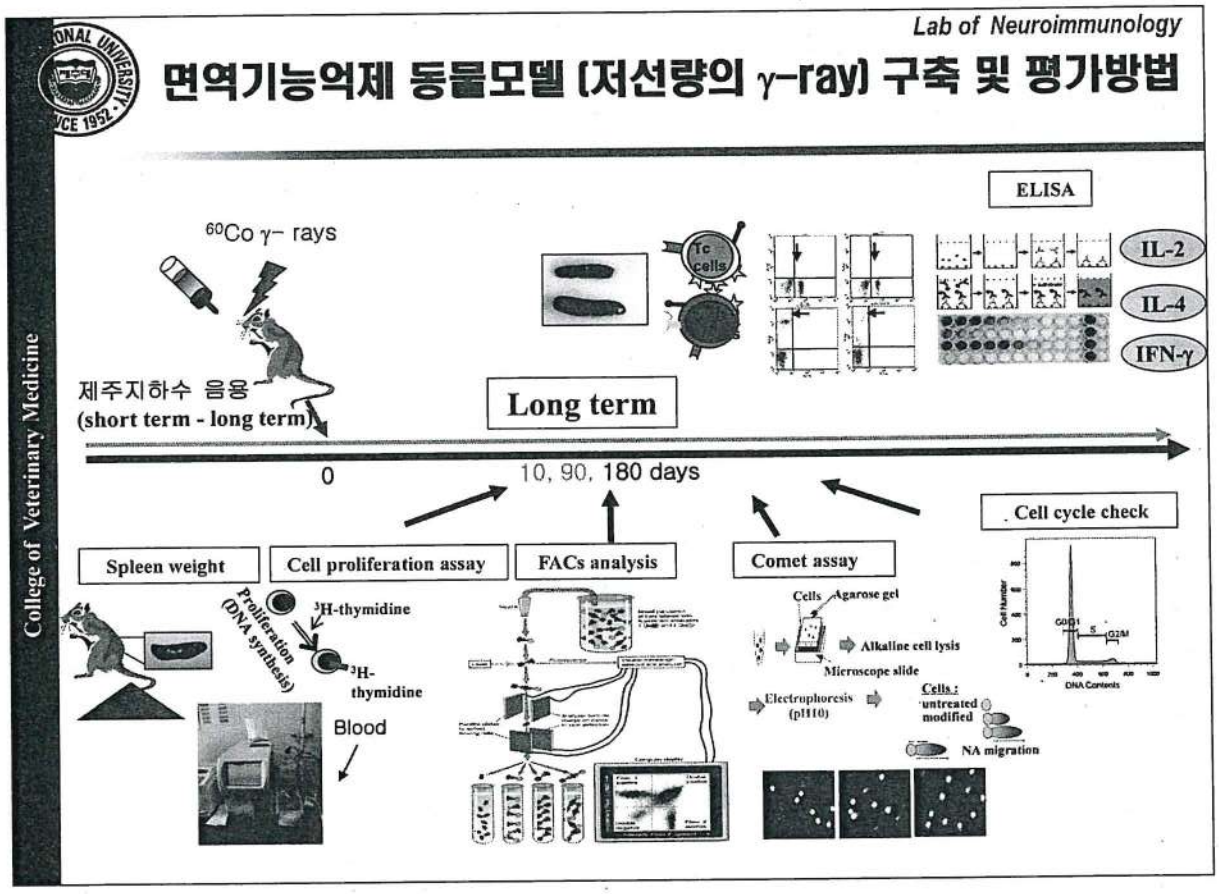
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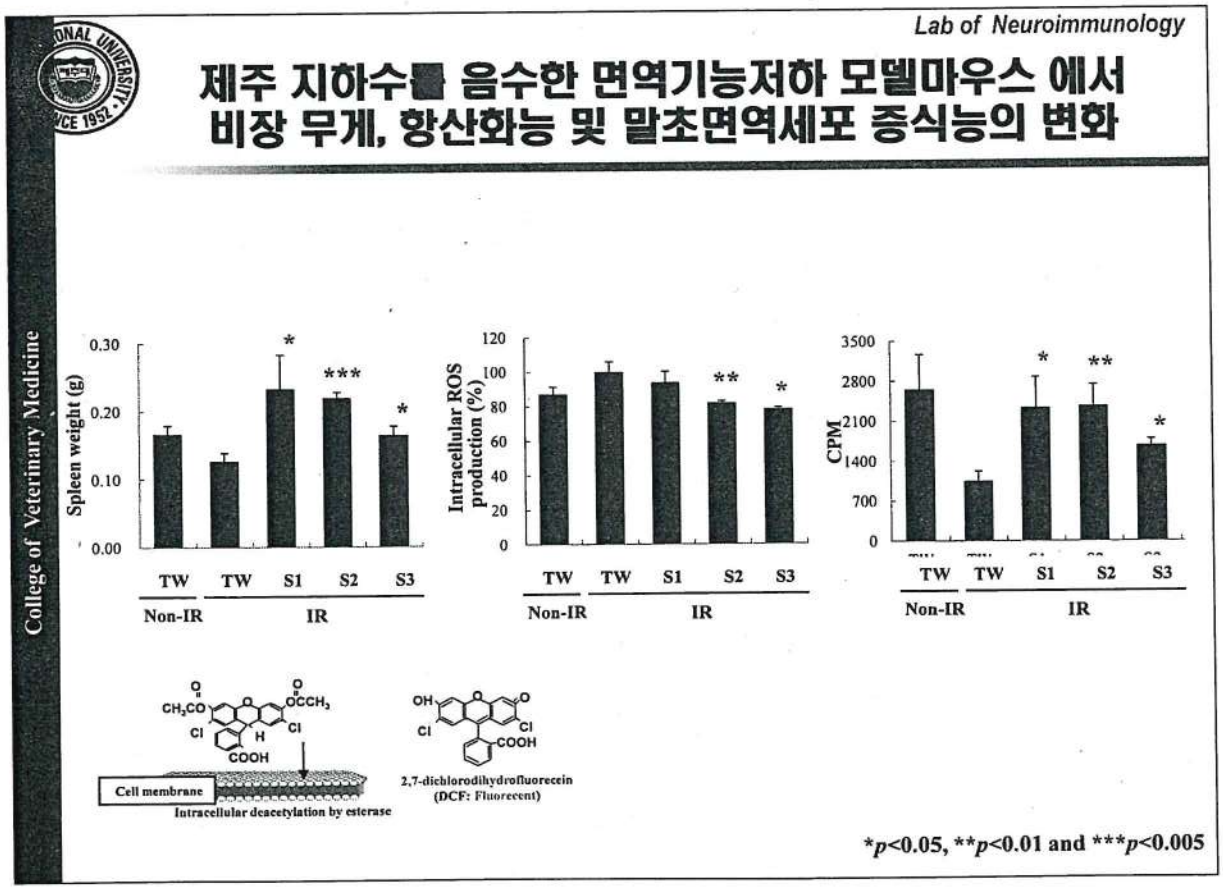
면역기능억제 동물모델 (저선량의 γ-ray) 구축 및 평가방법
College of Veterinary Medicine
ELISA
60Co γ- rays
Tc cells
IL-2
IL-4
IFN-γ
제주지하수 음용
(short term - long term)
Long term
0
10, 90, 180 days
Cell cycle check
Spleen weight
Cell proliferation assay
FACs analysis
Comet assay
Proliferation (DNA synthesis)
3H-thymidine
3H-thymidine
Blood
Cells
Agarose gel
Alkaline cell lysis
Microscope slide
Electrophoresis (pH10)
Cells :
untreated
modified
NA migration
DNA Contents


Lab of Neuroimmunology
제주 지하수를 음수한 면역기능저하 모델마우스 에서
비장 무게, 항산화능 및 말초면역세포 증식능의 변화
College of Veterinary Medicine
Spleen weight (g)
0.30
0.20
0.10
0.00
Intracellular ROS production (%)
120
100
80
60
40
20
0
CPM
3500
2800
2100
1400
700
0
TW
TW
S1
S2
S3
Non-IR
IR
Cell membrane
Intracellular deacetylation by esterase
2,7-dichlorodihydrofluorecein
(DCF: Fluorecent)
*p<0.05, **p<0.01 and ***p<0.005

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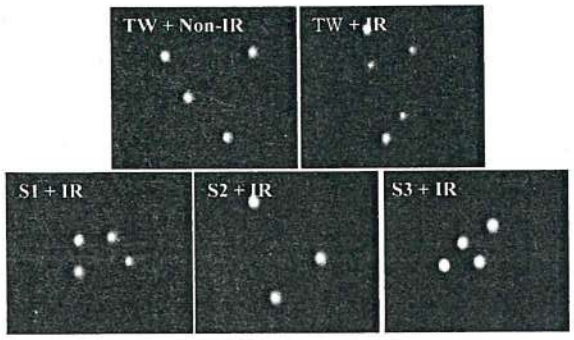
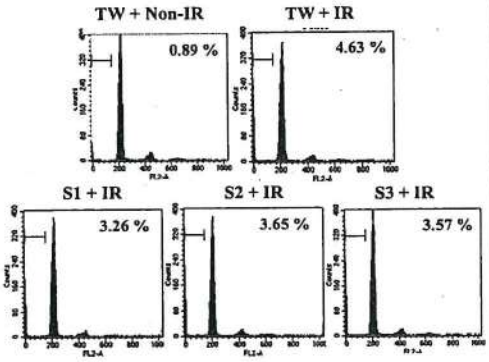
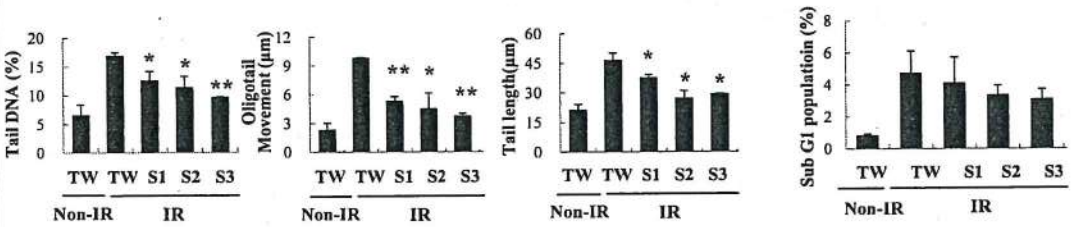
제주 지하수를 음수한 면역기능저하모델 마우스에서 면역세포 DNA 손상 및 세포자멸사(apoptosis) 억제효과







*$p<0.05$ and **$p<0.01$

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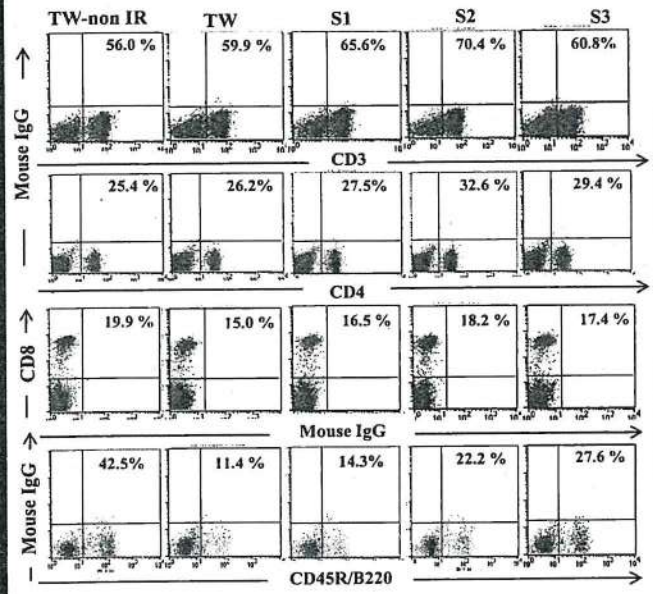
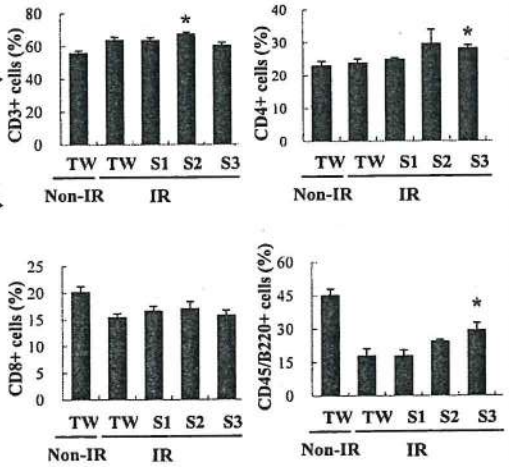
제주 지하수를 음수한 면역기능억제모델 마우스에서 말초면역세포의 수적 변화





*$p<0.05$

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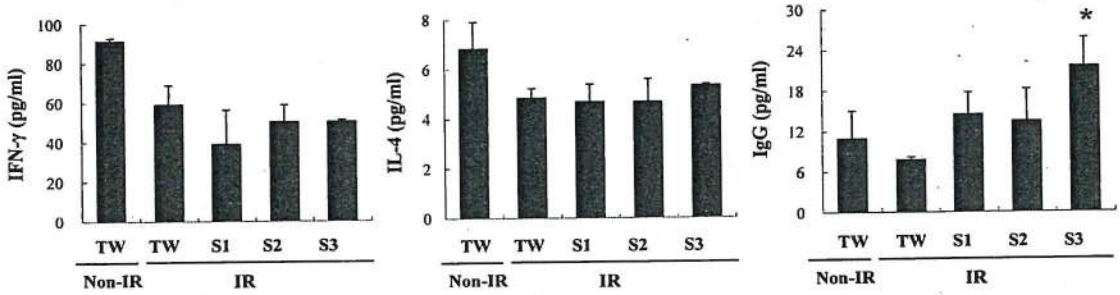
제주 지하수를 음수한 면역기능억제모델 마우스에서 cytokine 및 항체 생성량 변화



*$p<0.05$

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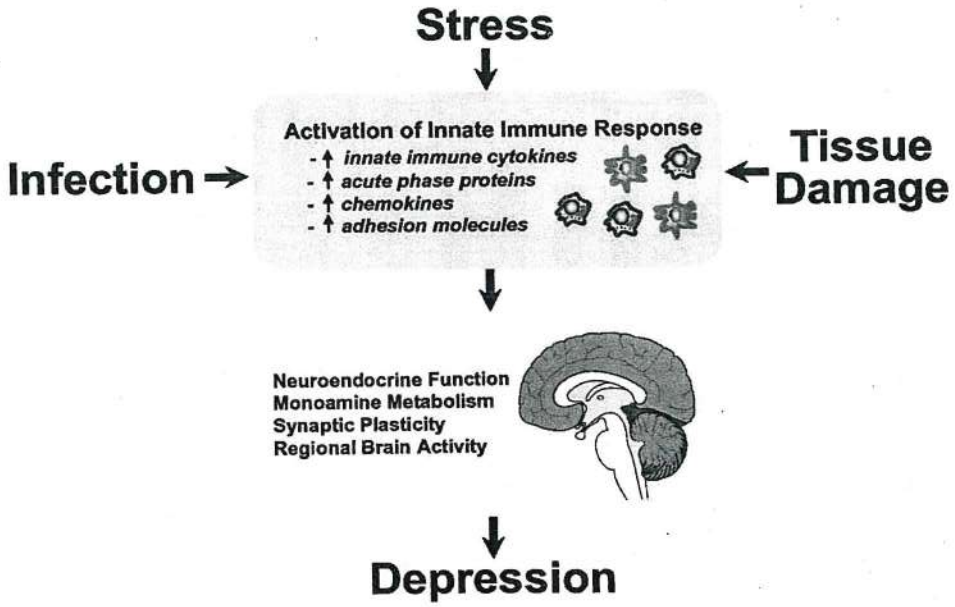
Immune System Contributes to the Pathophysiology of Depression



C. Tsigos et al.. J. Psychosomatic Res, 2002

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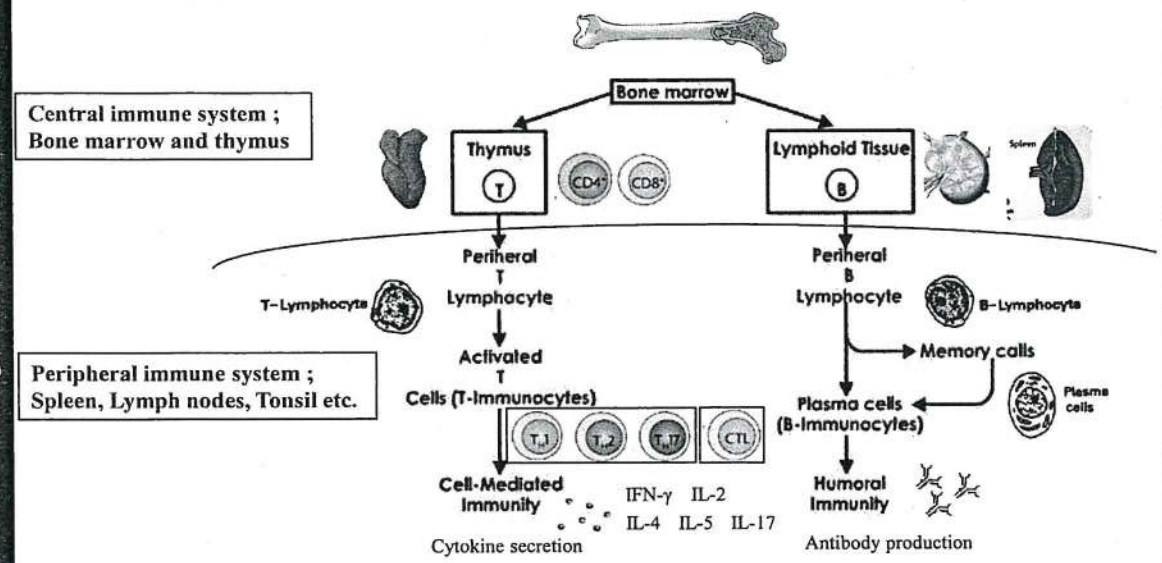
Immune Activation in Central and Peripheral Immune System



