PROGRAM 프로그램 안내

2. Korea-China International Symposium

KIOM-CACMS International Collaborative Researches
October 30 (Wed.) 2024, 9:30 ~ 12:00 I KIOM, Jema Hall

Day 2		
09:30~09:45	Opening	
Session 1. Chair : Siwoo LEE I KIOM		
09:45~10:00	Exploration and Utilization of Fungi and Medicinal Resources	Yuan YUAN I CACMS
10:00~10:15	Discovery of New Cosmetic Ingredients Using Herbal Medicine	Taesoo KIM I KIOM
10:15~10:30	Study on the Application of Acupuncture and Moxibustion in Sleep Health Management and International Dissemination	Yu ZHOU I CACMS
10:30~10:45	The Impact of Sleep Duration, Sleep Quality and Sleep Pattern on Cognitive Disorders	Jieun PARK I KIOM
10:45~10:55	Break	
Session 2. Chair : Yuan YUAN I CACMS		
10:55~11:10	The Establishment and Application of an Optical Imaging Method for the Skin Manifestation for the Efficacy of Traditional Chinese Medicine	Yi WANG I CACMS
11:10~11:25	Development of Skin Health LAB-based on Gut Function	Sunguk CHAE I KIOM
11:25~11:40	The Brain Mechanism of TaVNS on MCI by fMRI	Jiliang FANG I CACMS
11:40~11:55	Alteration of Anterior Cingulate Cortex Neurometabolites by Electro-acupuncture in Patients with Anxiety Disorder	Jieun KIM I KIOM
11:55~12:00	Closing	

* The 2024 KIOM Research Networking Day will be held simultanesouly (Dongmu Building, 1st Floor)

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2. Korea-China International Symposium

개 회 사

〈2024 한·중 국제 심포지엄〉

안녕하십니까. 한국한의학연구원장 이진용입니다.
올해로 14회째 개최되는 한국한의학연구원과 중국중의과학원과의 '한 · 중 국제심포지엄'을 오늘
우리 연구원에서 개최하게 되어 영광스럽게 생각합니다. 특히 올해는 우리 연구원이
개원 30주년을 맞아 개최하는 심포지엄에 이처럼 중국중의과학원의 귀빈 여러분들과, 특히 중국 재정부에서
참석 하는 자리가 되어서 더욱 뜻깊게 생각합니다. 존경하는 중국중의과학원 양홍쥔 부원장님,
중국 재정부 과학교육문화사 마홍빙 부사장님, 중의과학원 장홍메이 국제협력처장님, 바쁘신 중에도
심포지엄 참석을 위해 시간을 내어주신 보건복지부 정영훈 한의약정책관님, 주제발표를 위해 참석해주신
중의과학원 발표자 여러분들과 우리 연구원 발표자 분들께도 환영과 감사의 말씀을 드립니다.

한국한의학연구원은 중국중의과학원과 1998년 첫 MOU를 체결한 이후 2011년부터 상호교류,
공동연구 추진 등을 위한 국제 심포지엄을 매년 개최하고 있습니다. 양국의 전통의학분야 대표연구기관인
양 기관은 14번째 국제심포지엄을 진행하고 있고 2차례에 걸쳐 8개의 국제공동연구를 진행했으며,
6명의 연구인력교류를 진행하고 있습니다. 그리고 이번 심포지엄에서는 양기관이 관심을 가지고 있는
공동연구 주제를 탐색하고 공동의 관심사를 이끌어내 향후 세 번째 국제공동연구를
기획하는 방안의 일환으로 진행하고 있습니다. 저는 이번 심포지엄의 발표와 토론, 향후 이어질 협의가
양 기관의 발전적인 연구기회가 되기를 기대하며 이런 양기관의 노력이양국의 전통의학 발전,
미래전통의학 혁신에 기여할 수 있기를 희망합니다.

코로나19 팬더믹이라는 지구촌 초유의 사태가 발생한 시기에도 한 · 중 국 제심포지엄이 끊이지 않고
이어져 오고 있고 올해도 개최되는 것은 양 기관의 강력한 상호교류의 의지와 국가적인 지원이 있었기에
가능하다고 생각합니다. 우리 한국한의학연구원은 지난 30년동안 공을 들인 기초 원천연구의 기반 위에
다가오는 30년에는 인공지능을 활용한 연구, 뇌와 경혈의 융합연구, 만성난치성 질환의 치료기술,
난임 · 치매 · 우울증과 같은 사회문제 해결형 연구를 본격적으로 추진하겠습니다.

다시 한 번 멀리 중국에서 찾아주신 중의과학원 대표단 여러분들과
국 내외 귀빈 여러분들을 진심으로 환영하며 한 · 중 국제심포지엄의 성공적인 개최를 위해
양국, 양 기관이 함께 발전하는 시간이 되기를 기원합니다.

감사합니다.

2024. 10. 30

한국한의학연구원 원장 이 진 용

축 사

〈2024 한의학연 – 중국 중의과학원 국제심포지엄〉

안녕하십니까? 보건복지부 한의약정책관 정영훈입니다.
존경하는 중국중의과학원 양홍쥔 부원장님, 중국 재정부 마홍빈 부사장님. 한국한의학연구원 이진용 원장님,
그리고 오늘 발표하실 중의과학원과 한의학연구원 전문가 여러분, 관계자 여러분, 모두 반갑습니다.

먼저, 한국한의학연구원의 개원 30주년을 맞아 한국과 중국, 두 국가를 대표하는 전통의학
최고의 전문연구기관인 한의학연구원과 중의과학원의 국제심포지엄 개최를 진심으로 축하드립니다.
세계적으로 전통의학에 대한 관심이 증대되면서 의료수요가 늘어나고 있고 한국과 중국은 전통의학이
국가의료 체계의 한축으로 자리잡았습니다. 양국은 선조들로부터 전통의학에 대한 뛰어난 유산을 기반으로,
연구기관과 임상현장에서의 끊임없는 노력을 통해 전통의학을 발전시켜 온 결과라고 생각합니다.
한국한의학연구원은 한국 한의학 연구개발의 국가허브 연구기관으로 지난 30년 동안 우리나라 한의학 발전에
중요한 역할을 수행해왔습니다.

중국중의과학원도 중국 최고의 전통의학 연구기관으로 중의약 기초연구와 임상연구를 통해 중의약의 발전과
세계화에 중추적인 역할을 하고 있는 것으로 알고 있습니다. 저는 오늘 한 · 중 심포지엄이
전통의학 분야에서의 한국과 중국 양 국가 간 협력 발전 방향을 모색하고 인류의 미래를 위협하는 질병을
극복해 궁극적으로는 인류의 삶의 질 향상에 기여하는 기회가 되기를 희망합니다. 한국 정부도 여러분들의
노력이 헛되지 않도록 중국 정부와의 긴밀한 협조 속에서 양국의 연구 협력에 대한 지원을 아끼지 않을 것입니다.

다시 한번 한국한의학연구원과 중국중의과학원 전문가 여러분, 귀빈 여러분, 참여하신 연구자 여러분,
그리고 오늘의 심포지엄을 위해 보이지 않는 곳에서 노력을 기울여 주신
한의학연 관계자 여러분들께 감사를 드립니다.

감사합니다.

2024. 10. 30

보건복지부 한의약정책관 정 영 훈

祝 辭

〈2024 韩医学研究院 - 中国中医科学院国际研讨会〉

大家好!我是保健福祉部韩医药政策官Jeong Young-hoon。
尊敬的中国中医科学院副院长杨洪军先生，财政部科教和 文化司副司长马宏兵先生、
韩国韩医学研究院院长Lee Jin-Yong先生，以及今天即将发言的中医科学院和韩医
学研究院的专家、相关人士，十分荣幸与各位见面。

首先，在韩国韩医学研究院建院30周年之际，我衷心祝 贺代表韩国和中国两国传统医学最高
专业研究机构的韩医 学研究院和中医科学院召开此次国际研讨会。
随着全世界对传统医学的关注增加，医疗需求也不断增 加，韩国和中国传统医学已经成为国家
医疗体系中不可或 缺的重要组成部分。我认为，这是两国在继承祖先留下的优秀传统医学遗产
的 基础上，通过各自科研机构和临床实践的持续努力，推动 传统医学不断发展的结果。
韩国韩医学研究院是韩国韩医学研究开发的国家中心研究 机构，
近三十年来在韩国韩医学的发展中扮演了举足轻重 的角色。

中国中医科学院同样是中国传统医学研究的领军机构，通 过深入的中医药基础研究和临床研究，
对中医药的现代化 和全球化进程产生了深远的影响。我期望本次韩中研讨会能够成为探索两
国在传统医学领域 合作方向的重要平台，共同应对威胁人类健康的疾病挑 战，最终为提高全
球人类的生活质量贡献力量。为确保各位的辛勤努力能够结出丰硕的果实，韩国政府将
与中国政府保持紧密合作，对两国间的研究合作给予全力 支持。

再次感谢韩国韩医学研究院和中国中医科学院专家、贵 宾、参与研究者们，
以及为了今天的研讨会而在幕后默默 付出努力的韩医学研究院相关人士。

谢谢。

2024. 10. 30

保健福祉部韩医药政策官 **Jeong Young-hoon**

祝 辭

〈2024 韩中研讨会开幕式致辞〉

尊敬的韩国韩医学研究院李进容院长，韩国保健福祉部郑永勋韩医药政策官，各位专家、同仁：
大家好！正值秋风送爽，秋意浓浓之时，非常感谢李院长邀请中国中医科学院代表团来到风景如画的大田。今天，我们与韩医学研究院的领导、专家们又相聚在一起，共同出席2024“韩中研讨会”，我仅代表代表团全体成员对本次会议的顺利召开表示热烈祝贺！
此时又恰逢贵院30周年院庆，在此，请允许我代表中国中医科学院并以我个人的名义向贵院30年华诞表示衷心祝贺，并向为了会议举办而付出辛勤努力的人员表示诚挚谢意！

中韩两国是一衣带水的友好邻邦，两国传统医学交流源远流长。韩医学研究院是韩国韩医学领域的国家级综合性研究机构，注重韩医学理论、技术和医疗服务等领域的研发和成果转化。
中国中医科学院是目前中国规模最大、科研力量雄厚，集科研、医疗、教育于一体的国家级综合性中医药科研机构。两院均是两国传统医学研究领域的“国家队”。
自1998年开始签署合作备忘录以来，在中韩两国政府合作框架下，秉持“优势互补、合作共赢”理念，两院建立了稳定的合作机制，共同致力于促进传统医学的发展，
努力增进广大人民的健康福祉。通过开展互访交流、轮流举办研讨会、开展合作研究项目以及互派研修人员等方式，两国科研人员间的交流更加深入，合作更加务实。我了解到，20余年来，两院已在药用植物资源鉴定、传统医学基础理论、针灸临床研究、植物药产品研发等领域共同开展了2个阶段8个合作研究项目，轮流举办了13次传统医学研讨会，多名人员获得了研修机会。今年上半年，双方又启动了新一阶段合作研究。我院高度重视与贵院的合作，确定了4位专家。在今天的研讨会上，他们和贵院的共8位专家将进行报告。我希望借此机会两院专家进行深入有效的交流，为今后顺利合作奠定坚实基础。未来，随着人类对自然、健康、疾病认知的深化，传统医学提供的服务一定会越来越为各国广大民众所了解、认可和接受，同时很多未知的领域，因其存在的潜力和价值还有待我们去探索和挖掘。我建议两院继续深化在传统医学领域的交流与合作，携手应对全球卫生健康领域的挑战，共同推动传统医学的繁荣发展！

最后诚挚地祝愿本次会议圆满成功！

2024. 10. 30

中国中医科学院副院长 **杨 洪 军**

KOREA INSTITUTE OF ORIENTAL MEDICINE
INTERNATIONAL SYMPOSIUM

PRESENTATION

Yuan YUAN
CACMS

EXPLORATION AND UTILIZATION OF FUNGI AND MEDICINAL RESOURCES

菌物药资源的挖掘与利用

Utilization of Mycological Pharmaceutical Resources

中国中医科学院 袁媛

YUAN Yuan，China Academy of Chinese Medical Sciences (CACMS)

菌物是重要的食药用资源

Fungi are important edible and medicinal resources

- **自然界的菌物大约有150万种。**

  There are approximately 1.5 million species of fungi in nature.

- **菌物药是一类以菌物体或者从中提取的有效成分加工而成的有治疗疾病作用的药物。**

  Medicinal fungi refer to drugs processed from fungal bodies or their extracted active ingredients that have therapeutic effects on diseases.

2

菌物是重要的食药用资源
Fungi are important edible and medicinal resources

- 中国已知真菌1.7万种，其中具有药用价值的菌物近1000种，居世界第一位。
  China has 17,000 known species of fungi, among which nearly 1,000 species have medicinal values, ranking first globally.

- 菌物药是中药产业的重要组成部分，2020年版《中国药典》收录：8种（9类药材）。
  The 2020 edition of the Chinese Pharmacopoeia includes 8 species of fungi (corresponding to 9 medicinal materials)

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以菌物入药治病的历史悠久
The history of using fungi as medicinal ingredients for therapeutic purposes spans long time

神农像 · 辽
（山西密县佛宫寺木塔）
Portrait of Shen Nong, Liao Dynasty

- **《神农本草经》称久服灵芝，可“轻身、不老、延年、神仙”**
  The *Shennong Bencao Jing* states that long-term consumption of Ganoderma can "lighten the body, prevent aging, extend life, and attain immortality."

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以菌物入药治病的历史悠久

The history of using fungi as medicinal ingredients for therapeutic purposes spans long time

《神农本草经》

按照菌盖的颜色将灵芝分为：白(玉芝) 、黑(玄芝)、紫(木芝)、青芝(龙)、赤(丹芝)、黄(金芝)六类，并详细描述这六种灵芝的药性

In *Shennong Bencao Jing*, Ganoderma was classified into six categories by the color of its pileus: white, black, purple, cyan, red, yellow. The medicinal properties of these six types of Ganoderma are described in detail.

7

灵芝的起源考古研究

Archaeological Research on the Origin of Ganoderma

- **收集了12份史前灵芝样本**

  Twelve prehistoric samples of Ganoderma were collected.

Table 2-3 The list of prehistoric *Ganoderma* spp. Specimens and their appearance

Lab No.	Field No.	Basidiome shape	Pileus color	Context color
Hemudu Site				
G1	T304⑦	imbricate	black	chestnut brown
G2	T305⑦	irregularly half round	black	cocoa brown
G3	T406⑧	irregularly half round	black	chestnut brown
G4	T407⑧	half round	black	chestnut brown
Nanhu site				
G5	06YN Ⅰ L:1	irregularly round	yellow to reddish brown	chestnut brown
G6	06YN Ⅰ L:1	fanshaped	yellow brown	brown
G7	06YN Ⅰ L:2	fanshaped	reddish brown	chestnut brown
G8	06YN Ⅰ L:3	fanshaped	black	chestnut brown
G9	06YN Ⅰ L:4	irregularly round	reddish brown	chestnut brown
G10	06YN Ⅰ L:5	irregularly fanshaped	dark brown	chestnut brown
G11	06YN Ⅰ L:7	fan-shaped	dark brown	chestnut brown
Tadi site				
G12	Tadi	Half block	brown	-

Chinese Science Bulletin，*2018*

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田螺山遗址灰坑中发现史前灵芝样本

Prehistoric Ganoderma samples were discovered in ash pits at the Tianluoshan Site

➢ **G1出土于田螺山遗址中心区的第七层（T305⑦）灰坑中。**

G1 was unearthed from the ash pit located in the seventh layer (T305⑦) of the central area at the Tianluoshan Site.

□ **据此分析，在灰坑中发现的灵芝遗存应该是河姆渡文化时期古人的遗物，可以判断是人为采集带入村落。**

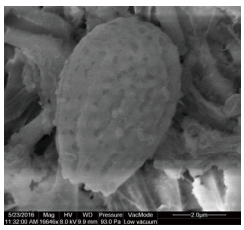
The remains of Ganoderma unearthed from the ash pit are relics from the Hemudu period, and it can be inferred that they were collected by the ancients.

Chinese Science Bulletin，2018

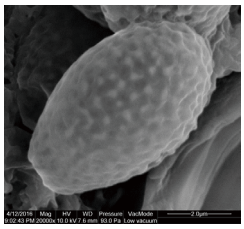
9

利用担孢子特征鉴定史前灵芝样本基原

Identifying botanical origin of prehistoric Ganoderma based on basidiospore characteristics



Prehistoric G1 samples

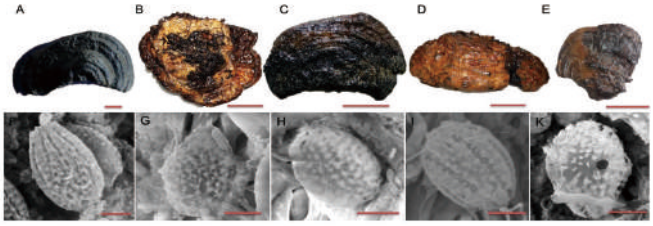


Ganoderma applanatum

□ **从担孢子纹饰、形状、长宽比等特征上，判断**

史前灵芝样本属树舌灵芝亚属

Based on the morphological characteristics of Ganoderma basidiospore, the prehistoric Ganoderma samples were authenticated as to belong to the *Ganoderma applanatum*.



Chinese Science Bulletin，2018

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利用同位素C14测定史前灵芝样本年代

Dating prehistoric Ganoderma samples by isotopic ^{14}C measurement

- **最早追溯到6800年之前，属新石器时代中晚期---河姆渡文化时期**

  Prehistoric Ganoderma samples could be dated back as early as 6,800 years ago, it belongs to the middle to late Neolithic period (specifically the Hemudu culture era).

Sample No.	Location	Measured Radiocarbon Age	Conventional Radiocarbon Age	Culture age
G1	Hemudu site	5975 ± 30	6817 ± 44	Hemudu culture
G2	Nanhu site	4615 ± 25	5379 ± 59	liangzhu culture
G5	Tadi site	4040 ± 30	4508 ± 50	liangzhu culture

- **河姆渡文化是中华文明起源的重要分支,该时期先民已经使用芦苇席，并种植茶树和水稻**

  The Hemudu culture is an important branch of the origin of Chinese civilization. During this period, ancestors already used reed mats and cultivated tea plants and rice.

Chinese Science Bulletin，2018

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中药起源与农业起源一脉相承

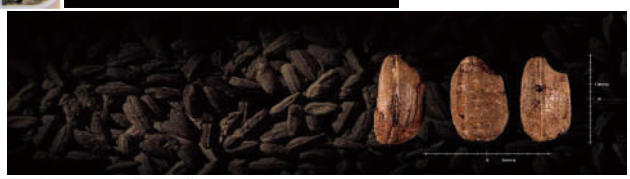
The origin of traditional Chinese medicine is closely linked to the origin of agriculture

- **在新石器时期的浙江地区，伴随着早期农业的形成，人们采集生物，用于食用或药用，由此开始了中药使用的历史**

  In the Neolithic period in Zhejiang, with the formation of early agriculture, ancestors began collecting organisms for food and medicinal use

遗存包括大量的植物遗存和动物遗骸
Numerous plant and animal relics

利用湿地种水稻
Utilizing wetlands for rice cultivation



发现最早人工种茶遗存
Relics of artificially cultivated tea
***Science*,2004**

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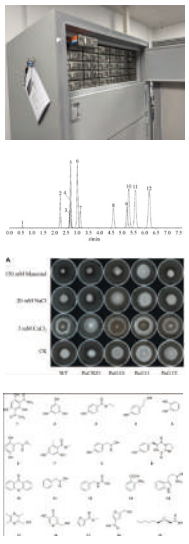
菌物药种质资源保藏库建设
Construction of Germplasm Resource Repository for Fungal Medicine



1. **资源保藏平台** Fungal Resource Preservation Platform — 建立菌物药种质资源保藏库，形成规范化的菌株保藏。
2. **标准提取物平台** Standard Extract Platform — 建立醇提物、水提物等粗提物保藏平台，进行功能初筛
3. **微生物发酵平台** Microbial Fermentation Platform — 解析活性成分的合成通路，构建高效表达载体，实现活性成分规模化大量生产
4. **活性评价研究平台** Activity Evaluation Platform — 筛选与抗氧化、抗衰老等功效相关的活性成分，解析物质基础

为大健康产品研发提供科技支撑
Provide scientific support for development of health products

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菌物药种质资源保藏库建设

Construction of Germplasm Resource Repository for Fungal Medicine

□ 菌物药资源目录：89科，203属，581种

Fungal Medicine Resource Directory: 89 Families, 203 Genera, 581 Species.

暗球腔菌科 竹黄属 竹黄

Shiraiaceae ***Shiraia bambusicola***

春季雨后寄生于短穗竹及其变种毛环短穗竹、白纹短穗竹。

分布于浙江、江苏、安徽、江西、福建、湖北、四川等地

白肉迷孔菌科 硫磺菌属 硫磺菌

Laetiporaceae ***Laetiporus sulphureus***

生于柳、云杉等活立木树干、枯立木上，阔叶林内

分布于吉林、内蒙古、陕西、新疆、福建、广东、江苏等地

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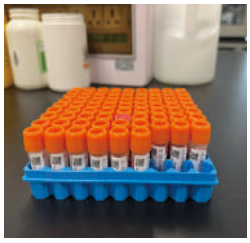
菌物药种质资源保藏库建设

Construction of Germplasm Resource Repository for Fungal Medicine

□ 2023年筹建菌物药种质资源保藏库

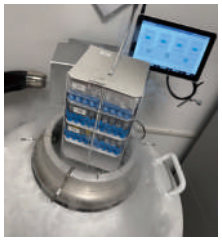
（地点：江西南昌 中国中医科学院健康产业研究所）

Construction of Germplasm Resource Repository for Fungal Medicine were commenced from 2023 at Institute of Traditional Chinese Medicine Health Industry, CACMS.