Yoshimura A et al., Nat Rev Immunol, 2007
Waldmann Herman et al., Science, 2004

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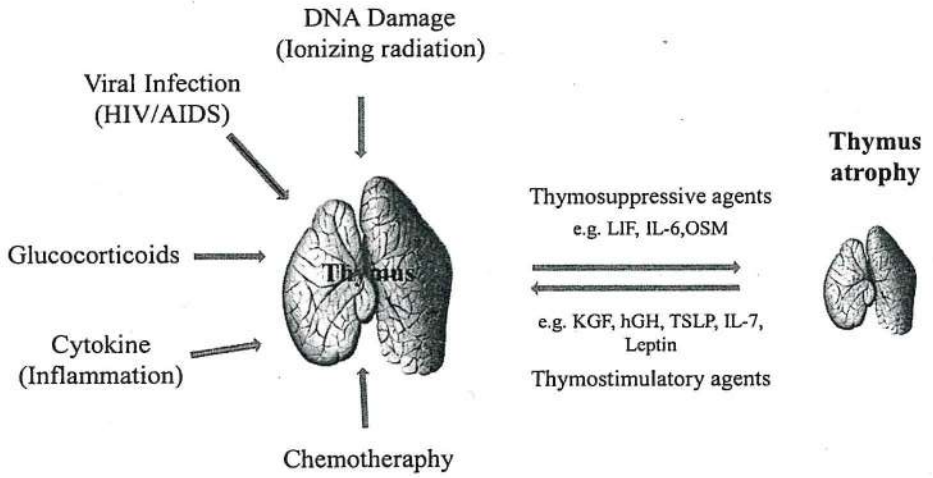
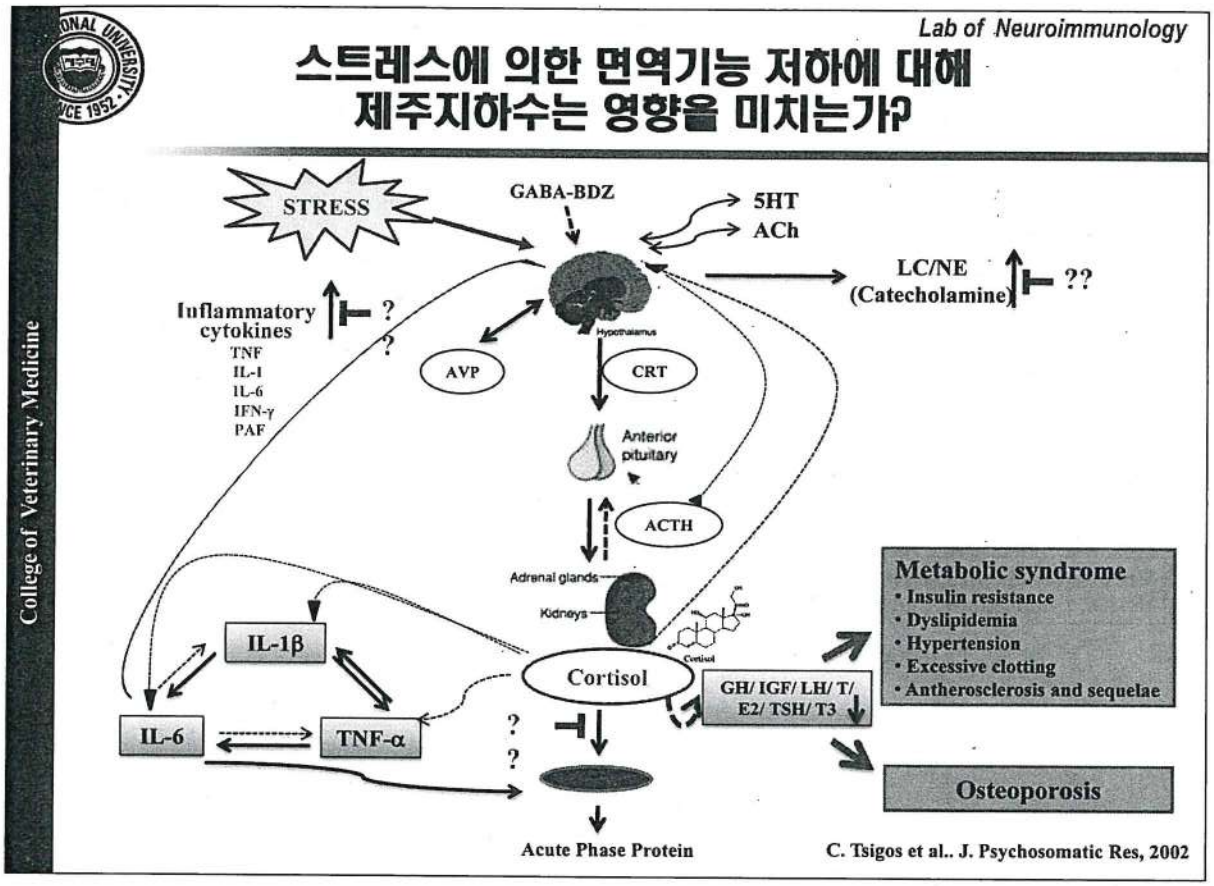
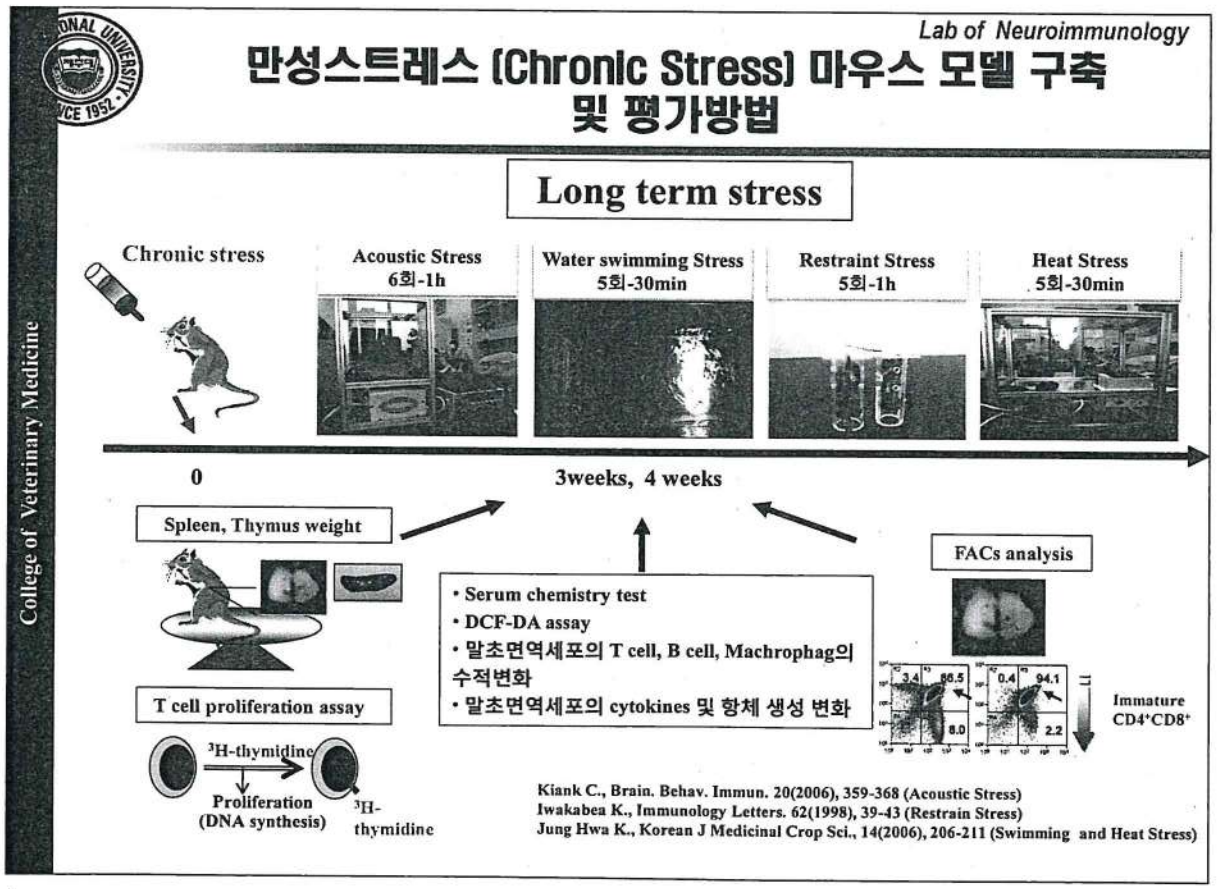
Stress-induced Thymic Atrophy



Gruver and Sempowski, J leukocyte Biology, 2008


Lab of Neuroimmunology
스트레스에 의한 면역기능 저하에 대해
제주지하수는 영향을 미치는가?
College of Veterinary Medicine
STRESS
GABA-BDZ
5HT
ACh
LC/NE
(Catecholamine)
??
Inflammatory cytokines
TNF
IL-1
IL-6
IFN-γ
PAF
AVP
CRT
Anterior pituitary
ACTH
Adrenal glands
Kidneys
Cortisol
IL-1β
IL-6
TNF-α
GH/ IGF/ LH/ T/
E2/ TSH/ T3
Metabolic syndrome
• Insulin resistance
• Dyslipidemia
• Hypertension
• Excessive clotting
• Antherosclerosis and sequelae
Osteoporosis
Acute Phase Protein
C. Tsigos et al.. J. Psychosomatic Res, 2002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만성스트레스 (Chronic Stress) 마우스 모델 구축
및 평가방법
College of Veterinary Medicine
Long term stress
Chronic stress
Acoustic Stress
6회-1h
Water swimming Stress
5회-30min
Restraint Stress
5회-1h
Heat Stress
5회-30min
0
3weeks, 4 weeks
Spleen, Thymus weight
FACs analysis
• Serum chemistry test
• DCF-DA assay
• 말초면역세포의 T cell, B cell, Machrophag의 수적변화
• 말초면역세포의 cytokines 및 항체 생성 변화
T cell proliferation assay
3H-thymidine
Proliferation
(DNA synthesis)
3H-thymidine
Immature
CD4+CD8+
Kiank C., Brain. Behav. Immun. 20(2006), 359-368 (Acoustic Stress)
Iwakabea K., Immunology Letters. 62(1998), 39-43 (Restrain Stress)
Jung Hwa K., Korean J Medicinal Crop Sci., 14(2006), 206-211 (Swimming and Heat Stress)

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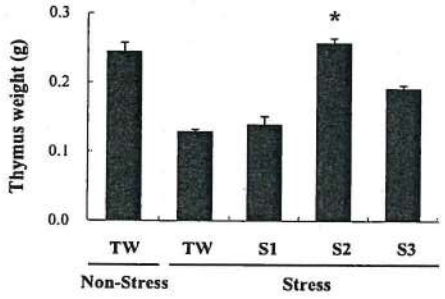
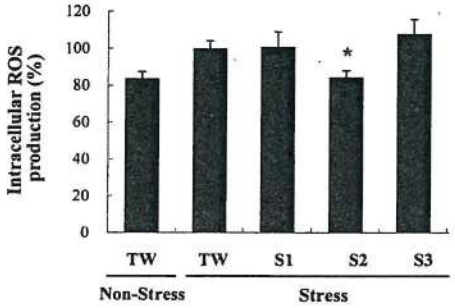
제주 지하수를 음수한 스트레스모델 마우스에서 흉선의 무게 및 항산화능의 변화





$*p<0.05$

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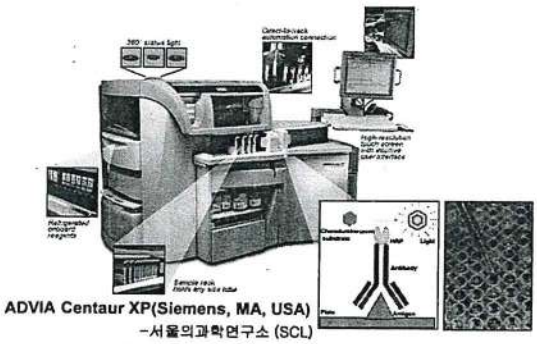
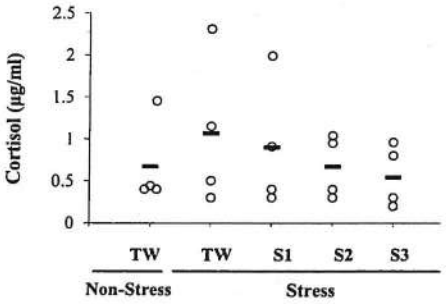
제주 지하수를 음수한 스트레스모델 마우스에서 혈중 corticosteron 농도의 변화

CLIA, Chemiluminescent Immunoassay



ADVIA Centaur XP(Siemens, MA, USA)
-서울의과학연구소 (SCL)



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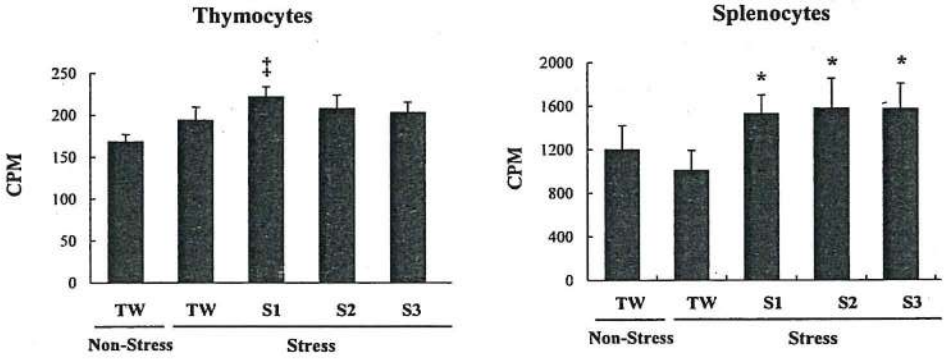
제주 지하수를 음수한 스트레스모델 마우스에서 중추 및 말초 면역세포의 증식능 변화



*p<0.05 and ‡p<0.1

Lab of Neuroimmunology

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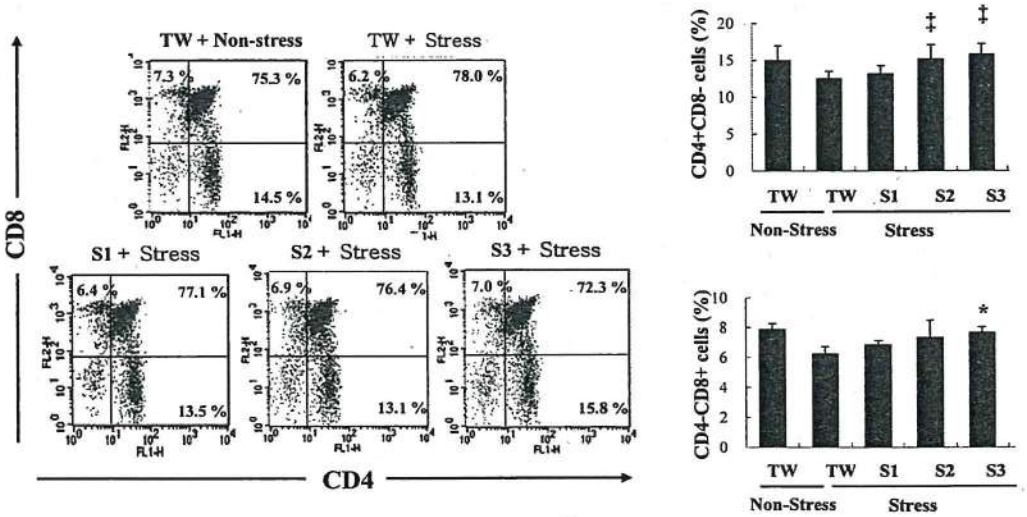
제주워터를 음수한 스트레스모델 마우스에서 중추면역세포의 분화능 변화



*p<0.05 and ‡p<0.1

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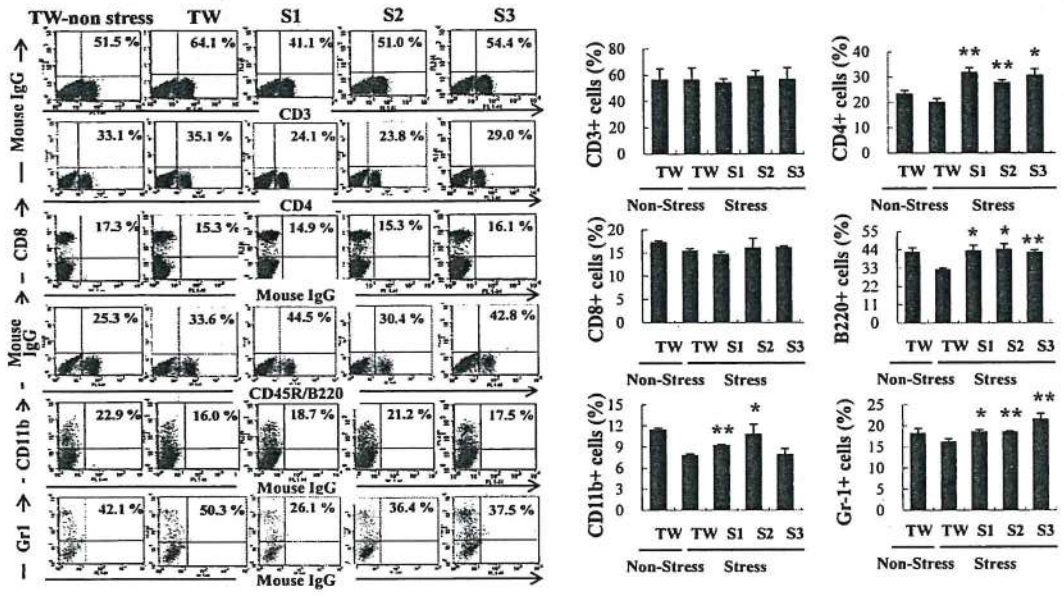
제주 지하수를 음수한 스트레스모델 마우스에서 말초면역세포의 수적 변화



*$p<0.05$ and **$p<0.01$

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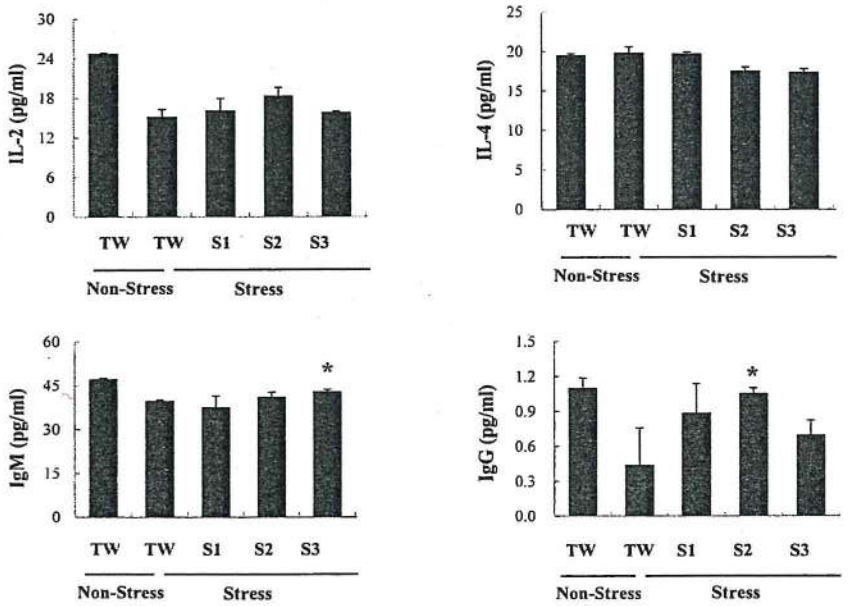
제주 지하수를 음수한 스트레스모델 마우스에서 cytokine 및 항체 생성량 변화



*$p<0.05$

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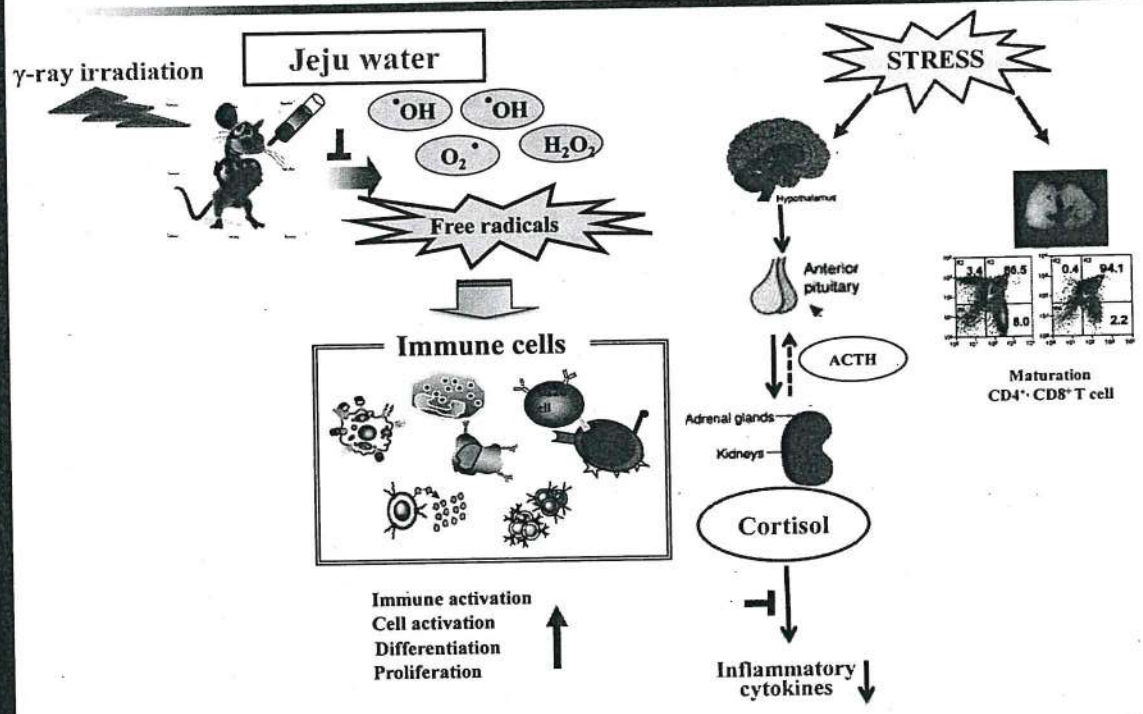
제주 지하수가 면역기능저하 및 스트레스모델 마우스에서 면역기능 향상에 미치는 영향