冻干法 (冻干粉)
Lyophilized powder

低温冻存法(-80°C)
Frozen at -80°C



液氮冻存法 (-195°C)
Frozen in liquid nitrogen

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菌物药种质资源保藏库建设
Construction of Germplasm Resource Repository for Fungal Medicine

- **截至目前：已分离纯化保藏 62 种、368 株菌物药菌株**

368 strains belonging to 62 species of medicinal fungi have been isolated, purified, and preserved

为药用真菌的资源开发和可持续利用奠定基础

A foundation for resource development and sustainable utilization of medicinal fungi

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菌物药种质资源保藏库建设
Construction of Germplasm Resource Repository for Fungal Medicine

综合信息库 Comprehensive Information Database	来源 (origin) 功效 (efficacy)
种质资源库 Germplasm Resource Bank	药用真菌种质资源库 (Repository for Medicinal fungi) 中药材伴生菌种质资源库 (Repository for TCM symbiotic fungi)
活体组织库 Living Tissue Repository	短期保藏库 (Short-term storage) 中期保藏库 (Medium-term storage) 长期保藏库 (Long-term storage)
基因信息库 Gene database	全基因组信息 (Whole genome) 特征片段信息 (Signature sequence) 改造信息 (Genetic Modification)
标准提取物保存库 Standard Extract Repository	水提物 (Aqueous Extract) 醇提物 (Alcohol Extract)

五库保育体系
Fungal Conservation and Breeding System

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菌物药化妆品极具市场潜力
Construction of Germplasm Resource Repository for Fungal Medicine

- **菌物药化妆品功能**
  Activities of medicinal fungi-derived cosmetics
  - 抗氧化作用 (antioxidant)
  - 抗衰作用 (anti-aging)
  - 保湿和滋养 (moisturizing)
  - 舒缓和修护 (repairing)
  - 美白 (whitening)
  - 抗刺激和抗炎 (anti-inflammatory)
  - 促进皮肤再生 (promoting skin regeneration)
  - 调节皮肤微生态 (modulating skin micro-condition)
- **菌物药化妆品产品**：桦褐孔菌菌核提取物、赤灵芝提取物、灵芝细胞油、灵芝三萜、灵芝多糖、白松露菌提取物、层孔菌提取物、松茸提取物、桦褐孔菌提取物。
  Representative products of medicinal fungi-derived cosmetics


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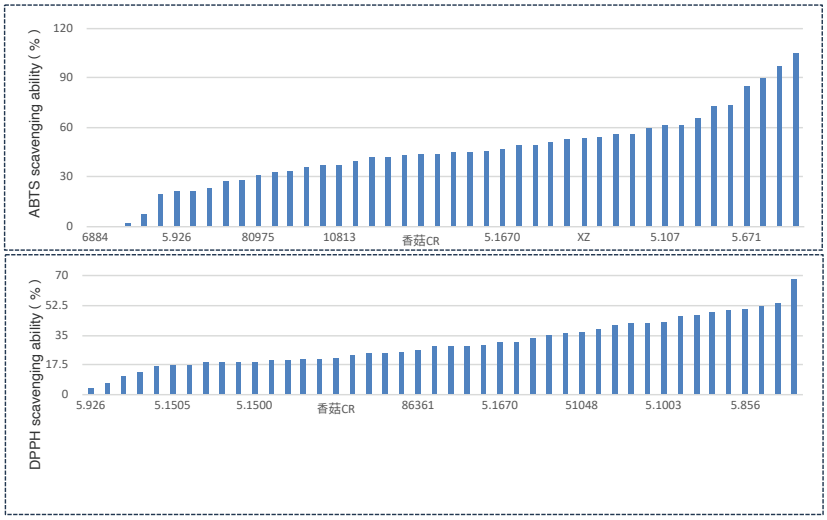
菌物药抗氧化作用筛选

Screening of antioxidative activity of fungal medicine

- **菌物药的ABTS和DPPH清除能力筛选**

  Screening ABTS and DPPH scavenging ability of fungal medicine



菌物药抗氧化作用筛选

Screening of antioxidative activity of fungal medicine

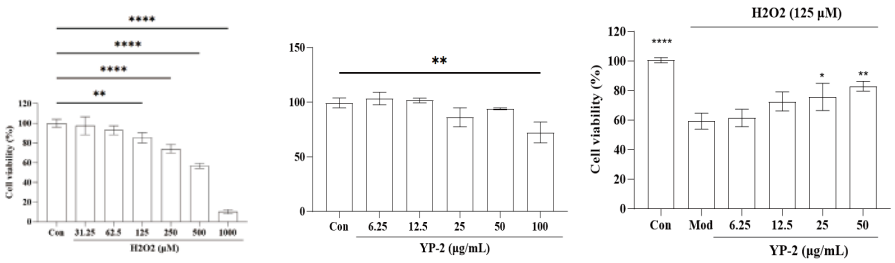
- 晶粒小鬼伞、隆纹黑蛋巢菌、杨树桑黄等**具有良好的抗氧化作用**

  Coprinellus micaceus, *Cyathus striatus*, and *Phellinus igniarius* exhibit high antioxidant activity.

菌物药抗氧化作用筛选

Screening of antioxidative activity of fungal medicine

- 晶粒小鬼伞 ***Coprinellus micaceus***
- 选择125 μM过氧化氢造模、6.25~50 μg/mL治疗，从25 μg/mL开始能够增加细胞存活率，且呈浓度依赖关系。
  Using 125 μM H_2O_2 for modeling and 6.25-50 μg/mL for treatment, the result indicated that concentrations starting from 25 μg/mL were able to increase cell viability in a concentration-dependent manner.
- 表现出抗氧化潜力，预测具有美白等作用。
  C. micaceus demonstrates antioxidant and skin-whitening potential.



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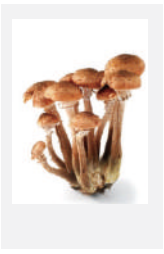
高卢蜜环菌良种选育

Screening and breeding of high-quality *Armillaria gallica*

高卢蜜环菌 (*Armillaria gallica*)

- 伞菌目、泡头菌科
- 分布较为广泛，森林病害
- 食药用真菌，中成药原料
- 与天麻的共生关系



A. gallica belongs to Agaricales order, Physalacriaceae family. *A. gallica* is a type of edible and medicinal fungus, which serves as a raw material of TCM and is often symbiosis with *Gastrodia elata*.

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高卢蜜环菌基因组特征分析

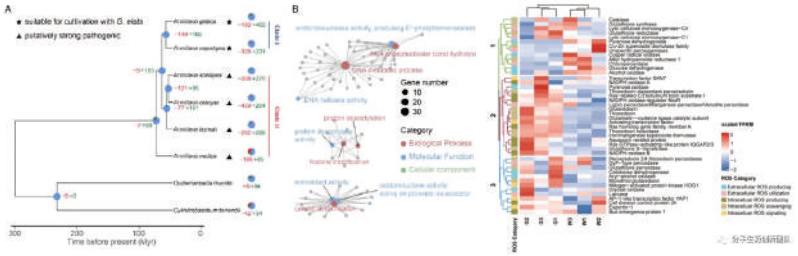
Screening and breeding of high-quality *Armillaria gallica*

来源：天麻块茎分离菌株NRC001

***A. gallica* strain NRC001 was isolated from the tuber of *G. elata*.**

- 属于低致病性蜜环菌
- 编码活性氧氧化还原酶等基因发生扩张，与活性氧相关的52个基因家族的218个基因
- 通过比较天麻共生蜜环菌和非共生蜜环菌的表达谱，发现其中63个基因表达水平差异显著

NRC001 is low-pathogenic *Armillaria spp.*, whose oxidoreductase gene family significantly expanded compared to high-pathogenic *Armillaria spp.* Among 218 genes from 52 ROS-related gene families, 63 genes differentially expressed after symbiosis with *Gastrodia elata.*



推测活性氧稳态在天麻与蜜环菌共生中发挥重要作用

ROS homeostasis plays a crucial role in *Armillaria-G. elata* symbiosis

Microbiological Research，2024

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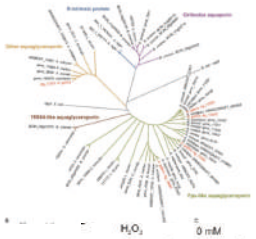
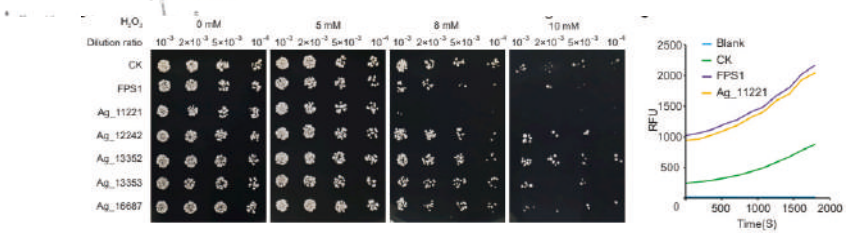
蜜环菌水通道蛋白AQPA通道孔径最大

The aquaporin AQPA in *A. gallica* has the largest pore diameter



- 在NRC001中共鉴定了5个水通道蛋白(AQPA~AQPE)
- AQPA属于“其他水甘油通道蛋白（Other aquaglyceroporin）”亚家族，尚未有对该家族基因功能的报道。

Five aquaporin were identified in NRC001. AQPA belongs to “Other aquaglyceroporin” subfamily, whose function has not been reported.



- 荧光探针实验表明，仅AQPA具有转运H_2O_2的能力。
- AlphaFold蛋白质结构预测，结合HOLE软件计算转运通道孔径大小，表明与其他4个AQP相比，AgAQPA的通道孔径最大，这可能是其可以运输H_2O_2的主要原因。

Only AQPA possesses the ability to transport H_2O_2. Compared to the other four AQPs, AgAQPA has the widest pore diameter.

Microbiological Research，2024

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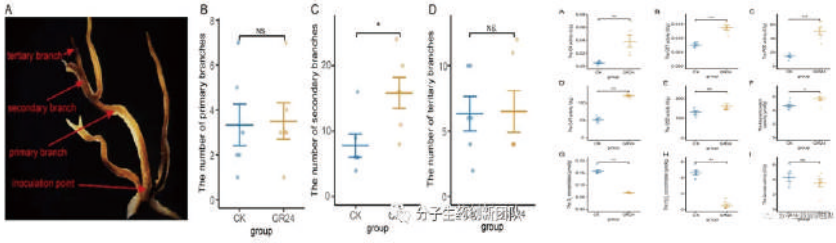
独脚金内酯调控天麻对蜜环菌活性氧稳态

Strigolactone are capable of regulating *A. gallica* ROS homeostasis

- **独脚金内酯（strigolactone）**：天麻吸引蜜环菌的关键信号物质。

  Strigolactone is the key signaling compound for *G. elata* attracting *A. gallica*



- 受控培养实验结果发现，独脚金内酯能够增强蜜环菌细胞内活性氧的清除作用，并促进细胞外活性氧的产生。
- 独脚金内酯处理后，细胞内活性氧或细胞外活性氧水平呈现相反的变化趋势，说明**蜜环菌细胞内外存在活性氧的交换。**

  SLs can enhance scavenging effect of ROS within *A. gallica* cells and promote extracellular ROS production, thereby influencing the exchange of intracellular and extracellular ROS.

Microbiological Research，2024

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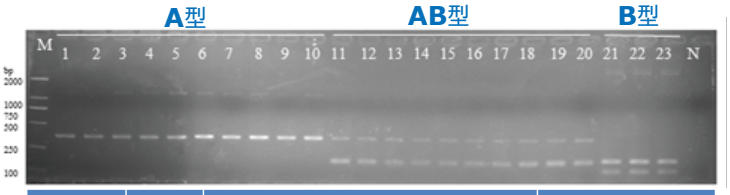
蜜环菌种质资源的基因型鉴定与应用

Genotype Identification and Application of *A. gallica* Germplasm Resources



基因型	等位基因	蜜环菌特征			伴栽天麻特征	
		单糖	生长量	抗逆性	坡地	平地
A型	纯合	葡萄糖高	高	弱	高	低
B型	纯合	海藻糖高	低	强	中	中
AB型	杂合	-	中	中	低	高

- **基于糖[illegible]基因[illegible]型**
- **受控实验条件下对不同基因型蜜环菌的生长量、抗逆性进行测量**
- **田间栽培实验对不同基因型蜜环菌伴栽天麻产量和指标成分进行比较**

Fourteen *A. gallica* strains were identified and classified into 3 genotypes. The yield, stress resistance, yield and valuable ingredients of combined-planting *G. elata* were measured and compared in different genotypes.

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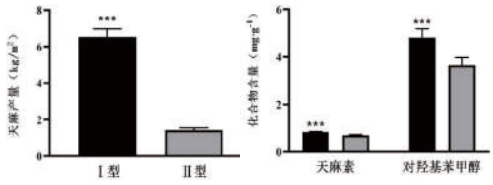
专利202010236665.8,201910419080.7

适合林下天麻栽培蜜环菌品种选育

Screening and Breeding of *A. gallica* Species Suitable for *G. elata* Cultivation

- 与对照相比：
  - 选育品种的产量显著增高；
  - 天麻素和对羟基苯甲醇含量显著增高



Compared with contrast, the yield and content of gastrodin and 4-hydroxybenzyl alcohol in *G. elata* co-planted with breeding *A. gallica* species were significantly increased.

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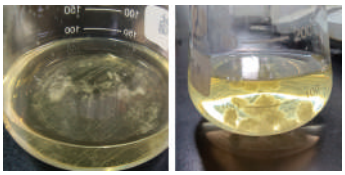
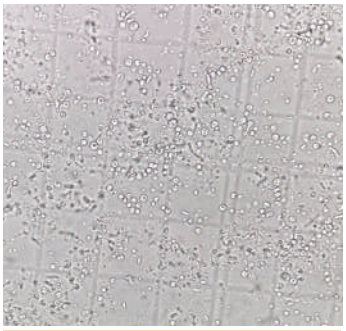
蜜环菌原生质体遗传转化体系研究

Genetic Transformation System of *Armillaria gallica* Protoplasts

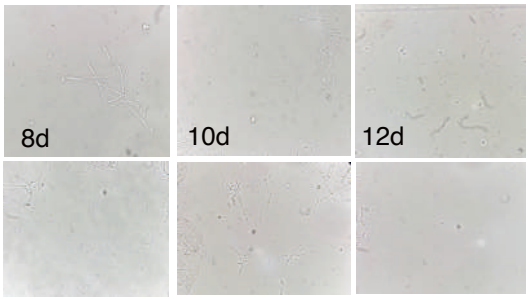
菌丝培养条件的优化





400倍显微镜下
血细胞计数板上的原生质体

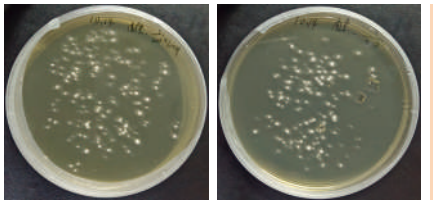
原生质体培养



1.5%溶壁酶 +1.5%复合酶

2%溶壁酶 +1.5%复合酶

2%溶壁酶 +2%复合酶



原生质体再生

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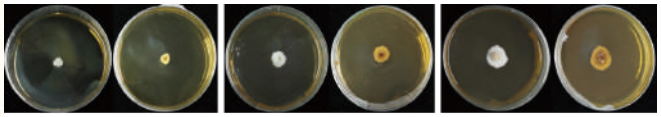
蜜环菌原生质体遗传转化体系研究

Genetic Transformation System of *Armillaria gallica* Protoplasts

pAg1-OE vector

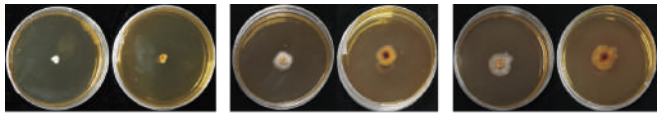
1.5 %潮霉素抗性培养基转化菌株生长情况

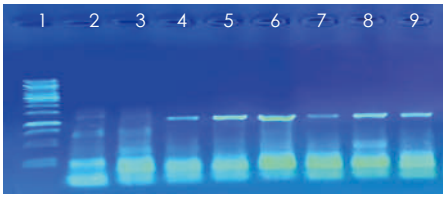
Transgenic strains on 1.5% hygromycin medium



3.0 %潮霉素抗性培养基转化菌株生长情况

Transgenic strains on 3.0% hygromycin medium





- **1：1kb marker**
- **2,3：Wild-type nontransgenic strain 1**
- **4,5,6：Transgenic strains on 1.5% hygromycin medium**
- **7,8,9：Transgenic strains on 3.0% hygromycin medium**

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真菌-细菌共生体研究

bacteria-fungi endosymbiosis

- **内共生关系**，即两种生物体在同一宿主内密切协作的现象，极大地推动了生物进化。
- 通过微注射技术，将细菌移植到真菌体内，从而诱导出一种全新的人工内共生关系。这一发现为探索合成内共生体提供了崭新的思路，也为未来设计具备特定代谢功能的内共生生物开辟了无限可能。

Article

Inducing novel endosymbioses by implanting bacteria in fungi

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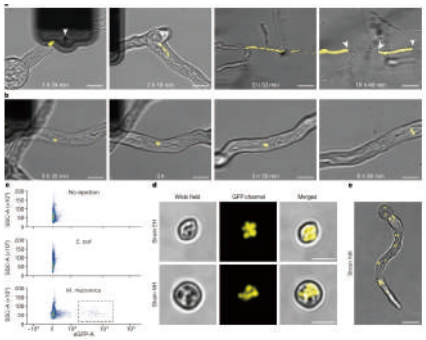
Giger, G.H., Ernst, C., Richter, I. *et al*. Inducing novel endosymbioses by implanting bacteria in fungi. Nature (2024).



Inducing novel endosymbioses by implanting bacteria in fungi provides a powerful experimental approach for synthetic approaches towards designing endosymbioses with desired traits.

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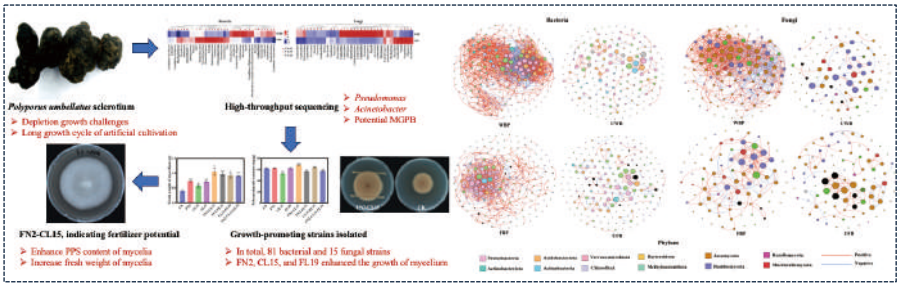
伴生细菌助力猪苓多糖生产

Bacteria facilitate the production of *P. umbellatus* polysaccharides

- **猪苓菌丝体中分离获得3株细菌菌株（FN2、FL19和CL15）具有促进猪苓菌丝生长的生物活性。**

Three bacterial strains (FN2, FL19 and CL15) were isolated from the mycelium of *P. polyporus* could promoting the mycelium growth.



Journal of Fungi , 2024

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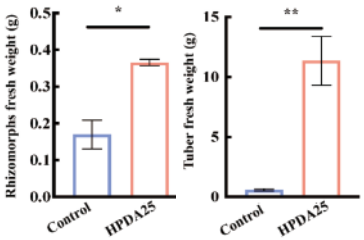
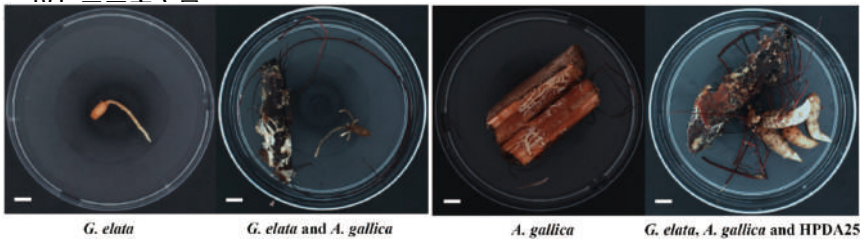
伴生细菌助力天麻与蜜环菌共生

Companion bacteria benefits the symbiosis between *A. gallica* and *G. elata*

- **从天麻中分离鉴定了菌株HPDA25**
- **可通过分泌植物生长激素IAA促进了高卢蜜环菌*Armillaria gallica*菌索生长和分支数增加、胞外漆酶活力增强**
- **并加快了蜜环菌与天麻共生关系的建立，**





HPDA25 isolated from *G. elata* can promote the rhizomorph growth and branch number of *A. gallica*. HPDA25 could also promote the establishment of symbiosis between *A. gallica* and *G. elata,* thereby improve the yield of *G. elata.*

Frontiers in Microbiology , 2022

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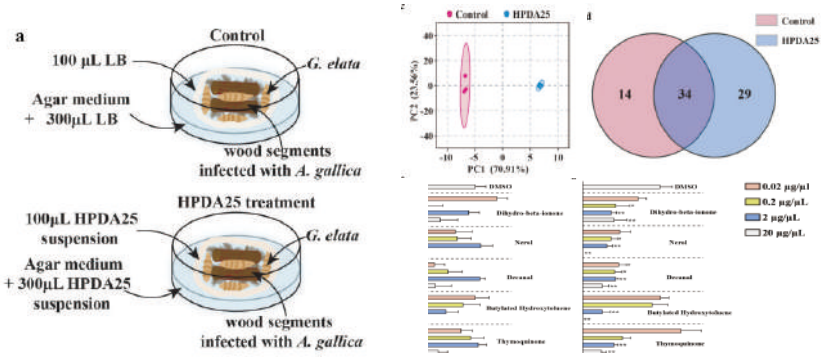
伴生细菌助力天麻与蜜环菌共生

Companion bacteria benefits the symbiosis between *A. gallica* and *G. elata*

- 菌株HPDA25可促进天麻VOCs成分谱的变化，
- 其中6 种 VOCs 对 *A. gallica* 具有生长抑制活性，而对菌株HPDA25 没有显著影响。



HPDA25 can promote changes in VOCs profile of *G. elata*, among which six VOCs could inhibit growth of *A. gallica*.

Plant Signaling & Behavior , 2024

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- 中国中医科学院科技创新团队“分子生药学”
- 中国中医科学院“卓越人才”专项

KOREA INSTITUTE OF ORIENTAL MEDICINE
INTERNATIONAL SYMPOSIUM

PRESENTATION

Taesoo KIM
KIOM

DISCOVERY OF NEW COSMETIC INGREDIENTS USING HERBAL MEDICINE

Discovery of New Cosmetic Ingredients Using Herbal Medicine

- Taesoo KIM I KIOM

한중 심포지엄 : KIOM-CACMS 국제공동연구 기획

[한의약융합연구부]

Discovery of New Cosmetic Ingredients Using Herbal Medicine
한약 소재를 활용한 화장품 신소재 발굴 연구

2024.10.30

KIOM 한국한의학연구원

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- Taesoo KIM I KIOM

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한국한의학연구원 KOREA INSTITUTE OF ORIENTAL MEDICINE

천연물 기반 화장품

천연물 기반 화장품 정의

» **천연화장품(Natural Cosmetics)**에 대한 정의와 기준은 국가마다 다르나 통상적으로는 식물, 동물, 미생물, 광물 등 **천연자원에서 얻어지는 소재** 자체로부터 얻거나, 물리· 화학·생물학적 공정에 따라 **가공한 천연유래 화장품**을 의미

» 천연화장품에 대한 중요성은 세계 공통으로 커지고 있으나, 이에 대한 규정 및 인증 취득 절차는 국가별·지역별로 상이

- 국가별로 '**오가닉**', '**유기농**', '**천연'화장품**' 등에 대한 개별적 규정 및 범위를 정하여 엄격한 요건 요구
- 천연화장품 인증 및 레이블 취득에 대한 요구가 강화되는 추세에 맞춰, 국가별 맞춤형 인증취득 필수

[천연화장품의 소재 워드클라우드]

천연화장품 산업 및 소재개발 트렌드

» **화학물질에 대한 우려**로 **유기농** 및 **천연유래** 화장품에 대한 관심이 고조되고, **동물권리의 보호, 친환경** 등의 사회적 이슈까지 더해져 인체와 사회, 환경에 모두 안전한 천연화장품의 산업 전망 이슈 증가

» 화장품 성분 이외에도 제조공정, 유통과정 등에서 **동물 임상실험 금지**, **탄소배출량 감소**, **생분해성 원료개발**(미세플라스틱 사용금지)의 확대 등 기업윤리와 환경적 책임을 요구하는 친환경 경영요구가 확대되며, 이를 소비성향에 반영하려는 움직임이 활발함.