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Characteristics of Jeju Water

	이화학 성분			음이온				주요미네랄					미량원소						
	pH	EC (μs/cm)	경도 (mg/L)	F (mg/L)	Cl (mg/L)	NO_3 (mg/L)	SO_4 (mg/L)	Ca (mg/L)	K (mg/L)	Mg (mg/L)	Na (mg/L)	SiO_2 (mg/L)	V (μg/L)	Al (μg/L)	B (μg/L)	Fe (μg/L)	Cr (μg/L)	Zn (μg/L)	Mn (μg/L)
S1	7.7	74.4	17.5	0.0	6.0	1.5	1.7	3.4	2.1	2.6	5.9	27.2	7.5	2.3	5.2	15.0	0.2	0.5	0.1
S2	8.2	105.5	23.1	0.1	5.3	1.2	1.8	2.7	4.2	3.5	9.7	27.4	19.4	6.7	7.6	17.3	0.3	8.3	0.0
S3	8.4	179.0	23.0	0.0	9.3	4.4	3.4	4.8	6.6	2.2	23.4	28.5	24.5	8.5	19.4	12.0	0.0	0.0	0.0
SS	7.4	130.1	40.5	0.1	12.4	9.7	8.6	11.6	2.4	2.5	6.3	8.0	1.5	24.3	8.2	64.2	0.3	12.7	1.7
BW-E	7.0	241.9	78.1	0.2	22.6	14.3	14.0	19.6	1.3	3.6	12.8	19.5	1.5	0.8	2.5	62.8	0.1	1.2	0.0
BW-I	7.4	554.1	301.2	0.0	6.4	3.1	11.9	88.5	1.1	26.9	7.2	11.2	0.6	0.2	14.6	0.4	0.1	0.1	0.7

2010년 제주개발공사 자체 분석결과

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물에 함유된 미량원소에 관한 면역활성 연구 사례

바나듐 (V)이 함유된 음용수의 면역활성 연구사례

- 바나듐 경구투여 시 실험동물의 면역체계와 뼈에서의 대사 효능 연구 [Sci Total Environ, 1993]
- 카드늄과 바나듐 이온이 CD4+ T cell의 대한 항원유도 신호전달에 미치는 효과 [Toxicology, 2001]
- 저농도의 바나듐이 사람의 면역세포 기능 향상 및 사이토카인 분비에 미치는 영향 연구 [Ann Clin Lab Sci, 2002]
- 실험동물에 바나듐 경구투여 시 말초혈액 내 T 세포의 증가 효과 [Biol Trace Elem Res, 2010]
- 바나듐수의 장기간 음수가 실험동물의 면역세포인 B cell의 증가에 미치는 영향 연구 [Sci Total Environ, 2002]

실리카 (Si)가 함유된 음용수의 면역활성 연구사례

- 실리카를 경구투여한 정상 실험동물에서 말초세포인 비장 면역세포의 증식능 향상에 대한 연구 [Biol Trace Elem Res, 2002]
- 실리카(SiO2) 투여 시 실험동물의 비장 T, B cell 의 증식능 및 항체(IgG) 생성 증가에 관한 연구 [Eur J Immunol, 1983]
- 정상마우스 비장세포에 실리카(SiO2) 처리 시 면역세포의 집단 (plaque forming cells, PFC) 의 증가 효과 [Immunology, 1982]

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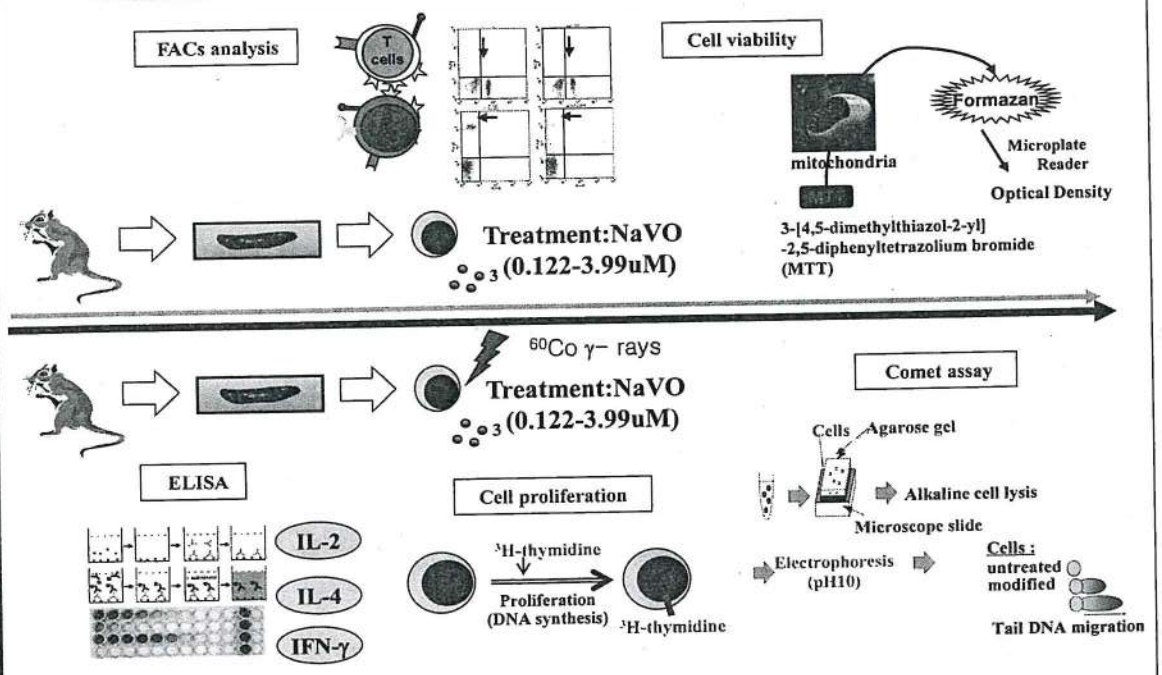
제주 지하수 내 함유된 유효성분 (vanadium)을 이용한 면역활성 기전 연구



* 0.122 and 0.245μM $NaVO_3$ = 14.88 and 29.87ppb (μg/L) ; 제주지하수 S2 및 S3 내 함유량 (15-20ppb, 20-25ppb) 유사

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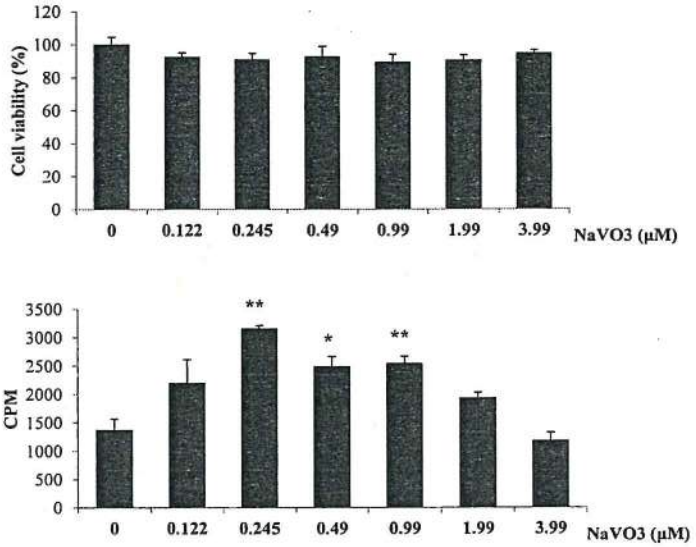
Vanadium에 의한 말초면역세포에서 세포 독성 확인 및 증식능 변화 관찰



* 0.122 and 0.245μM $NaVO_3$ = 14.88 and 29.87ppb (μg/L) ; 제주지하수 S2 및 S3 내 함유량 (15-20ppb, 20-25ppb) 유사

*p<0.05 and **p<0.01

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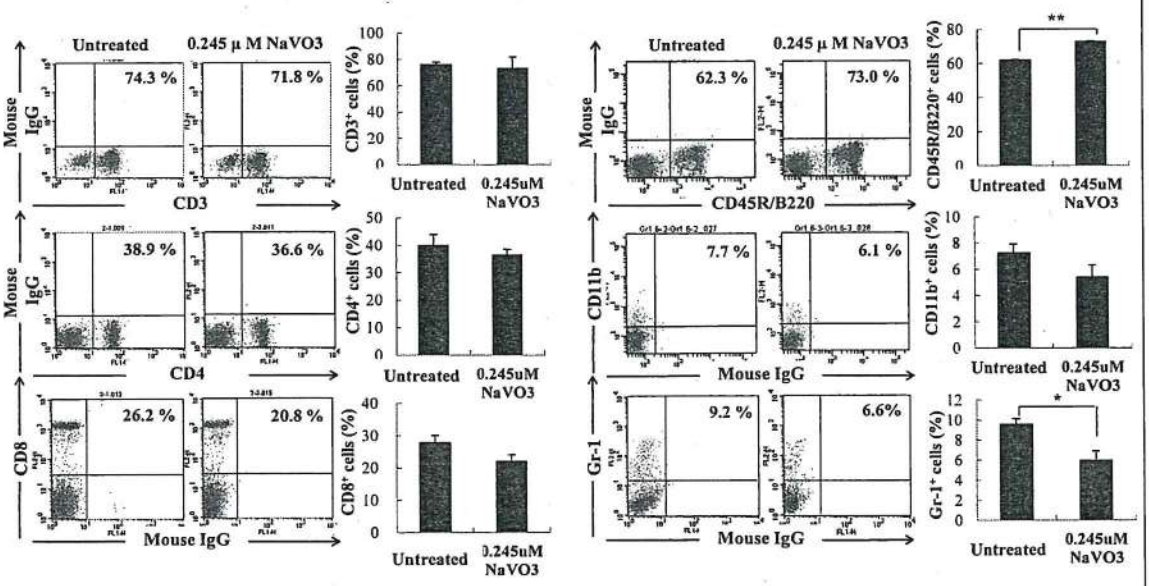
Vanadium에 의한 말초면역세포의 수적 변화



* 0.122 and 0.245μM $NaVO_3$ = 14.88 and 29.87ppb (μg/L) ; 제주지하수 S2 및 S3 내 함유량 (15-20ppb, 20-25ppb) 유사

*p<0.05 and **p<0.01

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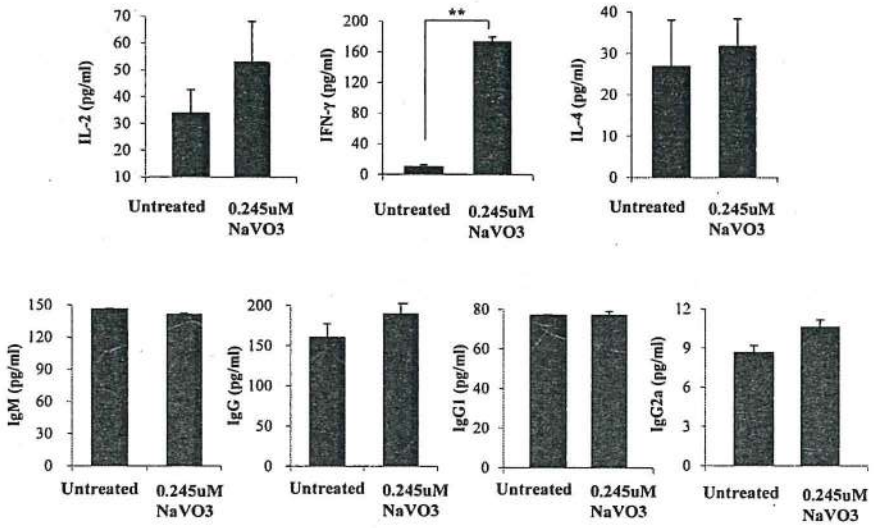
Vanadium에 의한 말초면역세포에서 cytokine 및 항체 생성량 변화



* 0.122 and 0.245μM $NaVO_3$ = 14.88 and 29.87ppb (μg/L) ; 제주지하수 S2 및 S3 내 함유량 (15-20ppb, 20-25ppb) 유사

$^{**}p<0.01$

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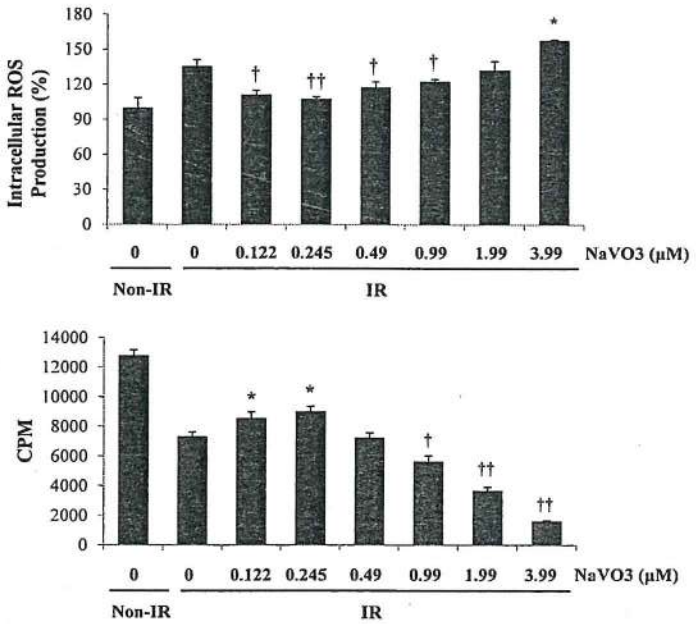
저선량의 방사선이 조사된 말초면역세포에서 Vanadium에 의한 항산화능 및 증식능 변화



* 0.122 and 0.245μM $NaVO_3$ = 14.88 and 29.87ppb (μg/L) ; 제주지하수 S2 및 S3 내 함유량 (15-20ppb, 20-25ppb) 유사

*, † $p<0.05$ and **, †† $p<0.01$

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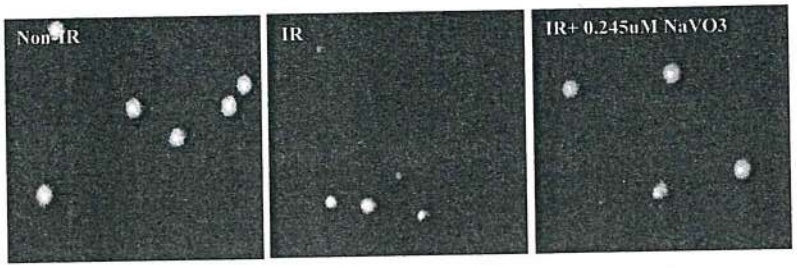
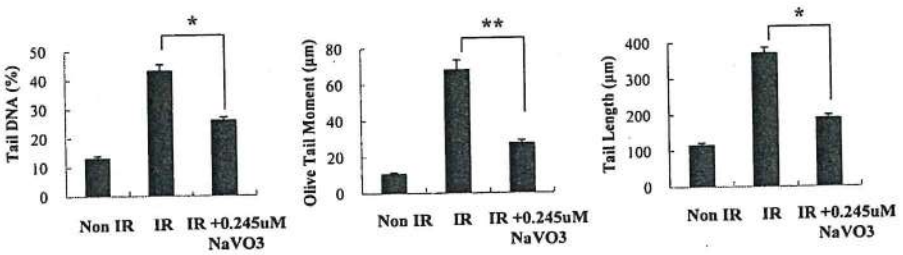
저선량의 방사선이 조사된 말초면역세포에서 Vanadium에 의한 면역세포 DNA 손상 변화





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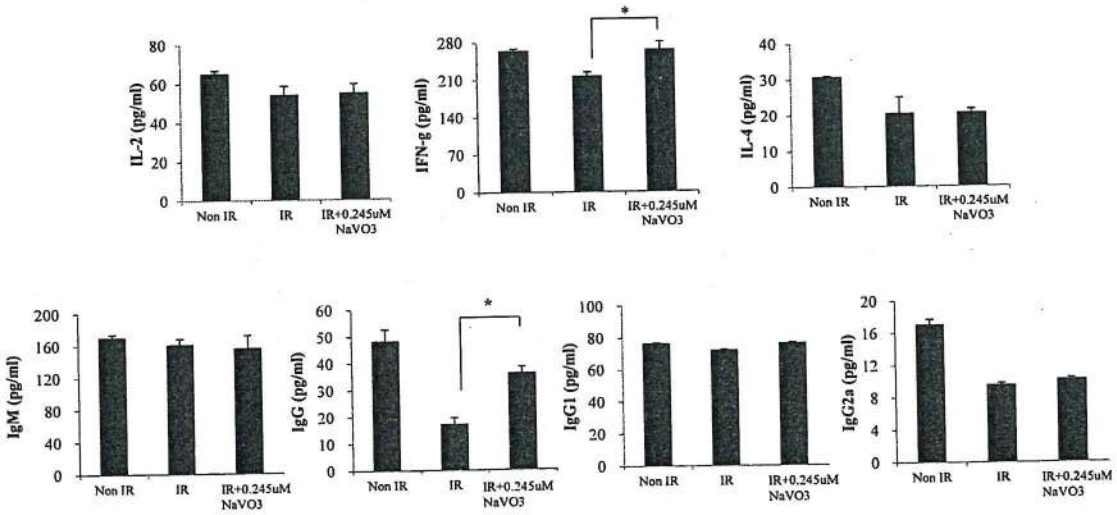
저선량의 방사선이 조사된 말초면역세포에서 Vanadium에 의한 cytokine 및 항체 생성량 변화



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*p<0.05

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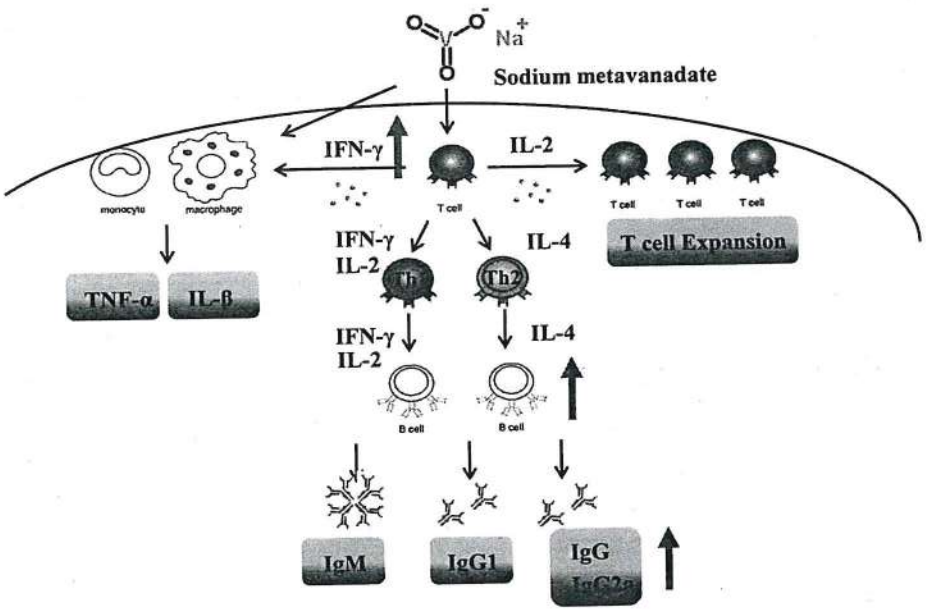
제주 지하수 내 함유된 유효성분 (vanadium)의 면역활성 기전



Gioacchino et al., Ann Clin Lab Sci, 2002; Shen et al., Toxicology, 2001

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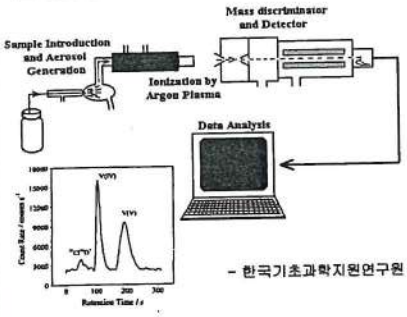
장기간 제주 지하수를 음수한 마우스의 실질장기 내 바나듐 독성 평가

ICP—Mass as per US EPA 6020A



- 한국기초과학지원연구원

Exp. period	Sample		MDL	Result(ppb)
90 Days	TW	Muscle	12	N.D.
	S3	Muscle	17	N.D.
230 Days	TW	Serum	60	549.9
		Liver	83	1981.7
		Kidney	287	1000.1
		Muscle	7	N.D.
	S3	Serum	79	353.6
		Liver	76	960.3
		Kidney	262	1167.3
		Muscle	6	N.D.
250 Days	S3	Serum	68	281.4
		Liver	107	834
		Kidney	240	630.1

MDL : Method Detection Limit (최저검출량); N.D. : Not detected (<MDL) (검출불가)

* Main organs of Vanadium accumulation ; Serum, liver, genital organs < kidney < bones< CNS
* Villani P., Toxicology Letters (2007), Leopardi P., Toxicology Letters (2005)

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최종 수행 실적

Available online at www.kvph.or.kr
Kor. J. Ver. Publ. Hlth., 35 (1). 49-59 (2011)

Korean Journal of Veterinary Public Health

<Original Article>

Immune activation of Jeju water containing vanadium on peripheral immunocytes of low dose gamma rays-irradiated mice

Danbee Ha, Min Ju Kim[1], Haejin Joo, Subeen Cho, So Jin Bing, Yoon-Kyu Lim, Jin Won Hyun[2], Youngheun Jee*

College of Veterinary Medicine, Jeju National University, Jeju 690-756, Korea
[1]Marine Bio Research Team, Korea Basic Science Institute (KBSI), Jeju 690-140, Korea
[2]School of Medicine, Jeju National University, Jeju 690-756, Korea
(Received , 2010 ; Revised , 2010 ; Accepted , 2010)

CANCER PREVENTION RESEARCH

□ORIGINAL ARTICLE□

Effects of Jeju Water Containing Vanadium on Antioxidant Enzymes *in vitro*

Areum Daseul Kim[1], Kyoung Ah Kang[2], Rui Zhang[2], Mei Jing Piao[2], Suhkmann Kim[3], Younghaun Jee[4], Nam Ho Lee[5], Ho Jin You[6], Kyoung Soo Ko[6] and Jin Won Hyun[2]

[1]Department of Marine Life Science, Jeju National University, [2]School of Medicine, Jeju National University, Jeju 690-756, [3]Department of Chemistry and Chemistry Institute for Functional Materials, Pusan National University, Busan 609-735, [4]College of Veterinary Medicine, [5]Department of Chemistry, College of Natural Sciences, Jeju National University, Jeju 690-756, [6]Department of Biomaterials, DNA Repair Center, Chosun University, Gwangju 501-759, [7]R&D Center, Jeju Special Self-Governing Province Development Co., Jeju 695-961, Korea

CANCER PREVENTION RESEARCH

□ORIGINAL ARTICLE□

Reactive Oxygen Species Scavenging Effects of Jeju Waters Containing Vanadium Components

Areum Daseul Kim[1], Kyoung Ah Kang[2], Rui Zhang[2], Chae Moon Lim[3], Youngheun Jee[4], Nam Ho Lee[5], Ho Jin You[6], Kyoung Soo Ko[6] and Jin Won Hyun[2]

[1]Department of Marine Life Science, [2]School of Medicine, [3]College of Veterinary Medicine, [4]Department of Chemistry, College of Natural Sciences, Jeju National University, Jeju 690-756, [5]Department of Biomaterials, DNA Repair Center, Chosun University, Gwangju 501-759, [6]R&D Center, Jeju Special Self-Governing Province Development Co., Jeju 695-961, Korea

Food and Chemical Toxicology

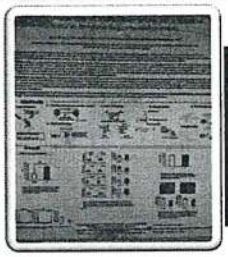
journal homepage: www.elsevier.com/locate/foodchemtox

Jeju ground water containing vanadium induced immune activation on splenocytes of low dose γ-rays-irradiated mice

Danbee Ha[a], Haejin Joo[a], Ginnae Ahn[a], Min Ju Kim[b], So Jin Bing[a], Subin An[a], Hyunki Kim[a], Kyung-goo Kang[c], Yoon-Kyu Lim[d], Youngheun Jee[a,*]

ARTICLE INFO

ABSTRACT



국내논문 3편, SCI 논문 1편, 국내외 학회발표 7건

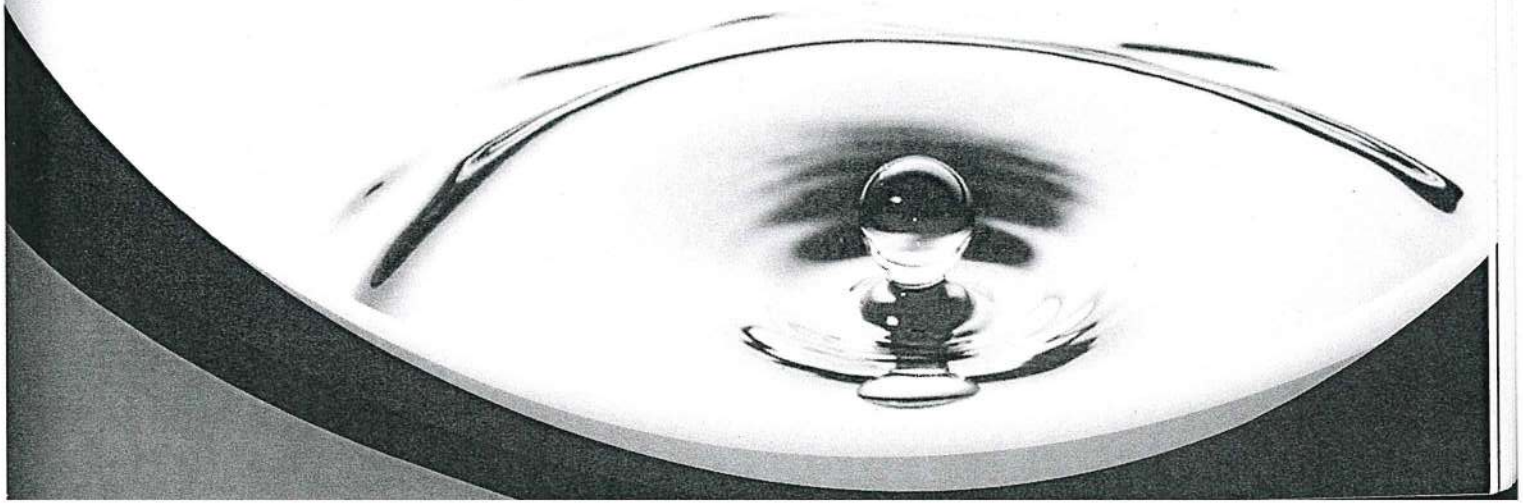
MEMO

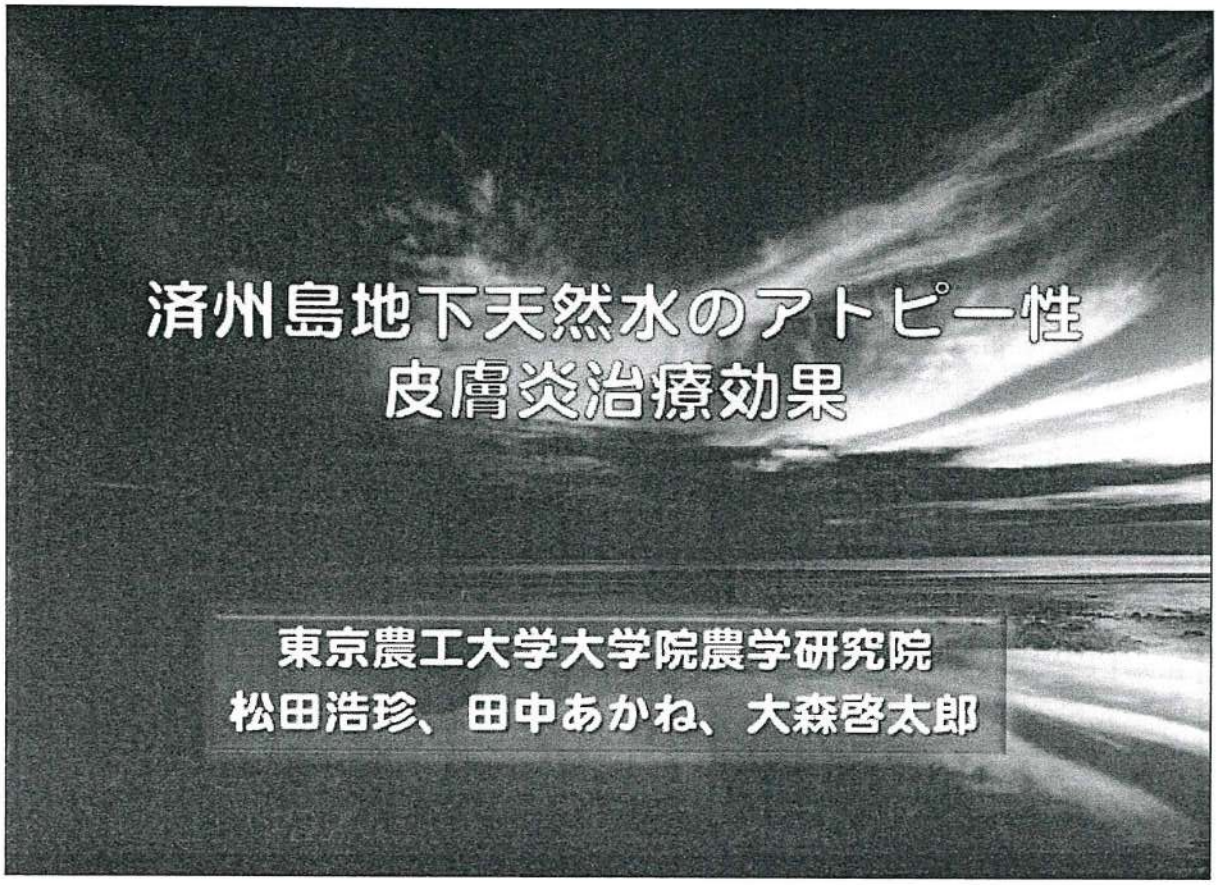
제주 천연 지하수의 아토피성 피부염증에 대한 효능

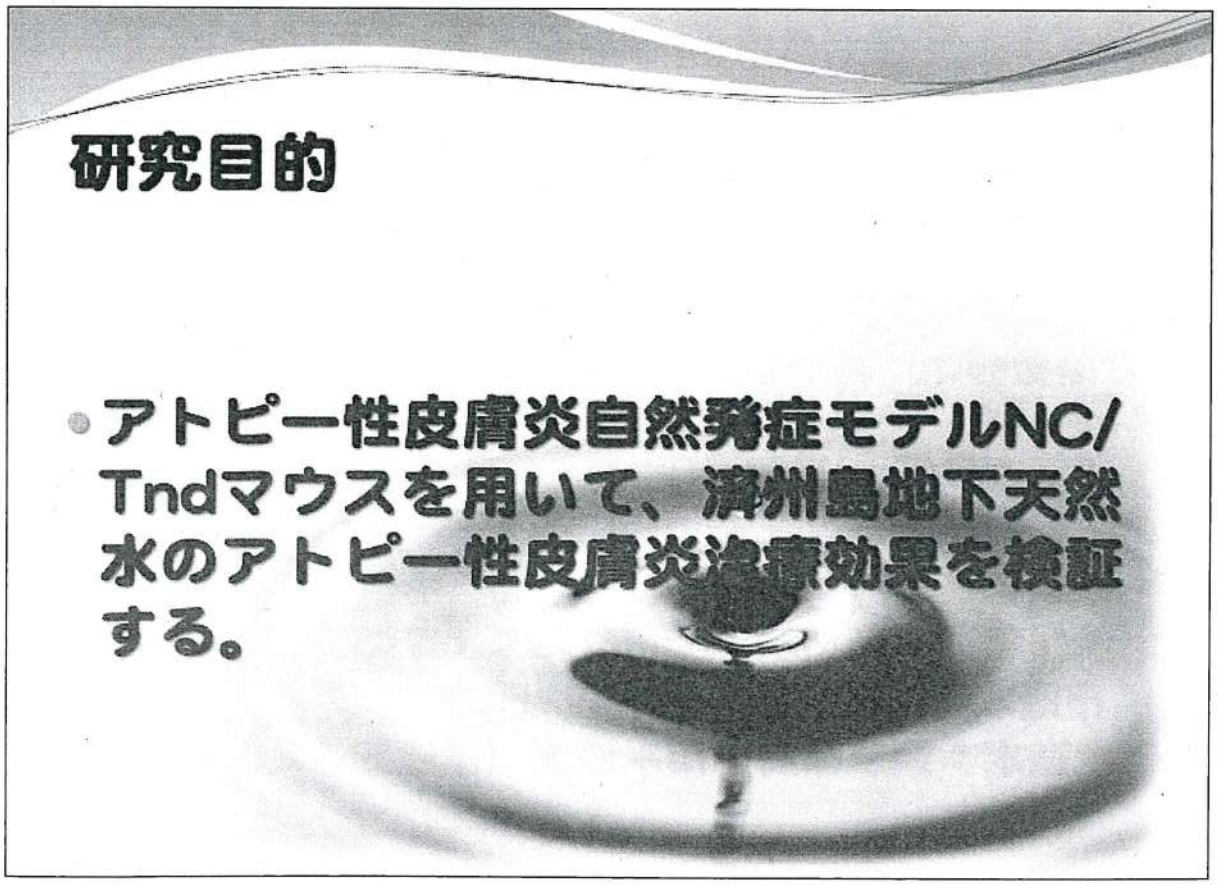
Effect of Jeju groundwater on atopic dermatitis

히로시 마쓰다 동경농공대 수의과대학 교수

Hiroshi Matsuda, Tokyo University of Agriculture and Technology




済州島地下天然水のアトピー性
皮膚炎治療効果
東京農工大学大学院農学研究院
松田浩珍、田中あかね、大森啓太郎


研究目的
アトピー性皮膚炎自然発症モデルNC/Tndマウスを用いて、済州島地下天然水のアトピー性皮膚炎治療効果を検証する。

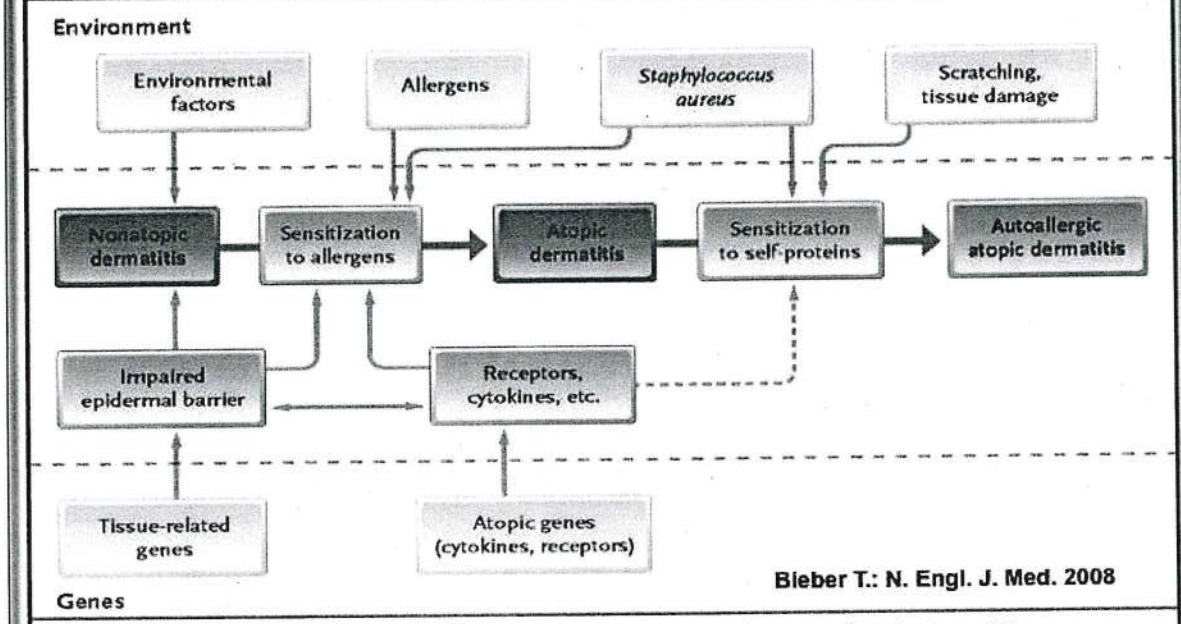
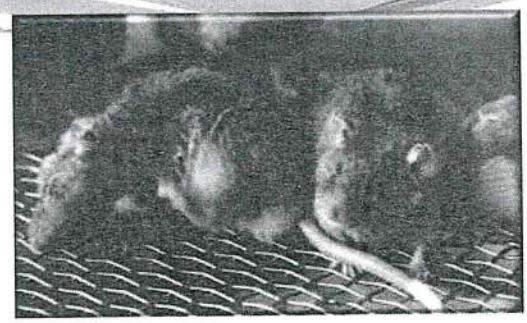


Figure 5. Gene–Gene and Gene–Environment Interactions in the Natural History of Atopic Dermatitis.
As a result of genetically determined epidermal-barrier dysfunction and the effect of environmental factors, nonatopic dermatitis is the first manifestation of atopic dermatitis. Subsequently, because of their genetic predisposition for IgE-mediated sensitization, patients become sensitized. This phenomenon is favored by *Staphylococcus aureus* enterotoxin products. Finally, scratching leads to tissue damage and the release of structural proteins, triggering an IgE response in patients with atopic dermatitis. This sensitization to self-proteins can be due to the homology of allergen-derived epitopes and human proteins in the context of molecular mimicry.