[국가별 천연화장품 인증마크]

INTRODUCTION

한국한의학연구원 KOREA INSTITUTE OF ORIENTAL MEDICINE

한약소재 기반 화장품 > 한방 화장품

한방 화장품 정의

» **「대한약전」, 「대약약전외한약(생약)규격집」 및 「기존 한약서에 대한 잠정 규정」**에 따른 기존 한약서에 수재된 생약 또는 한약재를 일정 기준 이상 제조 시 사용한 화장품

» 식품의약품안전청에서는 "한방화장품은 동의보감을 포함한 11대 한의학서적(본초강목, 향약집성방, 방약합편, 제중신표, 사상의학, 수세보원, 경약전서, 의약입문, 광제비급, 약성가)에 언급한 한약재를 함유한 화장품

국내 한방화장품 개발 동향

» **(1997) 설화수** : (주)태평양과 경희대 한의대가 공동연구 개발, 여성의 음기를 보해주는 자음단 처방의 한방원리에 따라 개발

» **(2000) 한방미인** : (주)코리아나화장품와 경희대 한의대가 공동개발, 사상의학에 근거하여 개발

» **(2001) 산심** : (주)한국화장품과 경희대 동서의학대학원이 공동개발, 산삼조직 배양 추출물을 함유한 화장품 개발

» **(2003) 수려한** : (주)LG 생활건강과 **한국한의학연구원** 공동개발, 경옥고와 비연목란단을 주성분으로 한방화장품 개발

INTRODUCTION

한국한의학연구원 KOREA INSTITUTE OF ORIENTAL MEDICINE

천연물 기반 화장품의 글로벌 시장 동향

지속적인 천연화장품 산업 및 시장의 성장 추세

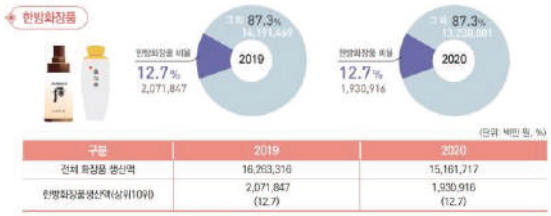
» 세계 천연화장품의 시장규모는 2022년 435억 달러에서 향후 5년간(2023-2028년) **6.15%의 CAGR(연평균성장률)**로 성장하여 610억 달러에 달할 것으로 예측 (Global Natural Cosmetics Market Outlook 2028, `23.05)

» 글로벌 천연화장품 시장은 2023년 486억 달러 수준에서 향후 10년간(2023-2033년) **CAGR 5.1%로 성장**하여 2033년에는 796억 달러까지 확대될 것으로 전망 (FMI(Future Market Insights))

국내 한방 화장품 생산 점유율은 2016년 7.1%에서 2020년 12.7%로 5.6%P 증가

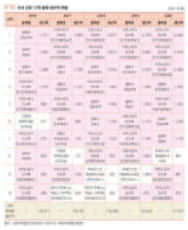
» 2020년 국내 화장품 생산 **상위 10개 품목 중 9개**가 한방 화장품이 차지

» 한방 화장품 생산 점유율은 2016년 7.1%, 2017년 6.7%, 2018년 10.2%, 2019년 12.7%, 2020년 12.7%로 매년 증가 추세



(단위: 백만 원, %)

구분	2019	2020
전체 화장품 생산액	16,263,316	15,161,717
한방화장품 생산액(상위10위)	2,071,847 (12.7)	1,930,916 (12.7)



INTRODUCTION

한국한의학연구원 KOREA INSTITUTE OF ORIENTAL MEDICINE

천연물 기반 화장품의 글로벌 특허 동향

지속적인 글로벌 천연화장품 분야의 특허 출원 증가

» 지난 반세기 동안(1974~2022) 화장품 관련 글로벌 특허출원은 연평균증가율(CAGR) 8% 성장하고 있으며, **천연화장품의 경우 11%**에 달해 일반화장품에 비해 더 높은 증가 추세

» **중국**은 천연화장품에 있어서 2012년 이후 최고점을 보인 **2018년까지** 연평균증가율 **43%**의 가파른 증가세를 보이다가 **최근 10년간은 17%의 높은 증가세**를 나타냄 (전세계 천연화장품 특허의 51%에 해당(46,569건)

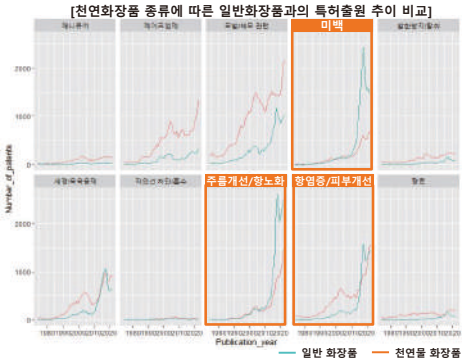
» 특허출원 점유율에 있어서 **중국, 일본**에 이어 미국을 제치고 **한국**이 16%의 점유율로 3위에 자리함으로써 자연친화적 기술의 천연화장품 분야는 **아시아 3국이 84%로 압도적 우위**로 나타남

식물유래 소재 중심으로 미백기능 가장 크고, 최근 주름개선/노화 분야 급증, 항염증/피부개선 진전

» 천연화장품의 종류에 따른 특허출원 추이를 일반화장품 종류와 비교해 본 결과 **미백, 주름개선/항노화, 항염증/피부개선** 분야에서 일반화장품에 비해 천연화장품의 비중이 확연히 높은 것으로 나타남

» 천연화장품의 원천소재 부분에 있어서 **식물유래 화장품이 대부분**을 차지하고 타 유래 분야(미생물, 동물 등)는 미미한 실정

[천연화장품 종류에 따른 일반화장품과의 특허출원 추이 비교]



Discovery of New Cosmetic Ingredients Using Herbal Medicine

- Taesoo KIM I KIOM

INTRODUCTION

한국한의학연구원 KOREA INSTITUTE OF ORIENTAL MEDICINE

천연물 기반 화장품의 기능성 연구 동향

생명공학 기술 발달에 따른 메커니즘 중심의 기능성 소재 개발 연구 증가

» **생명공학기술**의 발달로 **피부세포의 분화** 및 **노화현상의 규명**, 세포배양, 면역학 및 분자생물학적 기반 기술 등 피부과학분야 연구가 급진전하면서 미백과 보습, 자외선 차단과 흡수, 유해산소 제거 등 항산화 작용, 콜라겐 합성, 주름방지 등 항노화작용, 항염증작용을 포함한 피부장벽 개선 등 피부(모발 포함)에 다양한 효능·효과를 제공하는 **기능성화장품 소재 개발이 꾸준하게 증가**

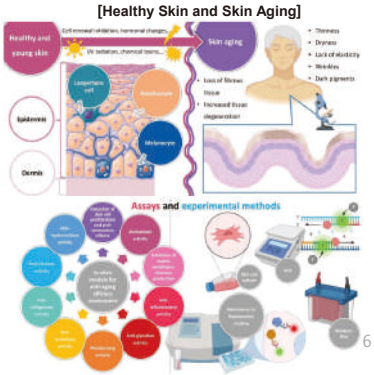
» 특히 최근에는 과학기술의 진보에 따른 **다양한 메커니즘의 규명**으로 **선택적으로 작용하는 효능·효과를 지닌 소재 발굴**의 움직임이 활발함

[Anti-wrinkle Mechanism and Some Representative Active Materials]

Mechanism	Examples	Remark
Control of differentiation of epidermal cell	Retinoids, α-Hydroxy acids, Mevalonolacton, Niacinamide	Stimulating skin turnover
Control of ECM components	Silicic acid, N-Methyl-L-serine Isoflavonoids Dehydroepiendrosteron	Inhibition of collagen metabolism (MMP-1 inhibition)
	Paoniflorin, Prangenidin-77	Collagen synthesis
	Retinoic-d-δ-tocopherol, 3-methylcyclopentadecanone	Hyaluronic acid synthesis
Scavenging of ROS	Benzastatins, Inoscavin, Melanocins, Coenzyme Q10, Astaxanthin	Inhibition of lipid peroxidation
Anti-inflammation	Glycyrrizic acid derivatives	
UV protection DNA Repair	Creatin, Photolyase (Photosome) Candlebush ext	Protection of gene
Other	Acetyl hexapeptide	Reduction of muscular motion

기능성화장품 연구개발 동향 (2010, KIC News, Volume 13)

[Healthy Skin and Skin Aging]



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INTRODUCTION

한국한의학연구원 KOREA INSTITUTE OF ORIENTAL MEDICINE

천연물 기반 화장품의 기능성 연구 동향

피부에 대한 기초 연구로부터 소재개발

» 화장품 소재 개발에 있어서 이미 활발하게 연구가 진행되고 있는 **genomics 등 다양한 ~Omics 기술을 활용한 제품, 타겟 유전자를 제어하는 기술을 활용이 활발히 진행중**

» **피부의 노화 기전을 규명**하여 노화를 늦추는 것에서 더 나아가 보호, 치유 등 피부를 건강하게 유지하기 위한 기전을 찾는 다양한 **기초연구**가 진행중

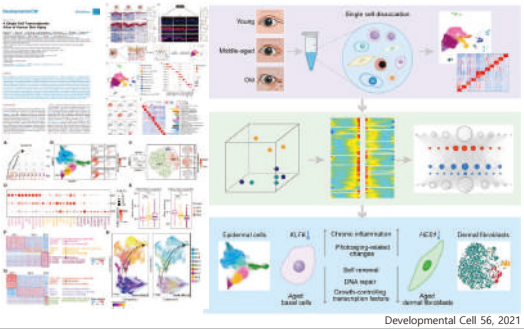
» 건강한 피부에 대한 연구뿐만 아니라 질환 등 문제를 안고 있는 피부에 대한 연구, 내부적 요인 뿐만 아니라 외부적 피부기전의 과학적 근거를 찾기 위한 연구가 활발히 진행되고 있으며 과학적인 분자 수준의 기전 연구를 바탕으로 한 근거 중심의 효능 연구 및 소재개발의 체인이 형성

단일세포 전사체 분석을 통한 인체 피부 노화 세포 분석

- **Single-cell transcriptional** landscapes of human skin aging
- Dysregulation of cell-type-specific transcriptional networks during skin aging
- Cell-type-specific downregulation of **HES1** or **KLF6** accelerates senescence
- **Quercetin** promotes the rejuvenation of aged dermal fibroblasts