材　料



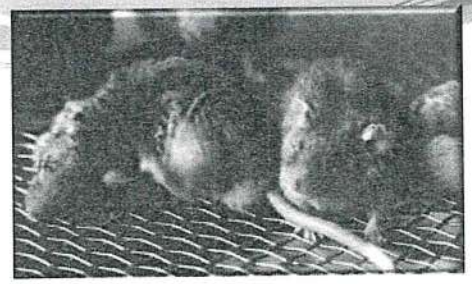
- **動　物**
  雌雄 NC/Tndマウス

- **被験物質**
  済州島地下天然水：Sam-Da-Soo (S1), S2, S3
  市販水１：硬水系（硬度約283）
  水道水：東京都府中市水道水（硬度約１26）

水質検査

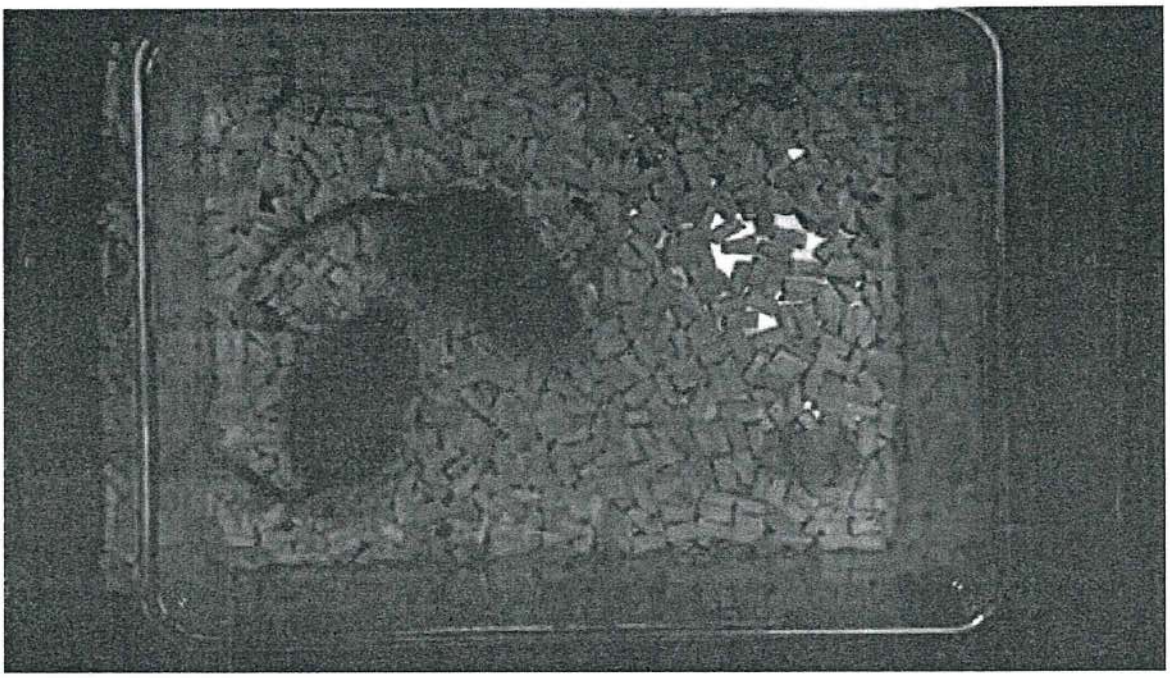
検査項目	試験水				
	水道水	S1	S2	S3	市販水
pH	7.0	7.8	7.0	7.4	7.2
硬度	126	10	22	17	283
Mineral ions (mg/L) Chloride	10	7	7	7	7
Silicate	39	28	28	35	15
Phosphate	0.04	0.09	0.15	0.10	< 0.03
Sodium	12.7	5.67	11.1	28.1	6.55
Potassium	2.76	2.33	4.57	7.71	1.14
Calcium	39.3	1.8	2.20	4.00	72.4
Magnesium	7.0	1.39	2.40	1.83	25.4
Vanadium	< 0.001	0.008	0.015	0.016	< 0.001
Endotoxin (EU/mL)	0.095	< 0.025	0.061	2.380	1.300

研究方法

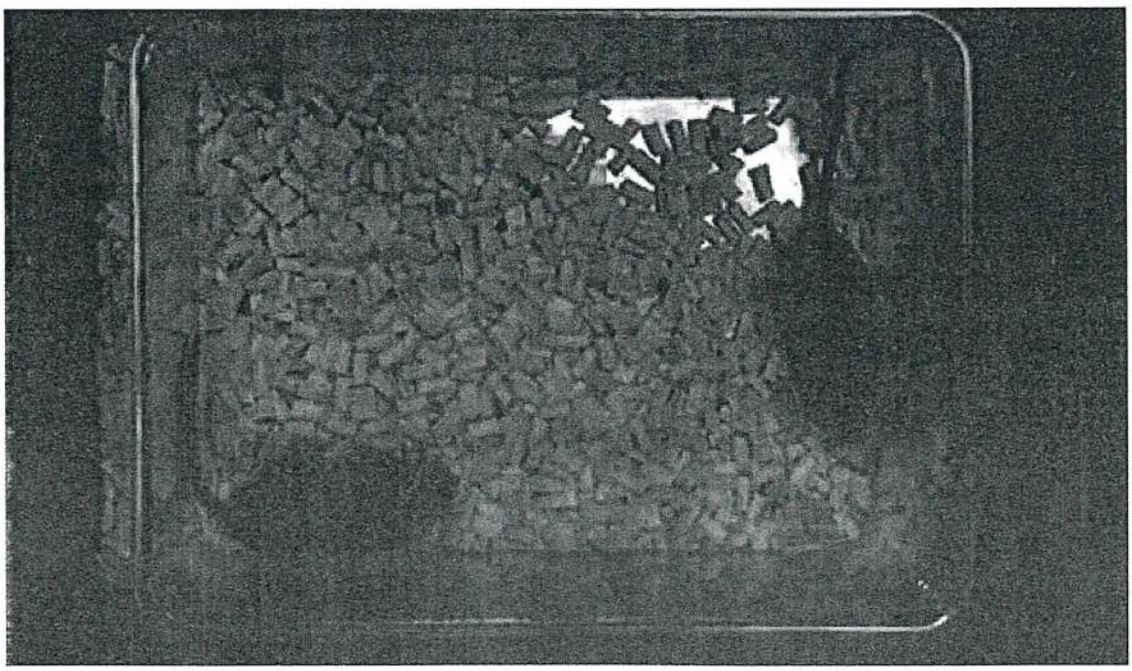


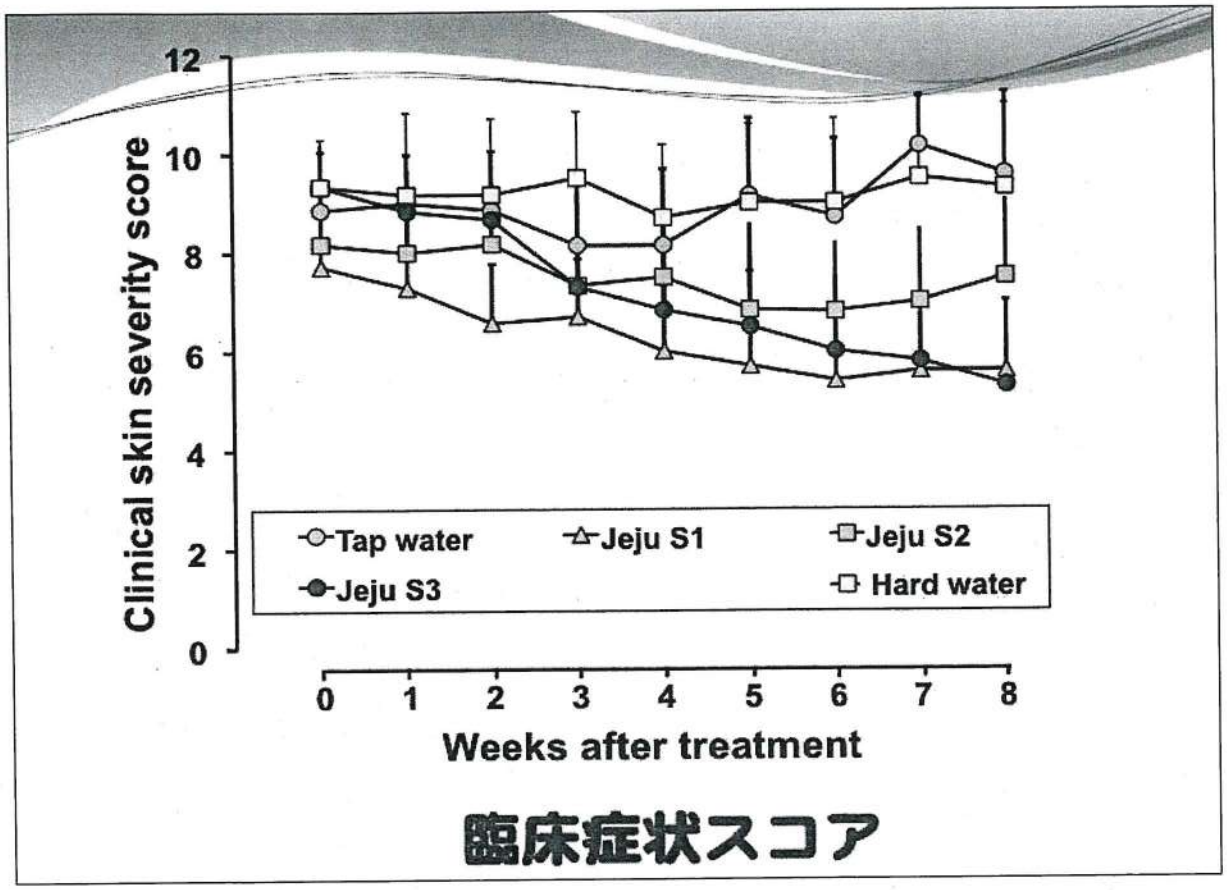
- *In vivo*試験
  8週齢から10週齢のNC/Tndマウス（中等度から重度発症）に、8週間各水を自由に摂取させた。
- 評価方法
  -臨床症状スコアの記録
  -引っ掻き行動の測定
  （自動測定装置SCLABA-Realを使用）
  -経皮水分蒸散量(TEWL)の測定
  -皮膚のreal time RT-PCR検査
  -組織病理学的検査

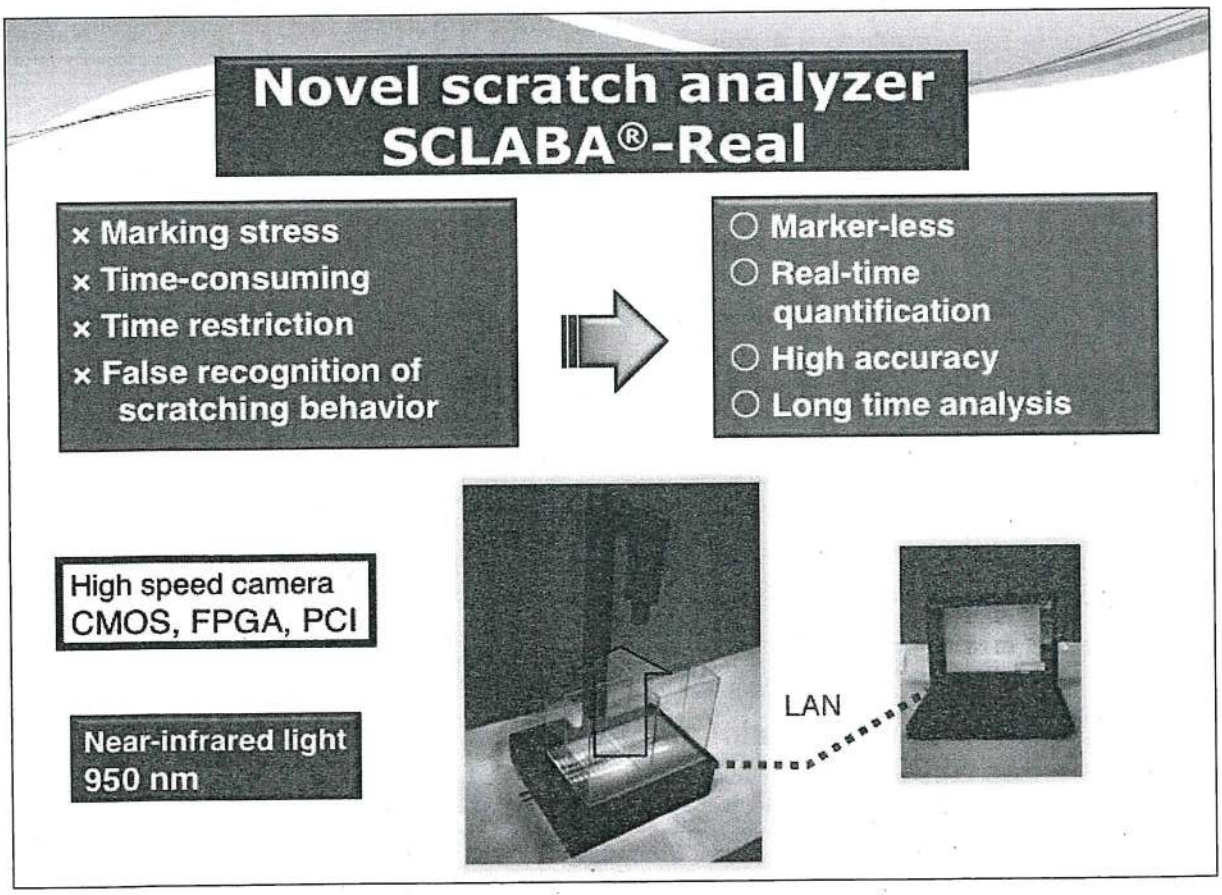
市販水（超硬水）



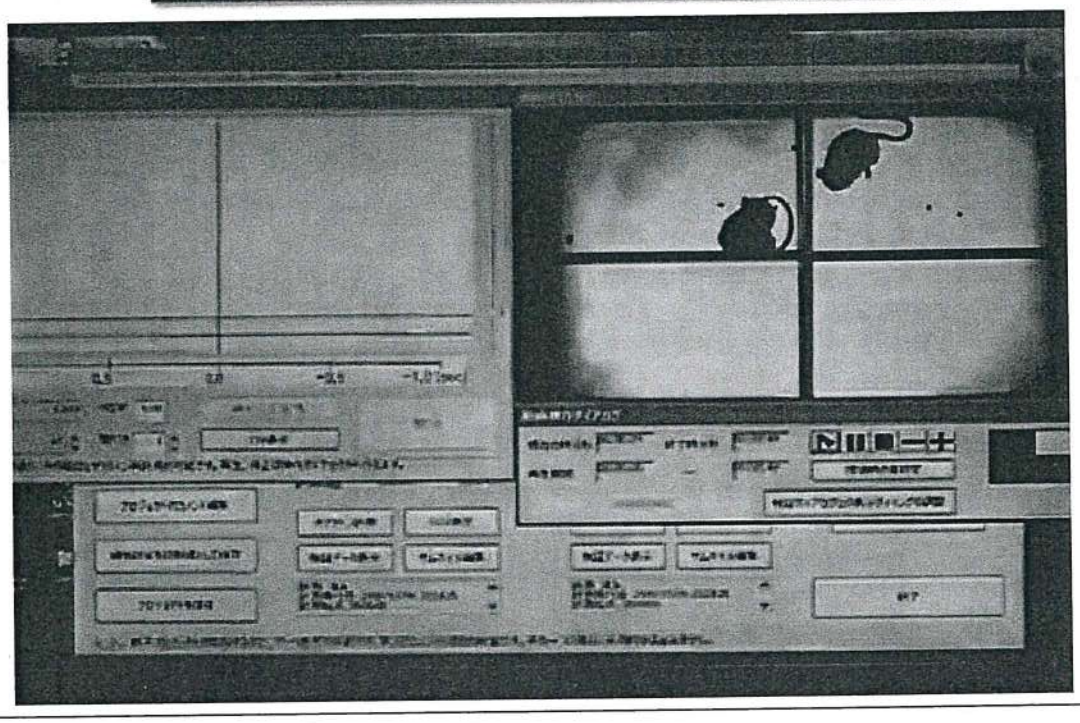
S1

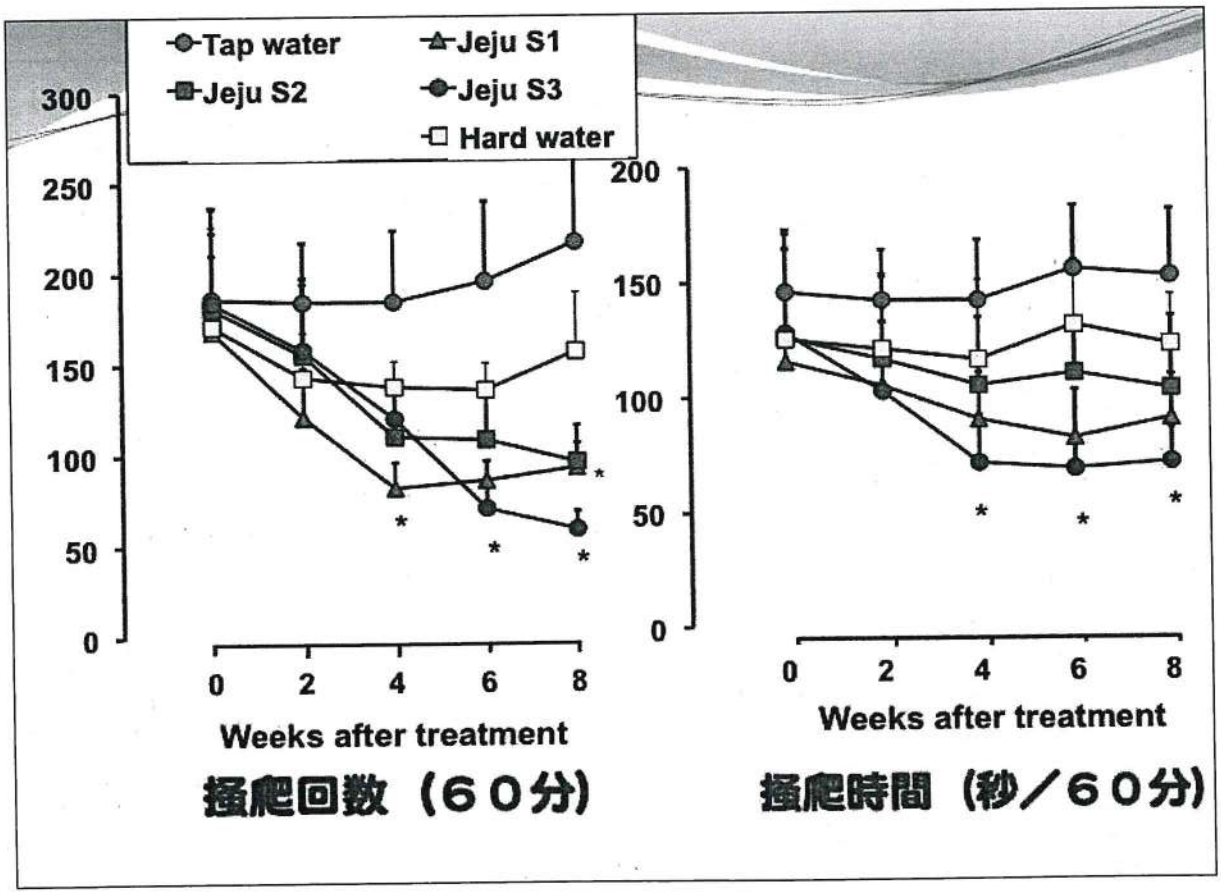


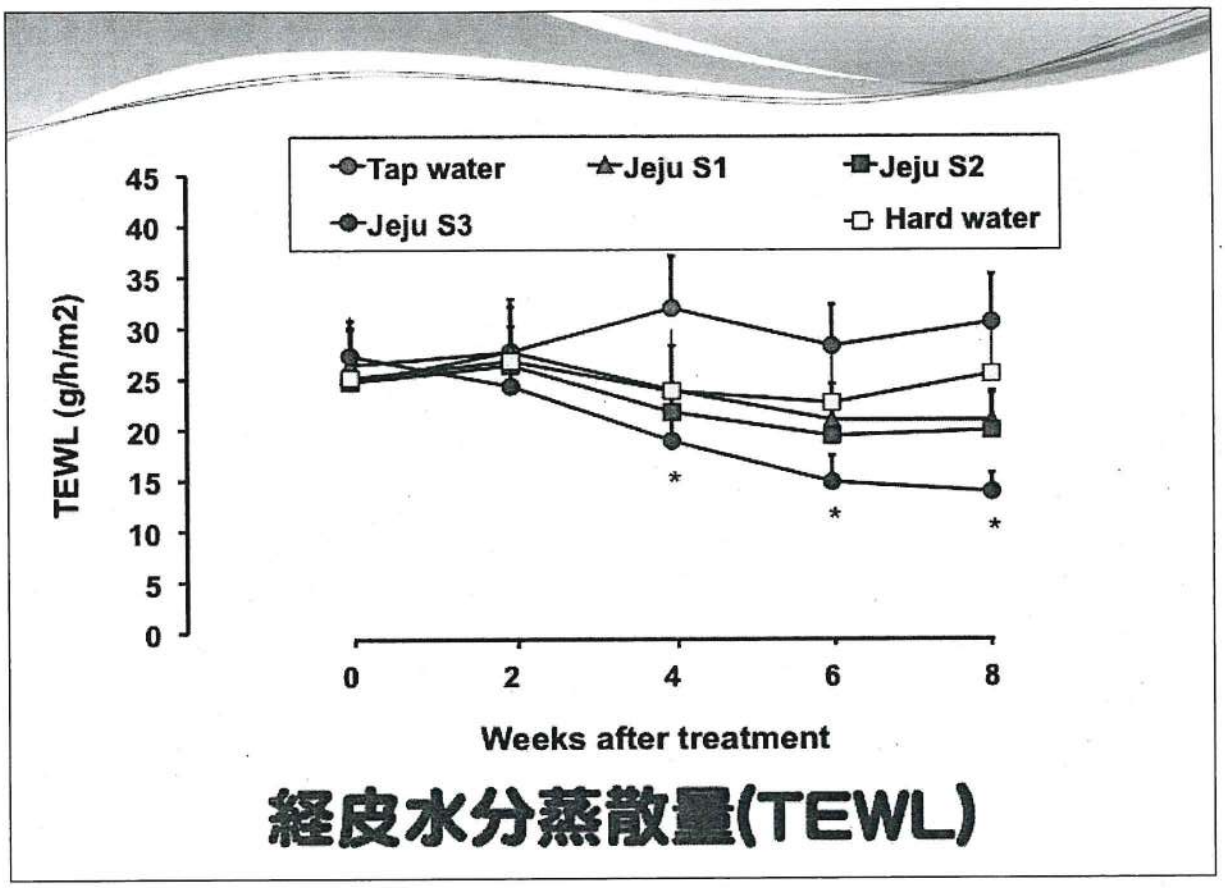

Clinical skin severity score
12
10
8
6
4
2
0
Tap water
Jeju S1
Jeju S2
Jeju S3
Hard water
0 1 2 3 4 5 6 7 8
Weeks after treatment
臨床症状スコア