✓ Chronic inflammation
✓ Photoaging-related changes

✓ Self-renewal
✓ DNA repair
✓ Growth-controlling transcription factors



Developmental Cell 56, 2021

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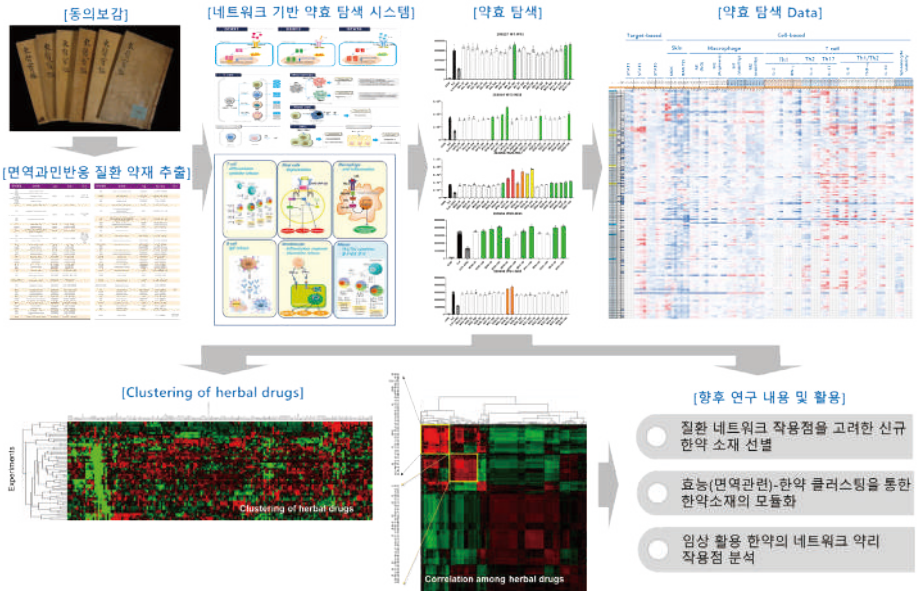
한국한의학연구원 KOREA INSTITUTE OF ORIENTAL MEDICINE

질환 네트워크 조절 다중표적 약리 작용점 및 효능 연구



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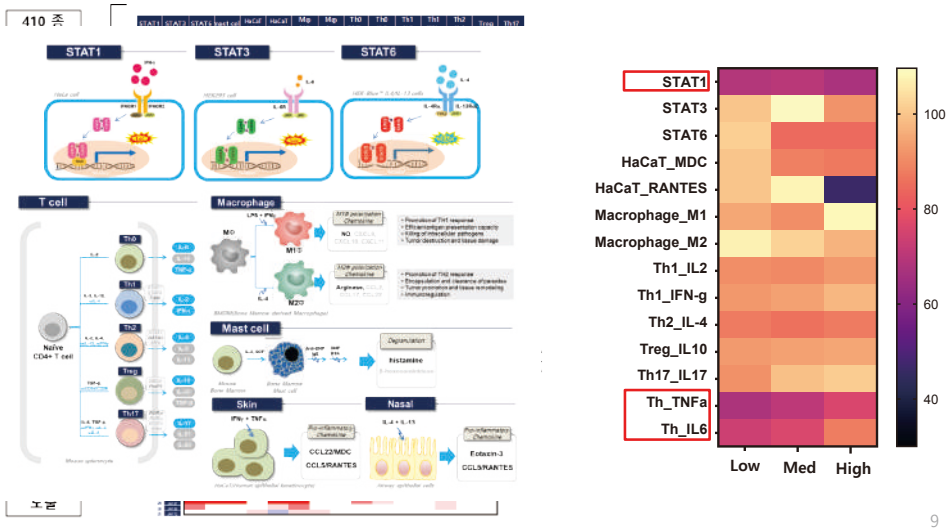
RESULTS

한국한의학연구원 KOREA INSTITUTE OF ORIENTAL MEDICINE

면역 네트워크 조절 다중표적 약리 작용점 및 효능

지모(知母)의 면역 조절 효능 : STAT1 & inflammatory cytokine(TNFa, IL-6) 억제



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한국한의학연구원 KOREA INSTITUTE OF ORIENTAL MEDICINE

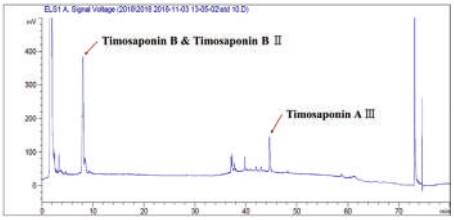
지모(知母, *Anemarrhena asphodeloides*) 소재를 활용한 피부건강 개선 소재 개발

지모(知母)의 특징 및 기원

과 : 백합과 Liliaceae
학명 : Anemarrhena asphodeloides
분포 : 한국, 중국(간쑤, 구이저우, 네이멍구, 랴오닝, 산둥 등), 타이완, 몽골
약용부위 : 뿌리줄기
공정서 : 대한민국약전외한약(생약)규격집(KHP)
향기 / 맛 : 특유한 냄새가 있고, 약간 달고 뒷맛이 씀
전통적 사용 : 갈증, 두통, 천식, 토혈(코피)/방광・간・신의 습열을 제거/허리와 다리가 붓고 아픈 증상

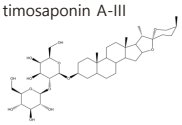
지모(知母) 구성 성분

[HPLC-ELSD chromatogram of *A. asphodeloides* extract]

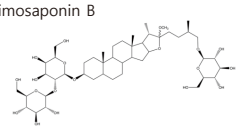


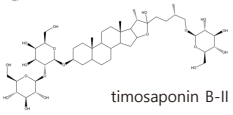
Biomedicine & Pharmacotherapy 133 (2021)

timosaponin A-III



timosaponin B





timosaponin B-II

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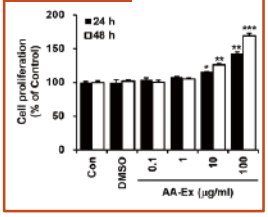
RESULTS

한국한의학연구원 KOREA INSTITUTE OF ORIENTAL MEDICINE

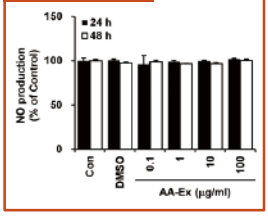
지모(知母, *Anemarrhena asphodeloides*) 소재를 활용한 피부건강 개선 소재 개발

지모(知母)의 면역강화 효능: 면역세포(macrophage) 증식 촉진

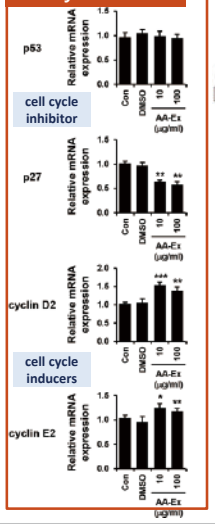
Cell Viability

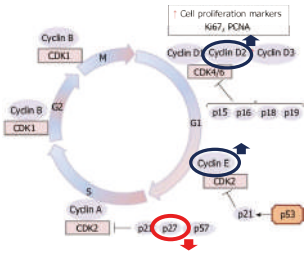


NO production

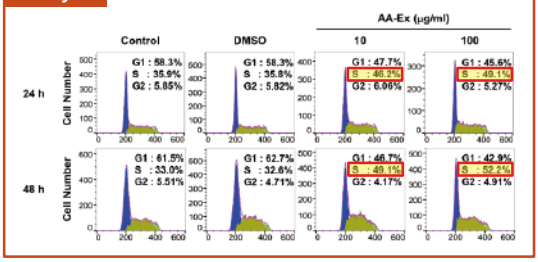


Cell Cycle markers





Cell Cycle



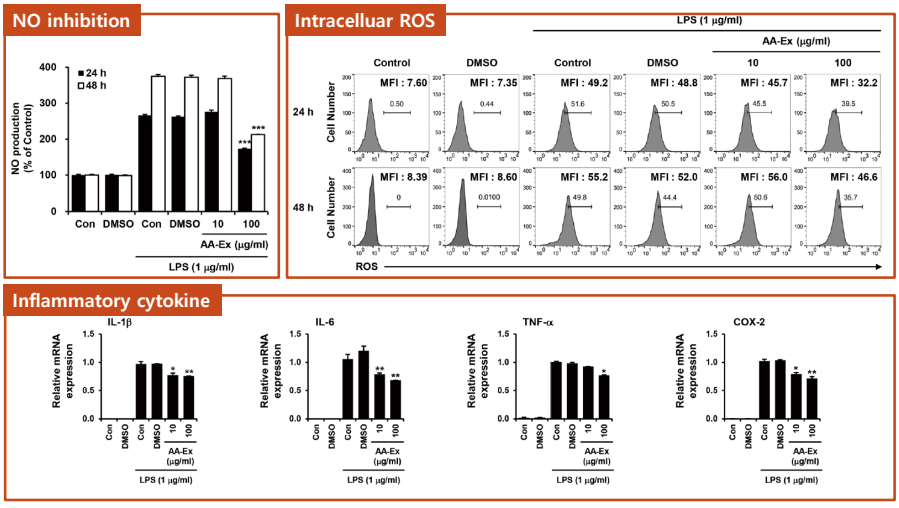
Phytomedicine 59 (2019)
The enhancing immune response and anti-inflammatory effects of *Anemarrhena asphodeloides* extract in RAW 264.7 cells

RESULTS

한국한의학연구원 KOREA INSTITUTE OF ORIENTAL MEDICINE

지모(知母, *Anemarrhena asphodeloides*) 소재를 활용한 피부건강 개선 소재 개발

지모(知母)의 항염 효능 : NO, iROS 및 inflammatory cytokine 생성 억제



RESULTS

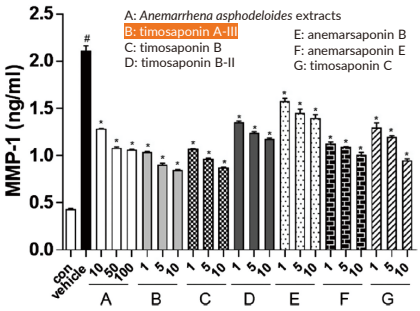
한국한의학연구원 KOREA INSTITUTE OF ORIENTAL MEDICINE

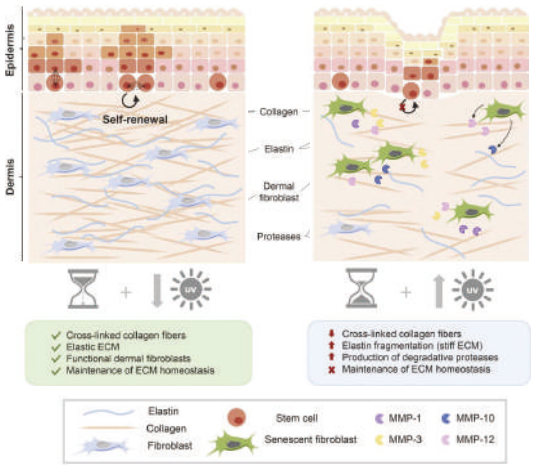
지모(知母, *Anemarrhena asphodeloides*) 소재를 활용한 피부건강 개선 소재 개발

지모(知母) 성분, timosaponin A-III의 주름억제 효능 : MMP-1 생성 억제

MMP-1(collaganase-1)

- Control of physiological collagen turnover
- Initiation of **collagen fragmentation** in human aged skin
- **Increased expression** upon transiently **UV** irradiation and TNF-α induction
- Up-regulated expression in human cornea upon UVB irradiation





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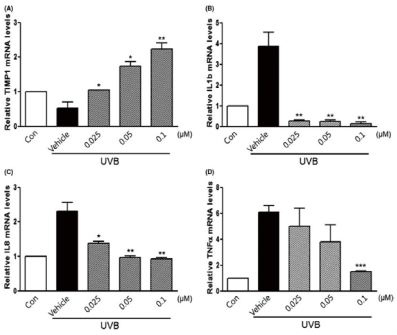
한국한의학연구원 KOREA INSTITUTE OF ORIENTAL MEDICINE

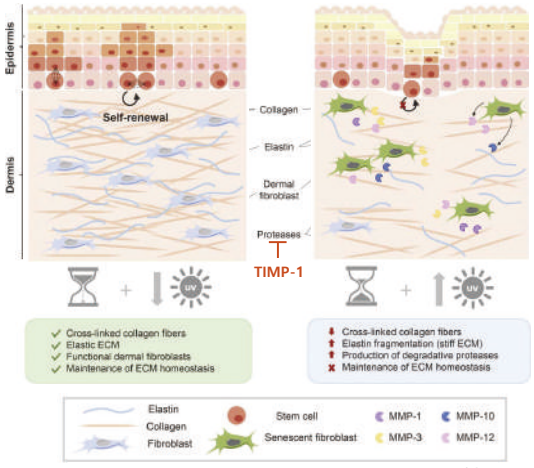
지모(知母, *Anemarrhena asphodeloides*) 소재를 활용한 피부건강 개선 소재 개발