Novel scratch analyzer
SCLABA®-Real
× Marking stress
× Time-consuming
× Time restriction
× False recognition of scratching behavior
○ Marker-less
○ Real-time quantification
○ High accuracy
○ Long time analysis
High speed camera
CMOS, FPGA, PCI
Near-infrared light
950 nm
LAN

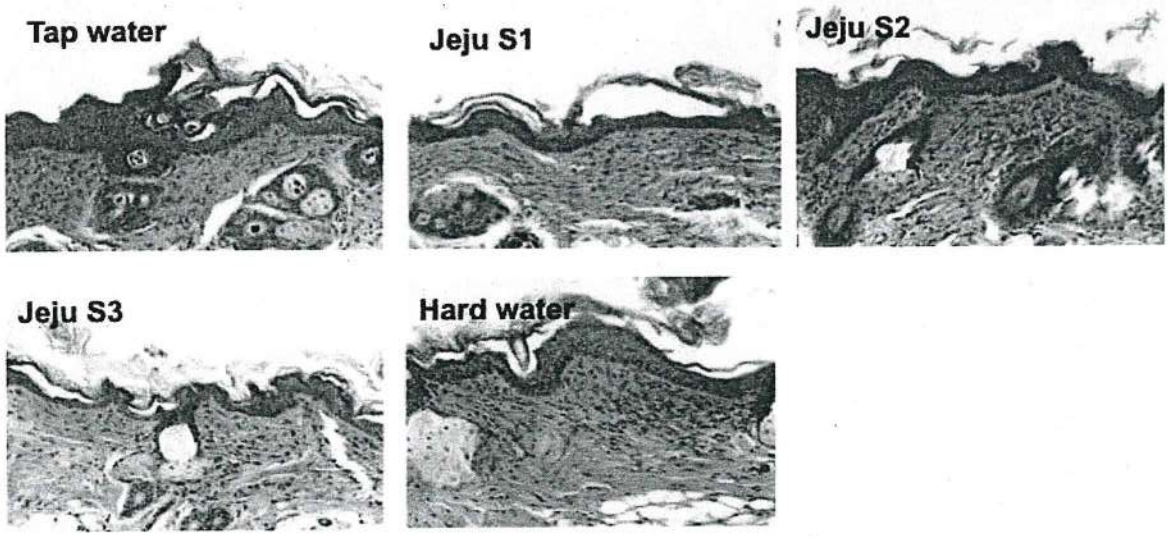
Extraction of scratching behavior with SCLABA-Real



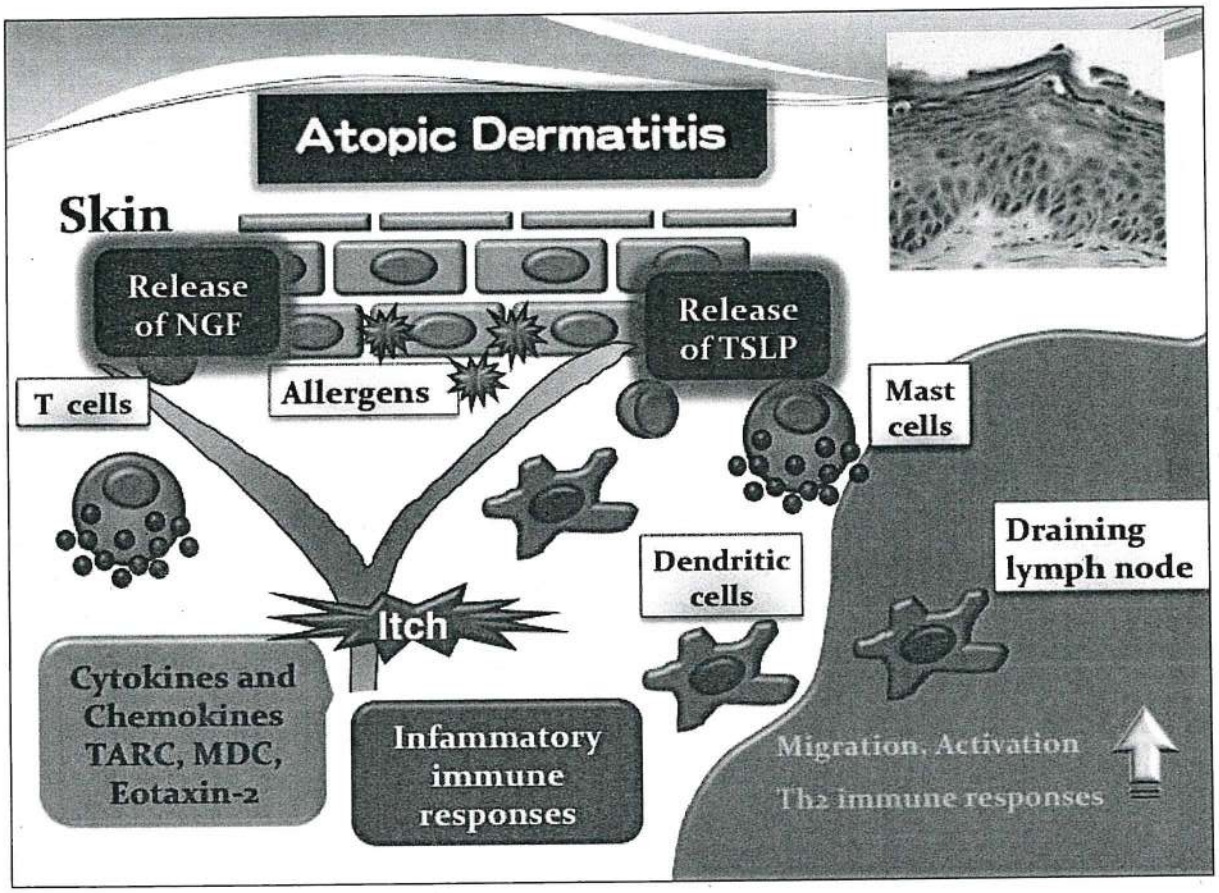


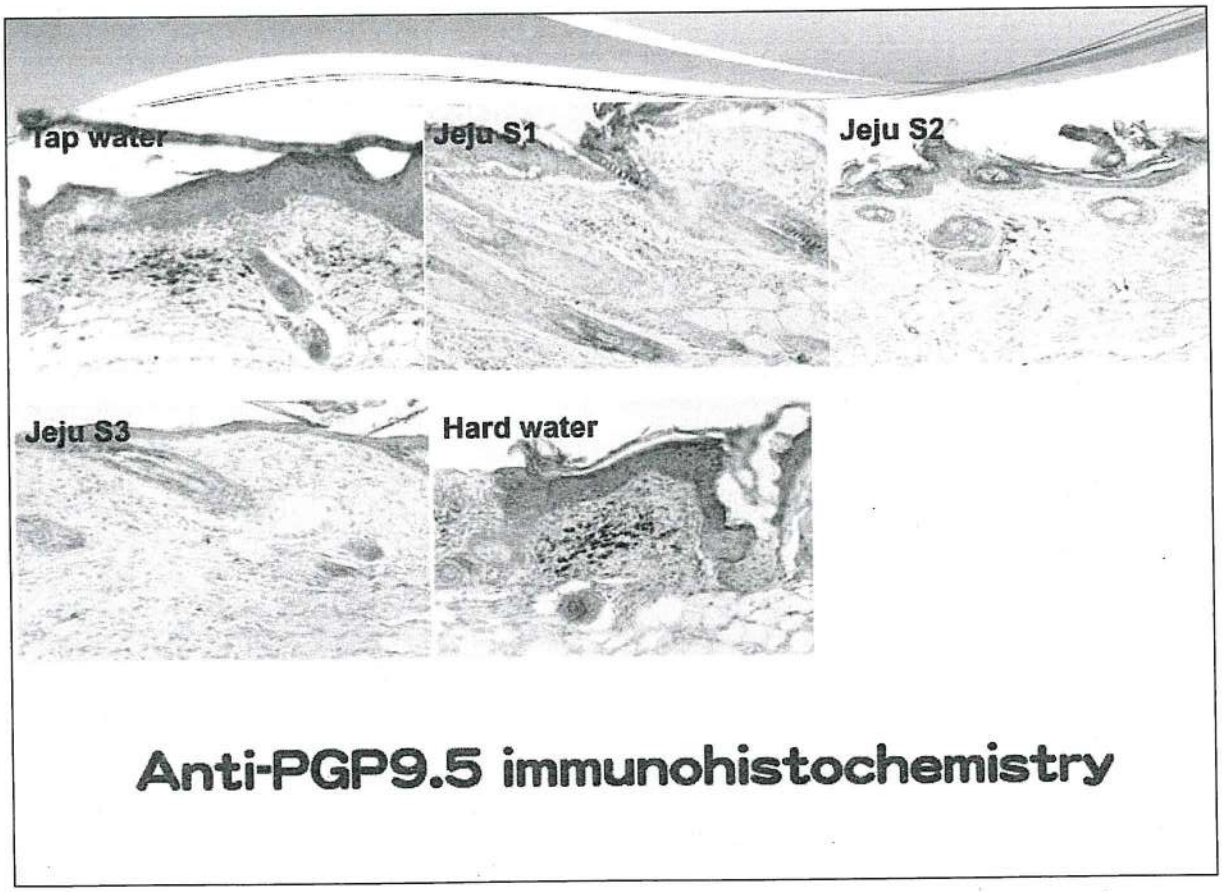


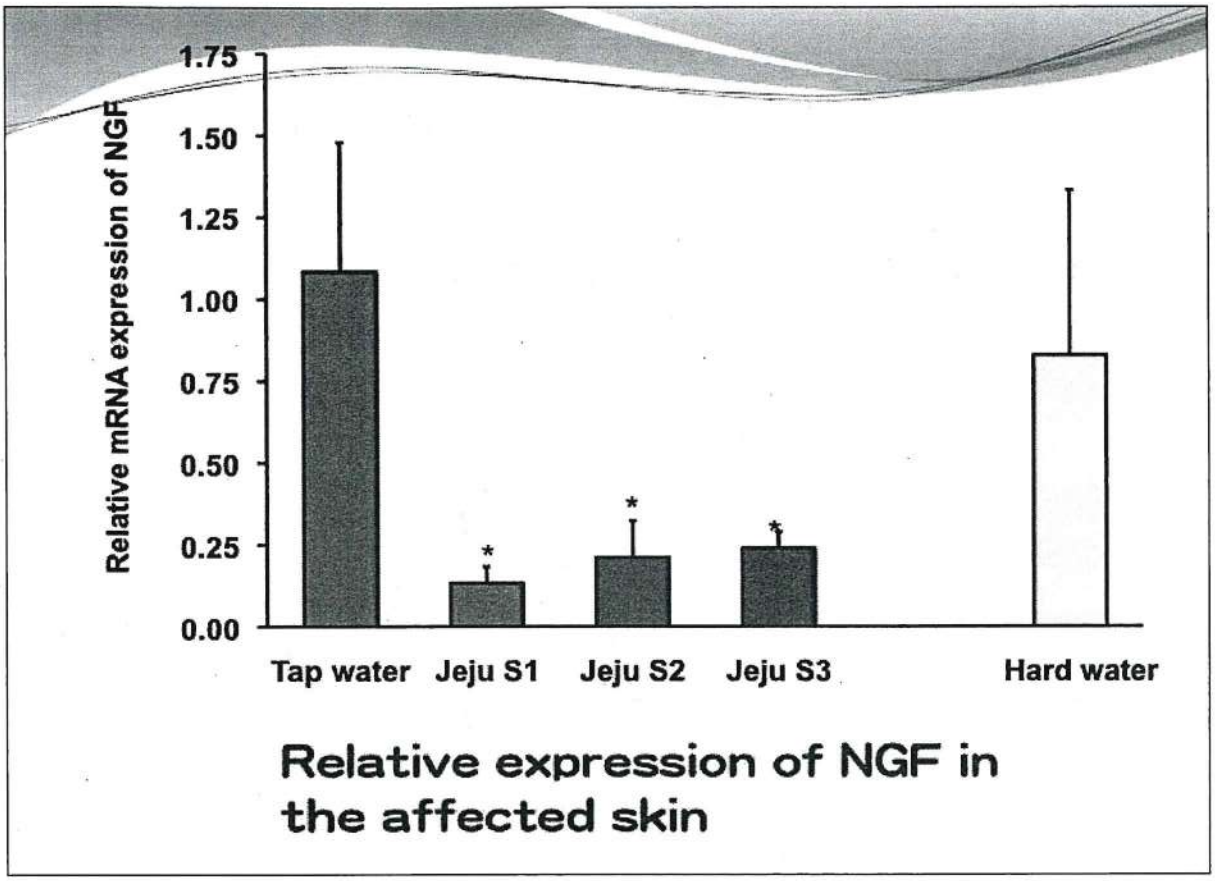
經皮水分蒸散量(TEWL)

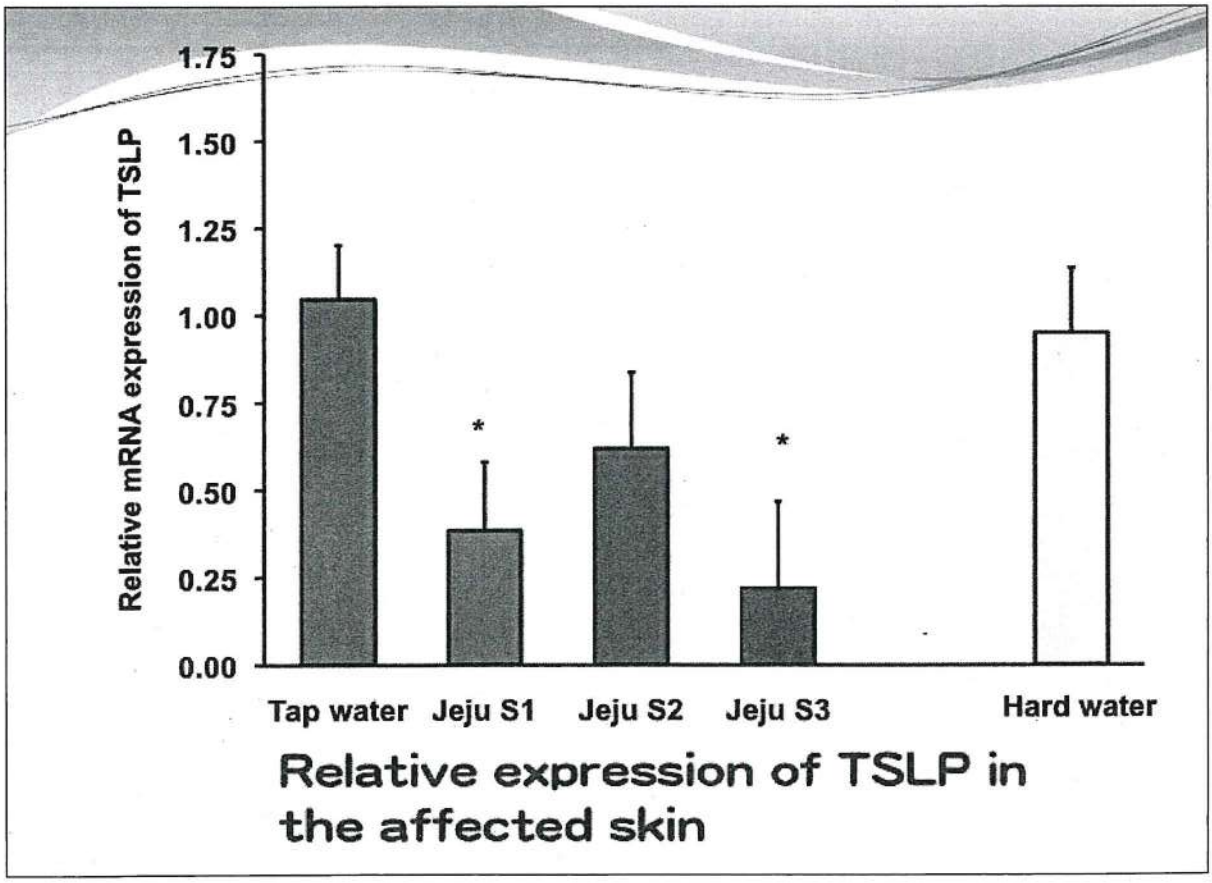


H & E staining


Atopic Dermatitis
Skin
Release of NGF
Release of TSLP
T cells
Allergens
Mast cells
Dendritic cells
Draining lymph node
Itch
Cytokines and Chemokines TARC, MDC, Eotaxin-2
Infammatory immune responses
Migration, Activation
Th2 immune responses


Tap water
Jeju S1
Jeju S2
Jeju S3
Hard water
Anti-PGP9.5 immunohistochemistry


Relative mRNA expression of NGF
1.75
1.50
1.25
1.00
0.75
0.50
0.25
0.00
*
*
*
Tap water
Jeju S1
Jeju S2
Jeju S3
Hard water
Relative expression of NGF in the affected skin


Relative mRNA expression of TSLP
1.75
1.50
1.25
1.00
0.75
0.50
0.25
0.00
*
*
Tap water
Jeju S1
Jeju S2
Jeju S3
Hard water
Relative expression of TSLP in the affected skin

結果と考察

- 済州島地下天然水の中でも、Sam-Da-Soo (S1)、S3は、アトピー性皮膚炎に対する明らかな治療効果を示した。
- 特に、S3は掻痒行動、などすべてのパラメーターに対して抑制効果を示した。

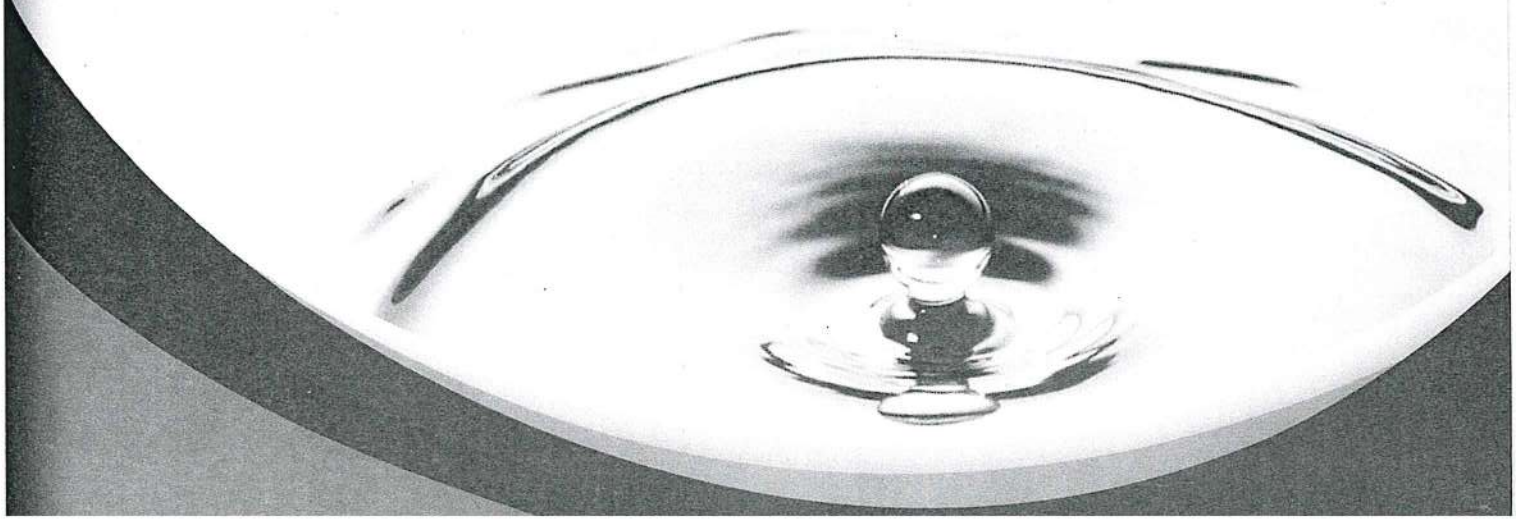
MEMO

제주 지하수의 혈당 조절 및 알러지 반응 조절 효과

Effect of Jeju groundwater on regulation of blood glucose and allergic response

장현욱 영남대학교 약학대학 교수

Hyun-Wook Chang, Yeongnam University



제주지하수의 혈당조절 및 알러지반응 조절효과

장 현 욱
영남대학교 약학대학

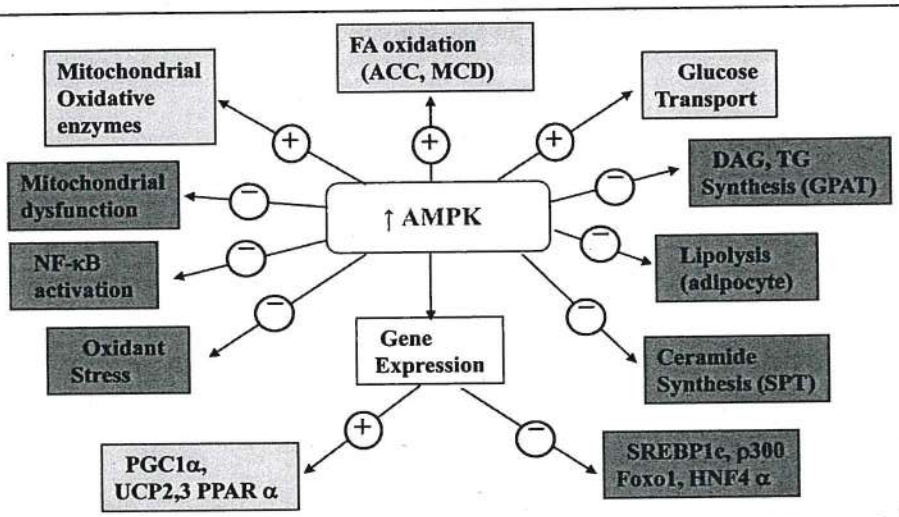
Part 1

제주지하수의 혈당조절 작용기전

AMPK (AMP-activated Protein Kinase)

◈ 대사성질환 치료의 새로운 Target - AMPK

AMPK는 에너지 대사 조절의 핵심 인자로 AMPK의 활성화는 지방산화 및 포도당 흡수를 촉진 시키며 세포내 중성지방 수치 저하 및 Insulin 민감성을 높여 대사질환의 치료를 가능케 함



Effects of AMPK activation on events that could account for its ability to diminish lipid accumulation, cell dysfunction and insulin resistance (Nature review 2004)

Condition ; Cell Based Assay in L6 myotubes

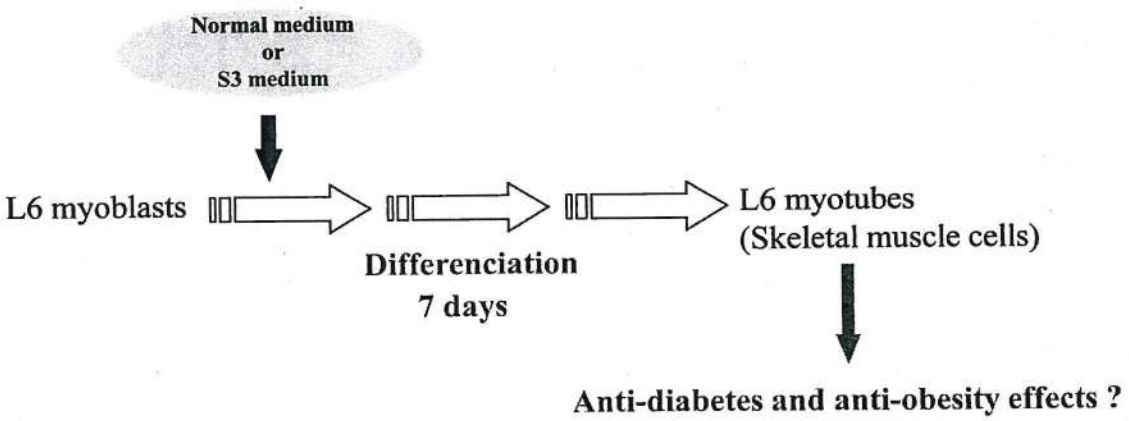


Fig. 1. Jeju ground water samples (S1, S2, and S3) increase glucose uptake in L6 myotubes

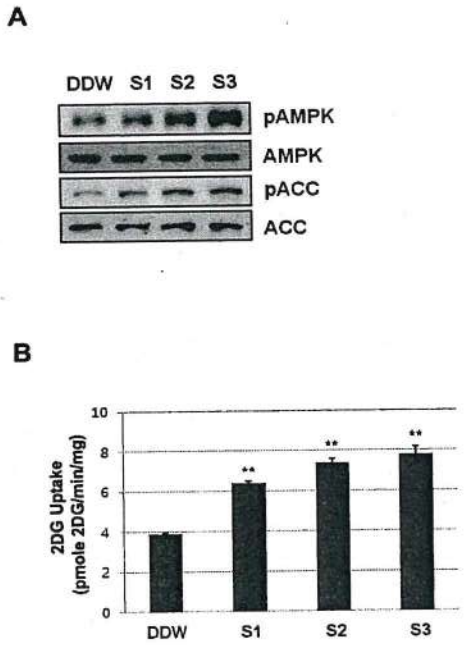


Fig. 2. S3 increases phosphorylation of AMPK and glucose uptake in L6 myotubes.

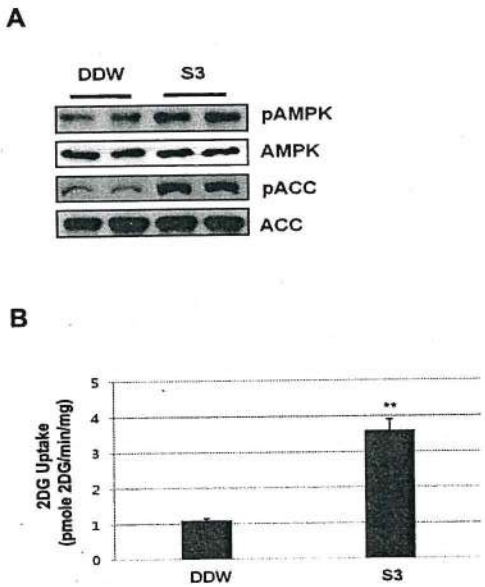


Fig. 3. S3 stimulates glucose uptake in an AMPK-dependent manner.

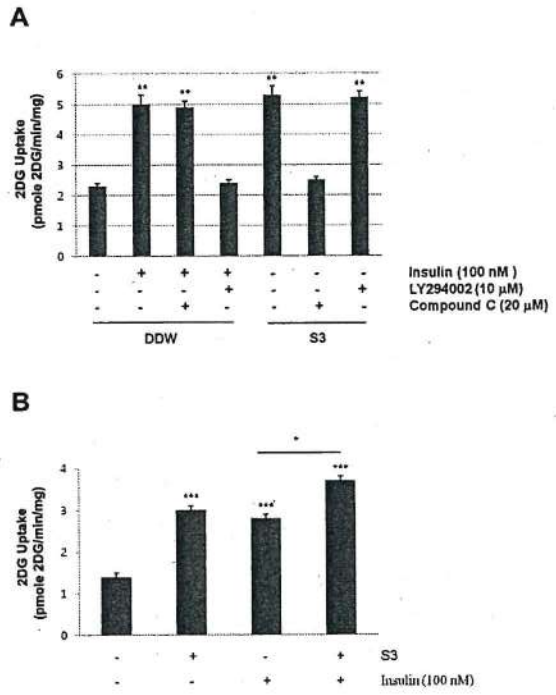


Fig. 4. Effects of pentaoxodivanadium (V_2O_5) on AMPK activity and glucose uptake in L6 myotubes.

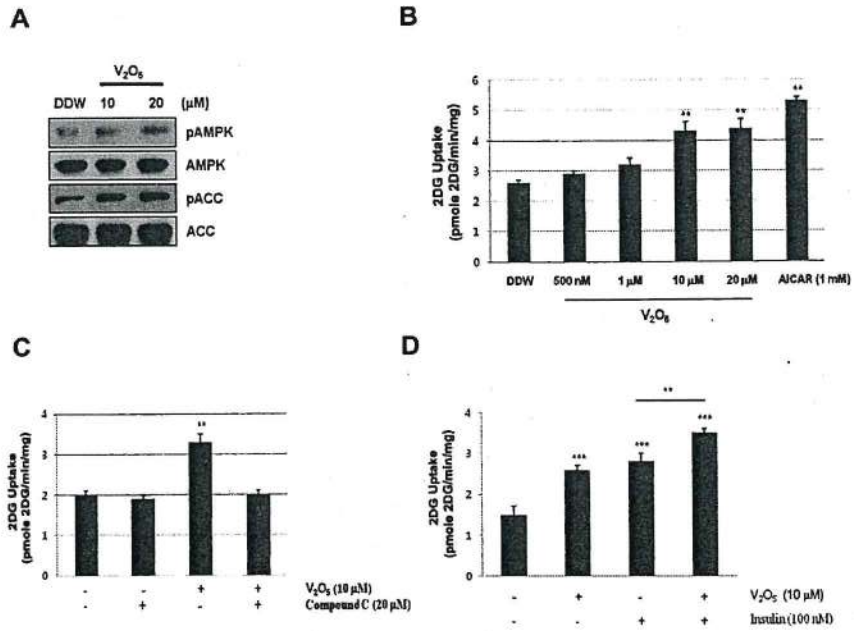


Fig.5. S3 activated AMPK induces glucose uptake through CaMKK-dependent signaling

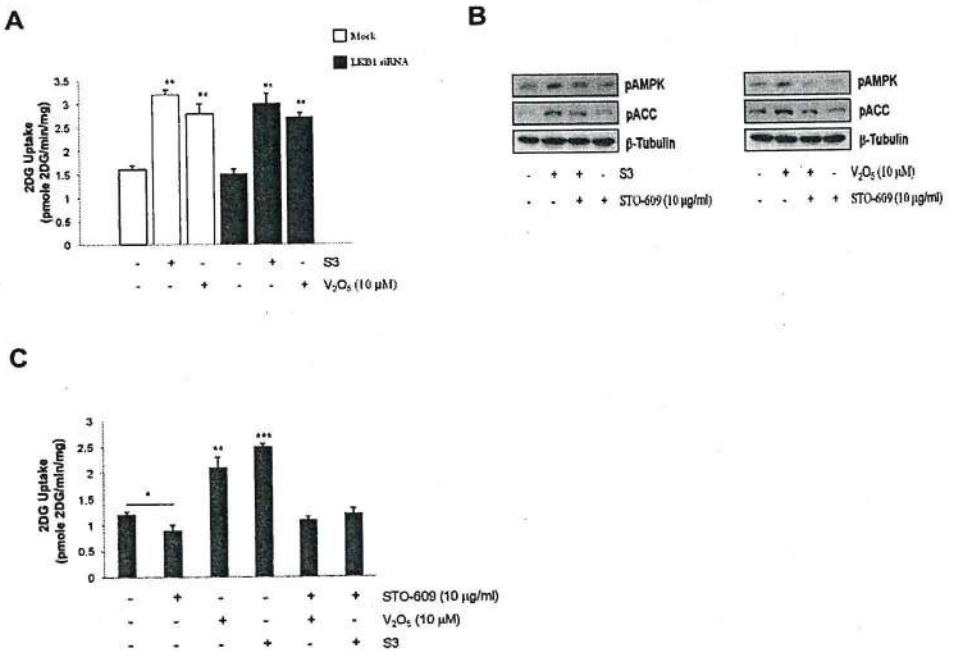
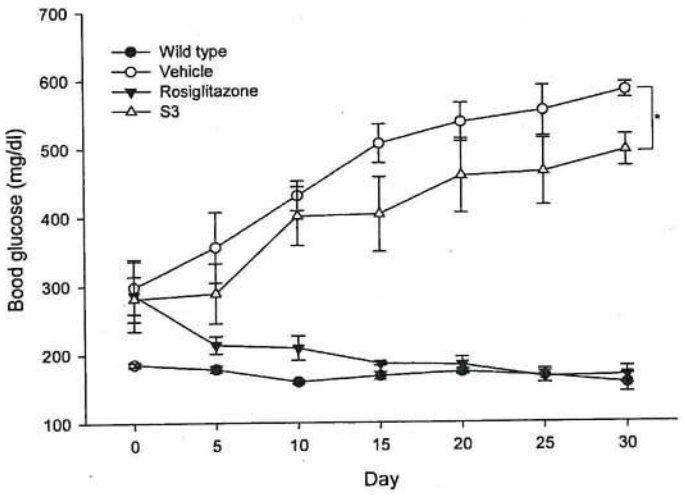
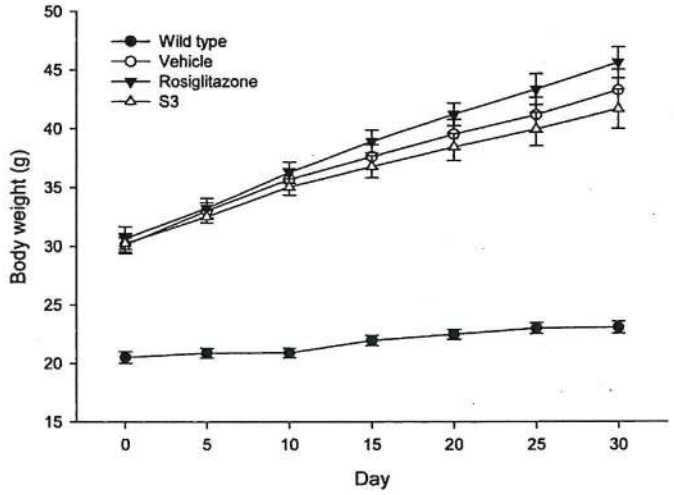


Fig.6. S3 decrease blood glucose level in db/db mouse for 4 weeks



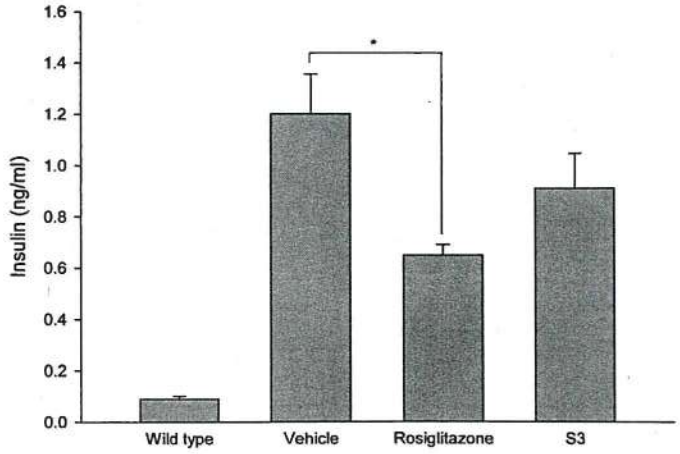
Each value is mean ± SE for 6 mice.
*P<0.05 compared with vehicle

Fig.7. S3 do not decrease body weight in db/db mouse for 4 weeks



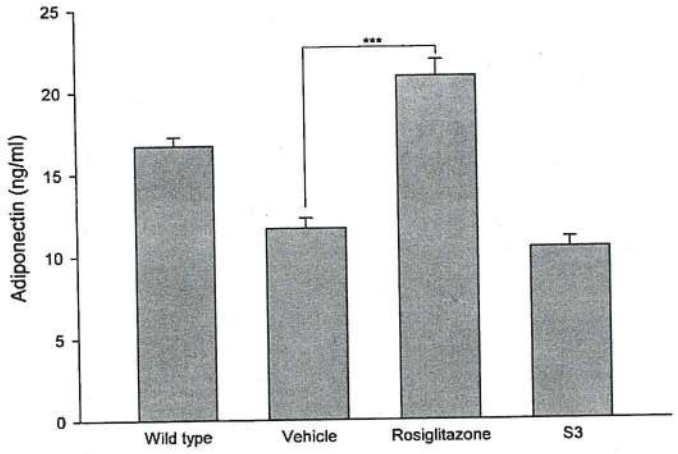
Each value is mean ± SE for 6 mice.

Fig.8. S3 do not decrease blood insulin level in db/db mouse for weeks



Each value is mean ± SE for 6 mice.
*P<0.05 compared with vehicle

Fig.9. S3 do not increase adiponectin level in db/db mouse for 4 weeks



Each value is mean ± SE for 6 mice.
***P<0.001 compared with vehicle

Table 1. Effects of S3 water on the plasma lipid level in db/db mice for 4 weeks.

Group	Total cholesterol (mg/dl)	Triglyceride (mg/dl)	HDL cholesterol (mg/dl)	LDL cholesterol (mg/dl) [1]	Atherogenic index [2]
Wild type	136.6±17.9	68.7±3.7	62.0±0.8	45.5±6.9	1.20±0.12
Vehicle	209.3±7.3	142.0±28.8	54.0±7.0	70.0±9.6	2.87±0.50
Rosiglitazone	307.4±29.1*	83.0±13.6*	79.6±1.8	152.6±29.2*	2.49±0.40
S3	213.3±22.6	127.6±13.2	96.0±2.6**	51.8±11.7*	1.22±0.23*

[1] Total cholesterol – HDL cholesterol – Triglyceride/5
[2] (Total cholesterol-HDL cholesterol)/HDL cholesterol
Each value is mean ± SE for 6 mice.
*P<0.05, **P<0.005 compared with vehicle

Mol Cell Biochem (2012) 360:401–409
DOI 10.1007/s11010-011-1062-4

Natural vanadium-containing Jeju ground water stimulates glucose uptake through the activation of AMP-activated protein kinase in L6 myotubes

Seung-Lark Hwang · Hyeun Wook Chang

Received: 10 May 2011 / Accepted: 8 September 2011 / Published online: 23 September 2011

Abstract The aim of this study was to elucidate the effects of natural vanadium-containing Jeju ground water on glucose uptake in L6 myotubes and adipogenesis in 3T3 L1 cells. The Jeju ground water samples containing vanadium components were designated as S1 (8.0 ± 0.9 μg/l), S2 (24.0 ± 2.0 μg/l), and S3 (26.0 ± 2.0 μg/l), respectively. To investigate the effects of the Jeju ground water on glucose uptake in L6 myotubes, L6 cells were differentiated in media containing deionized distilled water (DDW group) and the water samples (S1, S2, and S3 groups). After daily changes in cultured media containing the Jeju ground water samples for 1 week, all samples had increased glucose uptake compared to the DDW group and the order of glucose uptake increased in parallel with vanadium content (S3 > S2 > S1). In addition, S3 significantly stimulated the phosphorylation of the Thr-172 residue of the AMP-activated protein kinase-α subunit and the Ser-79 subunit of acetyl-CoA carboxylase compared to the DDW group. The effect of glucose uptake by S3 was reversed by pretreatment with Compound C, an AMPK inhibitor. Interestingly, vanadium pentoxide also increased glucose uptake and activated AMPK activity in a dose-dependent manner. Furthermore, as compared to the DDW treated group, S3 treatment inhibited adipogenesis of 3T3-L1 cells by down regulation of expressions of adipogenic transcription factors. Taken together, these findings suggest that S3 displays beneficial effects in the treatment of diabetes, at least in part through the activation of AMPK activity.

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Keywords Vanadium-containing Jeju ground water · AMP-activated protein kinase · Glucose uptake · Type 2 diabetes · Vanadium pentoxide · Adipogenesis

Introduction

In type 2 diabetes, insulin resistance leads to decreased glucose clearance and impaired glucose transport in the peripheral tissues, leading to dramatic hyperglycemia [1, 2]. Vanadium compounds have been of interest as a potential oral therapy for diabetes since their glucose-lowering effects were first discovered [3]. In human studies, vanadium administration has shown modest but positive effects in lowering blood glucose in type 2 diabetes [4].