지모(知母) 성분, timosaponin A-III의 주름억제 효능 : TIMP1 및 inflammatory cytokine 생성 억제

≫ TIMP-1(Tissue Inhibitor Of Metalloproteinase 1)

- Natural inhibitor of the matrix metalloproteinases (MMPs)
- Regulates cell differentiation, migration and cell death and activates cellular signaling cascades
- Down-regulation of TIMP-1 in aged human skin and transiently UV irradiation





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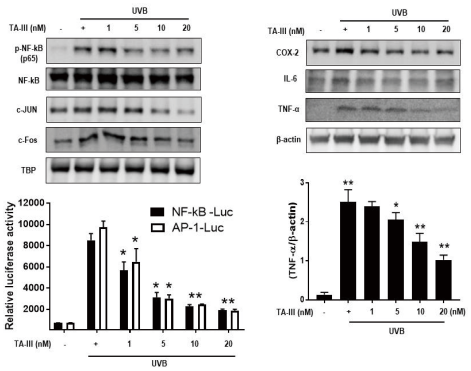
한국한의학연구원 KOREA INSTITUTE OF ORIENTAL MEDICINE

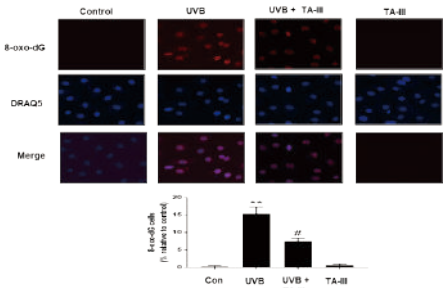
지모(知母, *Anemarrhena asphodeloides*) 소재를 활용한 피부건강 개선 소재 개발

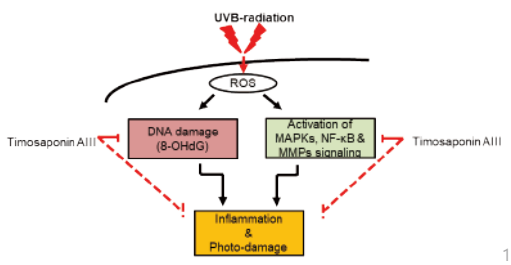
지모(知母) 성분, timosaponin A-III의 약리 기전

≫ TA-III의 전사인자 및 염증인자 억제효능

- Inhibition of UVB induced transcription factors (pNF-kB, c-Jun, c-Fos)
- Inhibition of UVB induced COX-2, IL-6 and TNF-a)
- Inhibition of UVB induced DNA damage







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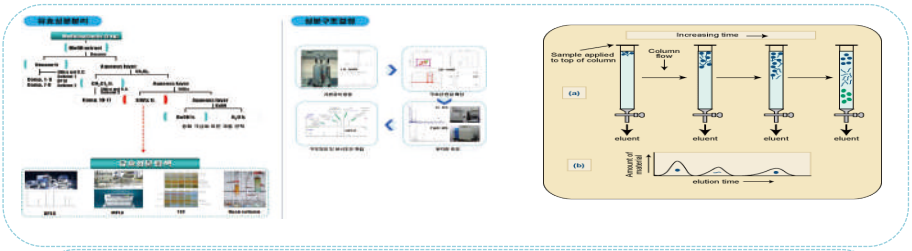
RESULTS

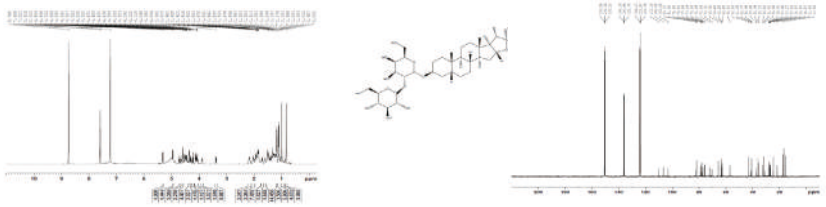
한국한의학연구원 KOREA INSTITUTE OF ORIENTAL MEDICINE

지모(知母, *Anemarrhena asphodeloides*) 소재를 활용한 피부건강 개선 소재 개발

지모 추출물 유래 효능성분 대량확보 및 구조결정

» 효능성분 분리를 위한 공정도





<[1]H-NMR Spectrum> <Timosaponin A-III> <[13]H-NMR Spectrum>

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한국한의학연구원 KOREA INSTITUTE OF ORIENTAL MEDICINE

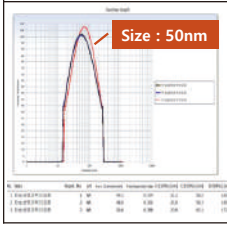
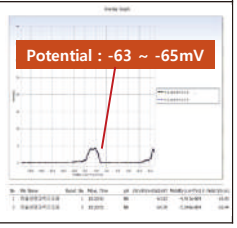
지모(知母, *Anemarrhena asphodeloides*) 소재를 활용한 피부건강 개선 소재 개발

Timosaponin A-III(TA-III) 리포좀 제형 개발

[TA-III(0.5% 함유) 리포좀 제조 및 구성 원료]

상	원료명	함량
A	DI-Water	To 100
	Glycerin	2.5
	Butyrospermum parkii(Shea) Butter	2.5
	Squalane	0.5
	Caprylic/Capric Triglyceride	7.5
	Hydrogenated Phosphatidylcholine	7.5
	Ceramide NP	0.1
	Pentylene Glycol	2.5
	Timosaponin A3	0.5

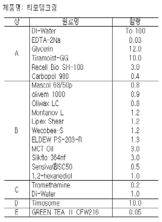
[TA-III(0.5% 함유) 리포좀 Size/Potential 측정]

Zeta Size	Zeta Potential
	
Size : 50nm	Potential : -63 ~ -65mV

※ Timosaponin A-III 리포좀은 피부 층 침투가 용이 할 것으로 판단되며 사이즈가 균일하며, Potential 결과도 안정한 값을 보임.

TA-III 리포좀 함유 크림 제형 안정성 확인

[TA-III(0.5% 함유) 리포좀 함유 크림]



[TA-III(0.5% 함유) 리포좀 함유 크림 안정성 시험]

※ Timosaponin A-III 리포좀 10% 함유 크림은 실온, 일광, 4도, 48도에서 장기간 안정함

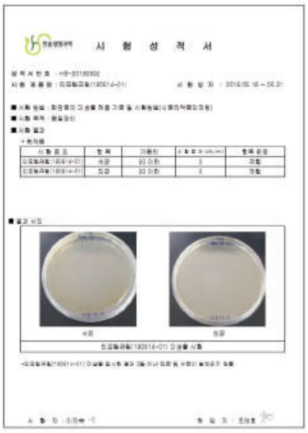
RESULTS

한국한의학연구원
KOREA INSTITUTE OF ORIENTAL MEDICINE

지모(知母, *Anemarrhena asphodeloides*) 소재를 활용한 피부건강 개선 소재 개발

크림 제형 안정성 평가

- Timosaponin A-III 리포좀 함유 크림 제형은 **균주 측정** 결과 안전함
- Timosaponin A-III 리포좀 함유 크림 제형은 **방부력 시험** 결과 안전함


시 험 성 적 서

<Timosaponin A-III 리포좀 함유 크림 제형 미생물 시험 성적서>

방 부 력 시 험 성 적 서		결재	작성	검토	승인
			18.06.14		18.06.14

시험의뢰 업체	한솔생명과학	시험의뢰 부서	연구소
의뢰자	정재욱	의뢰일	2018.05.14
검체명	티모템크림	검체량	80g
시험자	이지숙	시험기간	2018.05.17. ~ 2018.06.14
시험목적	시간에 따른 항균력 확인	시험방법	자사 미생물 시험방법 표준서 HBQM-511에 따른다
특이사항	*티모템크림 (180514-01)		

시 험 결 과

■ 시험 균주

Staphylococcus aureus(KCTC 2513)
Escherichia Coli(KCTC 2571)
Pseudomonas aeruginosa (KCTC 2513)
Aspergillus brasiliensis (KCTC 6317)
Candida albicans (KCTC 7965)

■ 시험 결과

생균수 / 실험균		Aerobic plate count (CFU/ml) after						종합판정
		초기균	0day	7day	14day	21day	28day	
티모템크림	Bac.	5.1x10⁶	4.2x10⁶	0	0	0	0	적 합
	Y/M	5.4x10⁶	4.2x10⁶	0	0	0	0	

■ 시험 소견

균수 측정 결과 7일 이내 99.9% 사멸도를 확인하였으므로 본 제품의 항균력을 증명함

<Timosaponin A-III 리포좀 함유 크림 제형 방부력 시험 성적서>

RESULTS

한국한의학연구원
KOREA INSTITUTE OF ORIENTAL MEDICINE

지모(知母, *Anemarrhena asphodeloides*) 소재를 활용한 피부건강 개선 소재 개발

임상용 시제품 크림 제형 개발

- Timosaponin A-III 리포좀 함유 크림 제형은 내부 품평(20대~50대)과 객관적인 피부진단기 측정을 통해 티모사포닌 A-III의 효능을 극대화 하며 사용감 좋은 제형으로 개발 하였음.

Timosaponin A-III 리포좀 함유 크림 실험군 대조군 품평테스트

제품명: 대조군

상	원료명	함량
A	DI-Water	To 100
	EDTA-2Na	0.03
	Glycerin	12.0
	Tiramoist-GG	10.0
	Recell Bio SH-100	3.0
	Carbopol 980	0.4
B	Mascol 68/50p	0.8
	olivem 1000	0.9
	Oliwax LC	0.8
	Montanov L	1.2
	Lipex Shear	1.2
	Wecobee-S	1.2
	ELDEW PS-203-R	1.3
	MCT Oil	3.0
	Silkflo 364nf	3.0
	Sensiva®SC50	0.5
	1,2-hexanediol	1.0
C	Tromethamine	0.2
	Di-Water	3.0
D	GREEN TEA II CFW216	0.05

제품명:실험군

상	원료명	함량
A	DI-Water	To 100
	EDTA-2Na	0.03
	Glycerin	12.0
	Tiramoist-GG	10.0
	Recell Bio SH-100	3.0
	Carbopol 980	0.4
B	Mascol 68/50p	0.8
	olivem 1000	0.9
	Oliwax LC	0.8
	Montanov L	1.2
	Lipex Shear	1.2
	Wecobee-S	1.2
	ELDEW PS-203-R	1.3
	MCT Oil	3.0
	Silkflo 364nf	3.0
	Sensiva®SC50	0.5
	1,2-hexanediol	1.0
C	Tromethamine	0.2
	Di-Water	1.0
D	Timosome	10.0
E	GREEN TEA II CFW216	0.05

티모템크림 품평 결과서

분류	평가 (1 나쁨 — 보통 — 10 좋음)	의견
사용감 평균 7.4점	1 2 3 4 5 6 7 8 9 10 / 나쁨 보통 좋음	자극 및 끈적임 無. 유분감 多
발림성 평균 7.6점	1 2 3 4 5 6 7 8 9 10 / 나쁨 보통 좋음	잘 발리고 흡수 빠름. 유분감 多. 번거로움
끈적임 평균 7.8점	1 2 3 4 5 6 7 8 9 10 / 나쁨 보통 좋음	끈적임 無. 건성피부에 적합
향 평균 4.9점	1 2 3 4 5 6 7 8 9 10 / 나쁨 보통 좋음	향에 대한 거부감 베이스취가 남. 산뜻한 취 원함.
기타 의견	전체적으로 만족하지만 향취가 강하고 미끈거림. 향이 유아용 같음(성인 취향의 향 원함) 약간의 백탁 현상이 남성에게는 적당하지 않은 것 같음.	