AMP-activated protein kinase (AMPK) is a phylogenetically conserved intracellular energy sensor that has been implicated in the regulation of food intake, body weight, glucose uptake, and lipid metabolism [5, 6]. Once activated, AMPK phosphorylates its downstream substrates to reduce ATP-consuming pathways, including fatty acid, cholesterol, and triacylglycerol synthesis, and increases ATP-generating pathways, including fatty acid oxidation and glycolysis [7–9]. Type 2 diabetes and obesity contribute to insulin resistance in skeletal muscle [10]. Recent reports have shown that AMPK activation may account for at least some of the beneficial effects of exercise, such as increased fatty acid oxidation [11, 12], increased mitochondrial biogenesis [13], and possibly glucose uptake [14]. AMPK is activated indirectly by metformin [15] and thiazolidinediones [16], widely used treatments for type 2 diabetes, suggesting that AMPK activity regulates insulin sensitivity and reduces plasma glucose and lipids. Previously, the Kato group reported that natural vanadium-containing Mt. Fuji ground water improved hyperglycemia by ameliorating

Part 1

제주지하수의 알러지반응 조절 작용기전

Mast cell as a major effector cell in allergy and inflammation

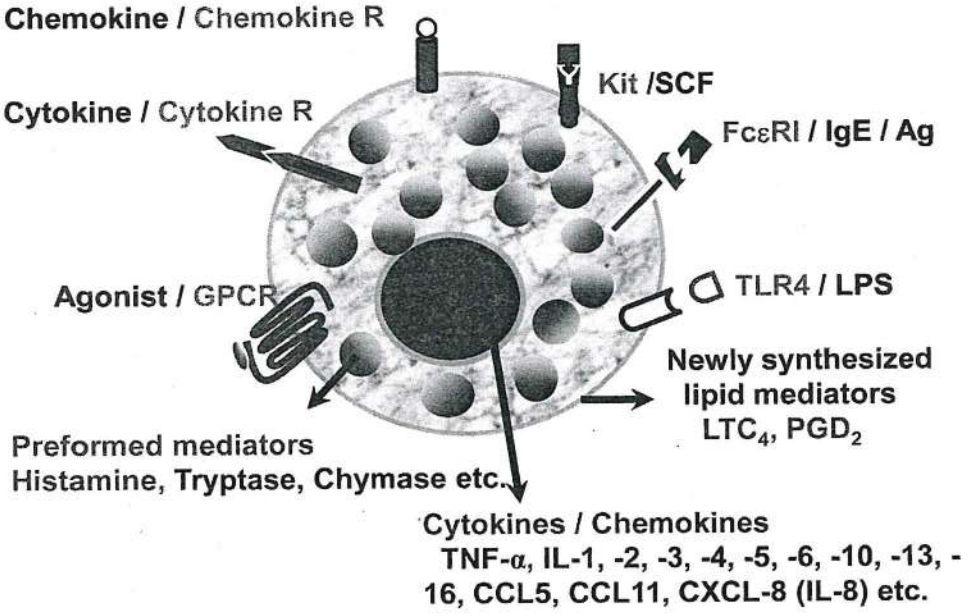

Fig. 1. JW (S1) Inhibits IgE/Ag-Mediated PCA reaction

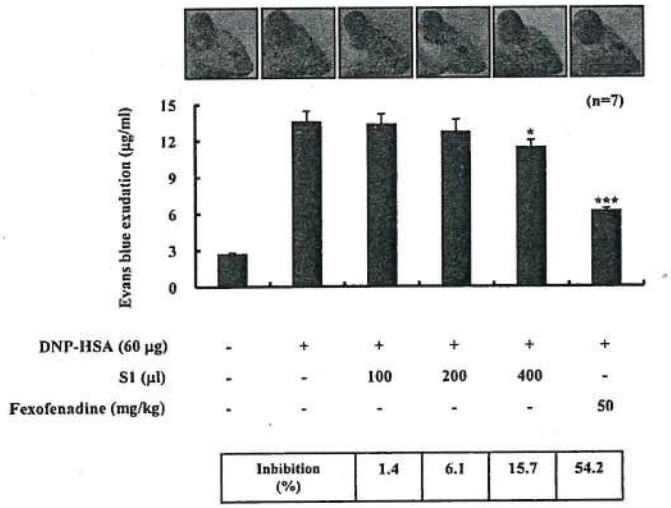

Fig. 6. JW (S3) Inhibits serum LTC_4 and PGD_2 production in IgE/Ag-induced PSA animal model

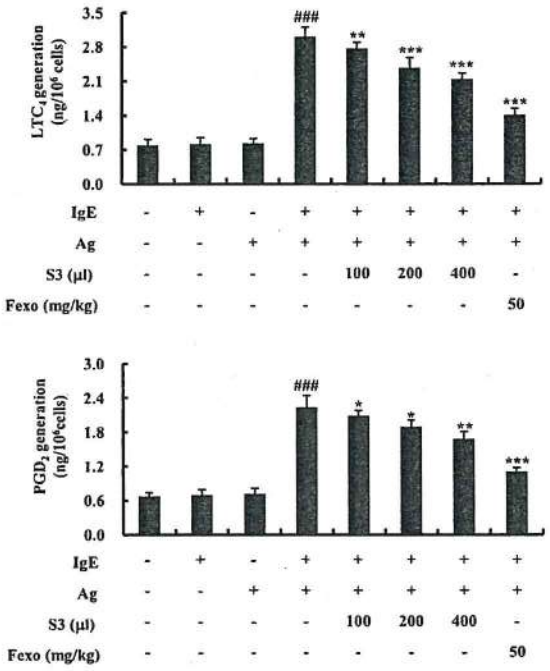

Fig. 7. JW (S3) Inhibits degranulation and Ca^{2+} Mobilization in IgE/Ag-induced BMMCs

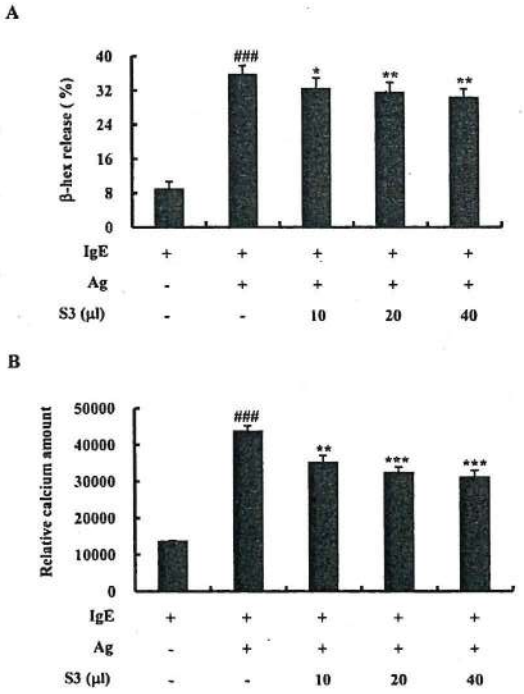

Fig. 8. S3 Inhibits COX-2 dependent PGD_2 and LTC_4 generation in IgE/Ag-induced BMMCs

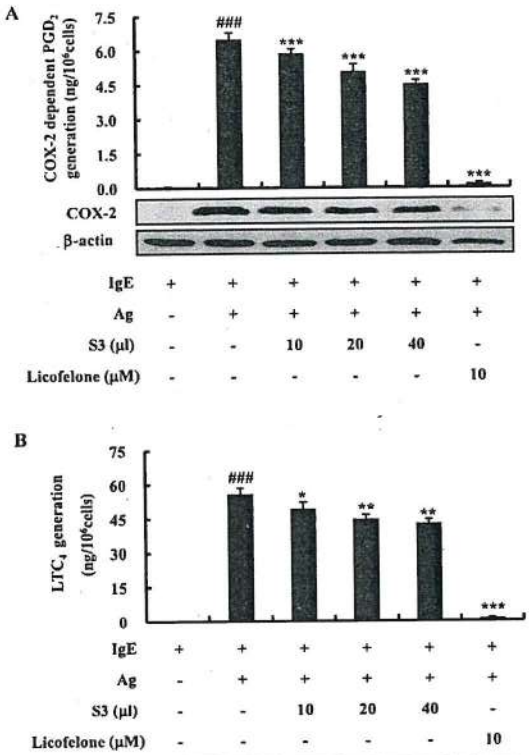

Fig. 9. V_2O_5 Inhibits IgE/Ag-Mediated PCA reaction

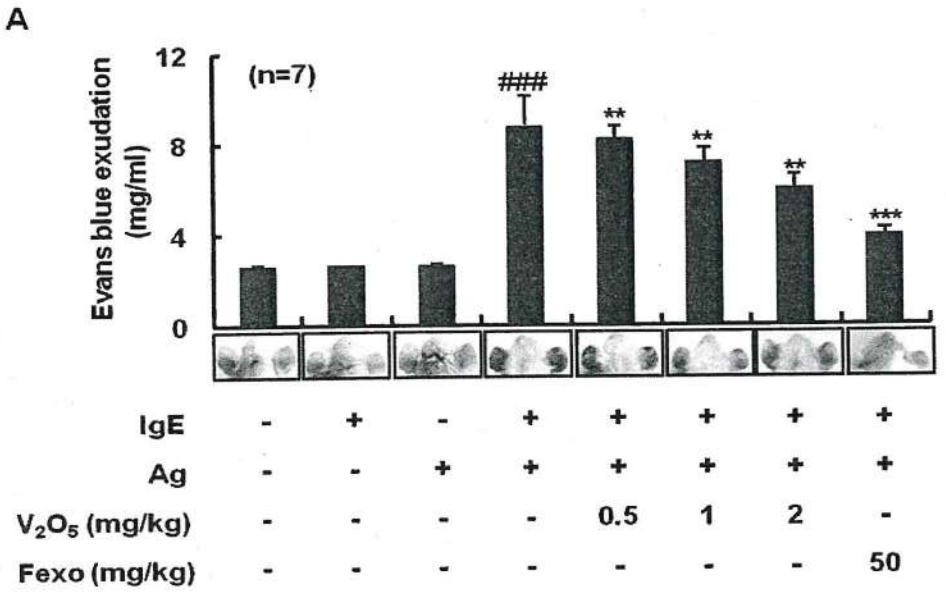

Fig. 10. V_2O_5 Inhibits COX-2 dependent PGD_2 and LTC_4 generation in IgE/Ag-induced BMMCs

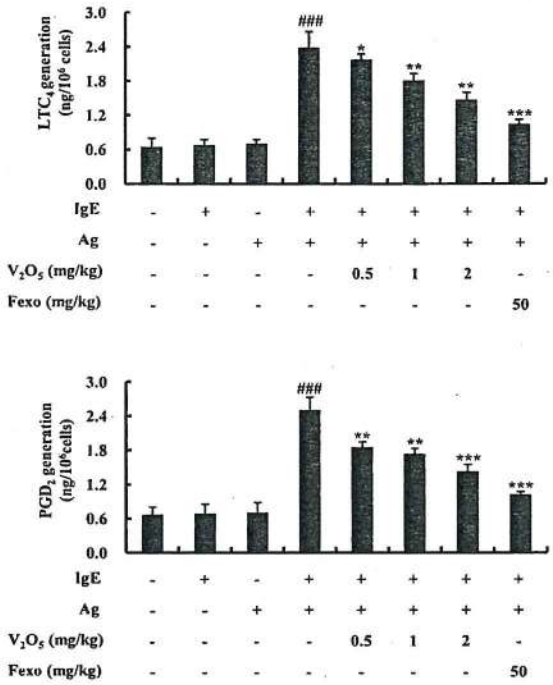

Fig. 11. V_2O_5 Inhibits degranulation and Ca^{2+} Mobilization in IgE/Ag-induced BMMCs

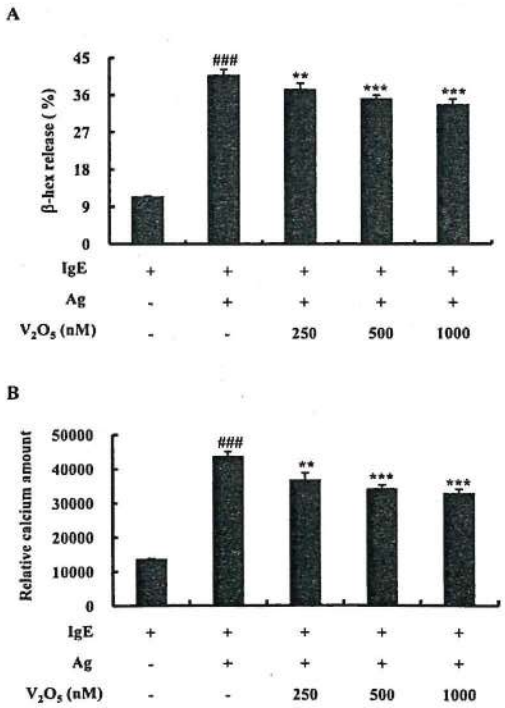

Fig. 12. V_2O_5 Inhibits COX-2 dependent PGD_2 and LTC_4 generation in IgE/Ag-induced BMMCs

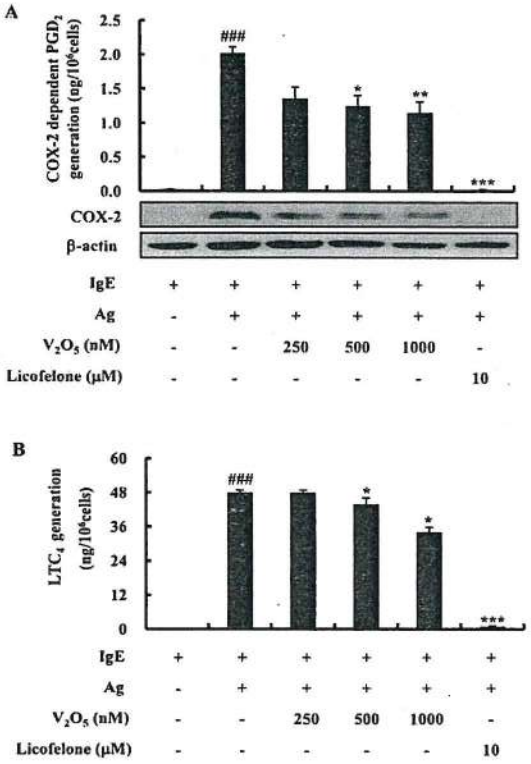

Table 1 Effect of JW on Compound 48/80-Induced Systemic Allergic Reaction

(n = 7/group)

	Compound 48/80 (8mg/kg)	Mortality (%)
None (2차 증류수)	+	100
S1	+	100
S2	+	100
S3	+	67 (*$p < 0.05$)

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Natural Vanadium-Containing Jeju Groundwater Inhibits Immunoglobulin E-Mediated Anaphylactic Reaction and Suppresses Eicosanoid Generation and Degranulation in Bone Marrow Derived-Mast Cells

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The high-affinity receptor for immunoglobulin E (IgE) (FcεRI)-mediated activation of mast cells plays an important role in various allergic diseases. To assess the anti-allergic activity of natural vanadium-containing Jeju groundwater (JW), an *in vivo* passive cutaneous anaphylaxis (PCA) animal model and *in vitro* mouse bone marrow-derived mast cells (BMMCs) was used. JW inhibited cyclooxygenase-2 (COX-2)-dependent prostaglandin D_2 (PGD_2) generation in a dose-dependent manner, with a concomitant reduction of COX-2 protein expression in IgE-induced BMMCs. In addition, JW inhibited 5-lipoxygenase (5-LOX)-dependent generation of leukotriene C_4 (LTC_4) as well as degranulation in a dose-dependent manner. These results demonstrate that JW has dual COX-2/5-LOX inhibitory activity. In addition, vanadium pentoxide (V_2O_5), which is the major vanadium component of JW, also inhibited PGD_2 and LTC_4 generation as well as degranulation in IgE-induced BMMCs. Furthermore, oral administration of JW dose-dependently inhibited mast cell-dependent passive anaphylactic reaction in IgE-sensitized mice. Taken together, these results suggest that JW may be useful in regulating mast cell-mediated allergic response through the suppression of eicosanoid generation and degranulation in mast cells.

Key words vanadium-containing Jeju groundwater, prostaglandin D_2, leukotriene C_4, degranulation, bone marrow-derived mast cell, passive cutaneous anaphylaxis

In recent years, there has been a growing realization that mast cells play a central role in the induction of allergic and inflammatory reactions. Mast cells are activated by allergen-specific immunoglobulin E (IgE) binding; upon interaction of high-affinity IgE receptor (FcεRI) or stem cell factor (SCF, also known as c-kit-ligand, KL) with c-Kit, mast cells release various preformed chemical mediators such as histamine, serotonin and proteoglycans, as well as newly synthesized inflammatory mediators, including prostaglandin D_2 (PGD_2) and leukotriene C_4 (LTC_4), through the activation of cyclooxygenase-2 (COX-2), 5-lipoxygenase (5-LOX), and various cytokines.[1-3] In murine bone marrow-derived mast cells (BMMCs), a biphasic PGD_2 biosynthetic response occurs over time. Immediate PGD_2 generation, defined as occurring within 2 h, is associated with the activation of COX-1, while delayed PGD_2 generation, observed following several hours of culturing (2—10 h), is associated with COX-2 after stimulation with either IgE/antigen (Ag) or a combination of cytokines and lipopolysaccharide (LPS).[4,5] It is well known that PGD_2 is the major prostanoid secreted from activated mast cells and has long been implicated in manifestation of inflammation and allergic diseases.[1] Leukotriene C_4 (LTC_4), another class of inflammatory lipid mediator, is synthesized from arachidonic acid by the action of 5-LOX.[6]

Previously, another group reported that natural vanadium-containing Mt. Fuji groundwater improves hyperglycemia by ameliorating liver insulin receptor activity.[7] Vanadate shows immunotoxicity through the production of inflammatory mediators, such as tumor necrosis factor-α (TNF-α), interleukin-1β (IL-1β), and PGE_2 in LPS-stimulated WEHI-3 cells.[8] In addition, sodium orthovanadate induces release of histamine from rat and mouse mast cells as well as vanadium-stimulated histamine release from mast cells and basophils at late phase in the presence of hydrogen peroxide.[9-12] However, the anti-allergic activities and underlying mechanisms of natural vanadium-containing groundwater have not been reported. We here describe for the first time the anti-allergic activity of natural vanadium-containing Jeju groundwater (JW) and the mechanism of its action in BMMCs. In our findings, JW clearly inhibited eicosanoid production and degranulation in mast cells *in vitro* and attenuated the IgE-mediated anaphylactic reaction through LTC_4 and PGD_2 production *in vivo*, suggesting that a low concentration of natural vanadium-containing JW has beneficial effects on the regulation of various allergic responses.

MATERIALS AND METHODS

Chemicals and Reagents JW containing vanadium components (V^{5+}: 26.0±2.0 μg/L, Na^+: 5.06±1.0 mg/L, Ca^{2+}: 3.4±0.3 mg/L, Mg^{2+}: 3.0±1.0 mg/L, K^+: 3.0±0.5 mg/L) was provided by the Jeju Special Self-Governing Province Development Corp. (Jeju, Korea).

Induction of IgE-Mediated Passive Cutaneous Anaphylaxis (PCA) in Mice Seven ICR mice (Hyochang Science, Daegu, Korea) were placed in each cage within a laminar airflow cabinet and were fed with standard laboratory chow (Purina, Seoul, Korea) and water *ad libitum*. The mice were kept at a temperature of 22±1°C and at a relative humidity of 55±10% and 12 h/12 h (light/dark) cycle for at least 7 d prior to the experiments throughout the study. For PCA, 80 ng of mouse anti-dinitrophenyl (DNP) IgE (Sigma-Aldrich, St. Louis, MO, U.S.A.) was intradermally injected into the ears of 6-week-old, male ICR mice (Hyochang Science, Daegu, Korea), followed 18 later by oral administration of 400 μL of JW or 0.5—2 mg/kg vanadium pentoxide (V_2O_5) or 50 mg/kg

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