성별	남	여	연령대	20대	30대	40대	50대
	4	8		2	7	2	1

총 12명에게 설문한 결과임.
2018.10.08. 허정민 연구원

<Timosaponin A-III 리포좀 함유 크림 제형 품평 결과서>

<Timosaponin A-III 리포좀 함유 크림 제형 피부진단기 측정>

RESULTS

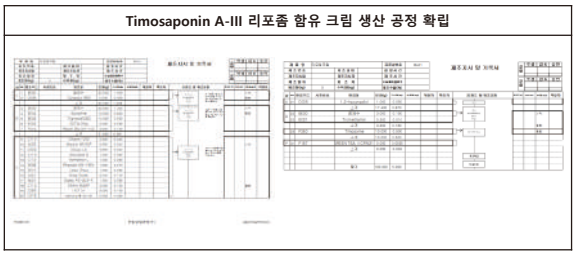
한국한의학연구원 KOREA INSTITUTE OF ORIENTAL MEDICINE

지모(知母, *Anemarrhena asphodeloides*) 소재를 활용한 피부건강 개선 소재 개발

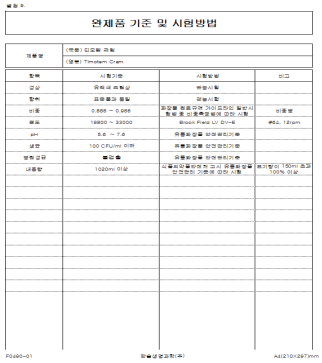
임상 시제품 제조 및 완제품 개발

- Timosaponin A-III 리포좀 함유 크림 제형의 대량생산 공정 확립 및 시제품 개발 완료함

Timosaponin A-III 리포좀 함유 크림 생산 공정 확립



<Timosaponin A-III 리포좀 함유 크림 시제품>



〈Timosaponin A-III 리포좀 함유 크림 시제품 성적서〉

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RESULTS

한국한의학연구원 KOREA INSTITUTE OF ORIENTAL MEDICINE

지모(知母, *Anemarrhena asphodeloides*) 소재를 활용한 피부건강 개선 소재 개발

피부 첩포에 의한 피부 일차 자극 인체 적용 시험

- 피시험자 33명을 대상으로 피부첩포시험 결과 30분, 24시간, 48시간 경과후 자극이 관찰되지 않음
- 평균 피부반응도는 0.00으로 판정기준에 따라 **무자극으로 판정**

1) 시험물질 정보

(1) 시험물질명 : 티모좀 크림

(2) 시험물질 관리번호 : M-KDS-AQ-P01-HSS

(3) 의뢰기관 : 한솔생명과학(주)

(4) 제형 : 미색의 불투명한 크림타입

(5) 전성분 : 별첨 2 참조

2) 시험물질의 용법·용량

(1) 시험담당자가 시험부위인 피시험자의 등부위를 70% 에탄올로 닦아내고 건조시켰다.

(2) 시험물질 20 ㎕를 직경 8 ㎜의 Finn Chamber에 적하하고 시험부위에 부착하여 고정하였다.

(3) 첩포는 24시간 경과 후 제거하였다.

표 3. 피시험자 기본정보

등록 피시험자	33명
최종 완료 피시험자	33명
성별	여성
평균연령	45.61세
표준편차	6.76

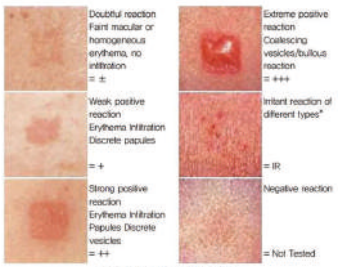
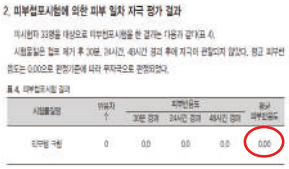
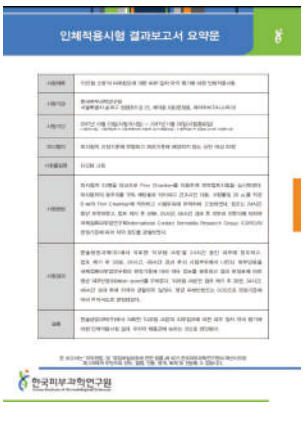


그림 1. 국제접촉피부염연구회의 판정기준.

2. 피부첩포시험에 의한 피부 일차 자극 평가 결과





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한국한의학연구원 KOREA INSTITUTE OF ORIENTAL MEDICINE

지모(知母, *Anemarrhena asphodeloides*) 소재를 활용한 피부건강 개선 소재 개발

인체 피부 주름개선 임상 시험 진행

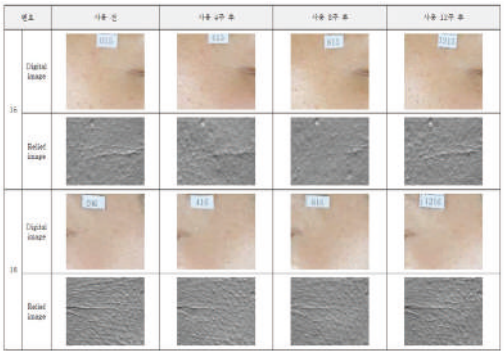
2. 시험 제품

2-1. 제품명: TAIII-0.05
(1) 시험군: Timosaponin AIII 0.05% 함유 크림(Lot No. TAIII-0.05(20180)
(2) 대조군: Timosaponin AIII 미함유 크림
2-2. 제품의 성상: 크림
2-3. 제품의 보관: 실온 보관
2-4. 제품의 유효성분: Timosaponin AIII 0.05%
2-5. 제품의 사용방법
12주 동안 1일 2회(아침, 저녁) 세안 후 스킨, 로션 다음단계에서 시험제품과 대조제품을 이중맹검 상태로 지급하고, 블록무작위배정(block randomization)에 따라 안면 좌, 우측 정해진 부위에 사용하도록 하였다.

3. 시험 방법

시험제품 관리자는 시험제품을 피험자가 내용물의 차이를 인식할 수 없도록 동일한 제형, 동일한 용기에 제공받은 후 독립적으로 시험제품 관리실에서 시험코드 라벨 작업을 수행하였으며, 시험자는 블라인드 상태로 시험제품 관리자로부터 시험제품을 제공받아 피험자에게 지급하여 이중맹검으로 수행되었다.
또한, 블록 무작위 배정(Block Randomization) 방법을 이용하였으며, DDPP, DPDP, DPPD, PPDD, PDPD, PDDP인 블록 무작위 배정표를 생성하여 피험자에게 제공, 선택하도록 하여 시험제품 D 또는 P를 12주간 사용하도록 하였다.
모든 피험자는 방문 시마다 시험부위를 세척한 다음에 항온항습실(22±2℃, 50±5%)에 입실하였으며 30분 동안 안정을 취한 후 시험에 참여하였다.
평가는 제품 사용 전과 사용 후 각 시점(4주, 8주 및 12주)에서 육안평가, 피부주름 파라미터 측정, 피험자에 의한 설문평가 및 시험자의 관찰과 문진을 통해 피부 이상반응을 평가하였다.

평가지표	- 피부주름의 육안평가 - 레플리카를 이용한 주름 파리미터 평가 - 사진 촬영 (안면 피부 촬영장치) - 설문평가 - 피부 이상 평가



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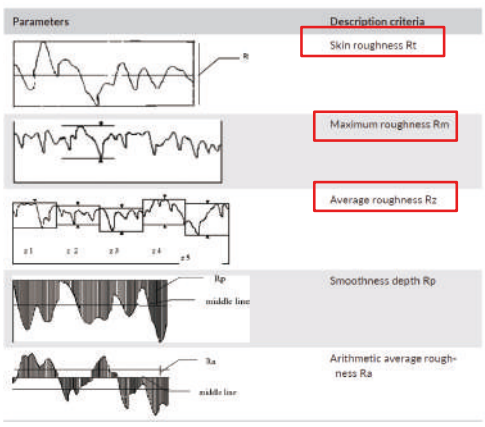
RESULTS

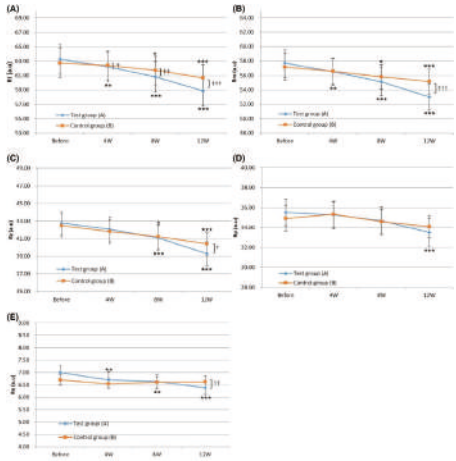
한국한의학연구원 KOREA INSTITUTE OF ORIENTAL MEDICINE

지모(知母, *Anemarrhena asphodeloides*) 소재를 활용한 피부건강 개선 소재 개발

인체 피부 주름개선 임상 시험

- 피부주름 개선효과 평가 결과 육안평가 및 3종의 주름 파라메타 (skin roughness, Maximum roughness, Average roughness)에서 유의한 개선 효능을 확인하였고, 모든 피험자에게서 피부 이상반응은 나타나지 않음





RESULTS

한국한의학연구원 KOREA INSTITUTE OF ORIENTAL MEDICINE

지모(知母, *Anemarrhena asphodeloides*) 소재를 활용한 피부건강 개선 소재 개발

식약처 기능성 자료 ; 식약처 제출을 위한 티모사포닌 A-III 리포좀 함유 크림(티모템 크림) 제형 별첨 서류

<Timosaponin A-III 리포좀 함유 크림 시험일지>

<Timosaponin A-III 리포좀 함유 크림 성적서>

<Timosaponin A-III 리포좀 함유 크림 기준 및 시험법 확립>

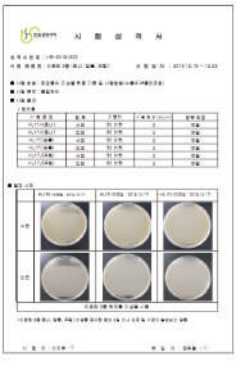
RESULTS

한국한의학연구원 KOREA INSTITUTE OF ORIENTAL MEDICINE

지모(知母, *Anemarrhena asphodeloides*) 소재를 활용한 피부건강 개선 소재 개발

완제품 출시 및 사업화 ; 제품명-셀린저 아르헨 3종 세트

<아르헨 3종 세트 완제품>



<아르헨 3종 세트 미생물 시험성적서>

<아르헨 3종 세트 방부력 시험성적서>

Discovery of New Cosmetic Ingredients Using Herbal Medicine

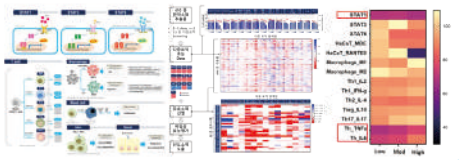
- Taesoo KIM I KIOM

SUMMARY

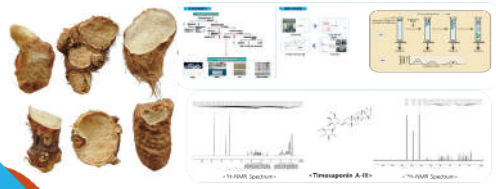
한국한의학연구원
KOREA INSTITUTE OF ORIENTAL MEDICINE

지모(知母, *Anemarrhena asphodeloides*) 소재를 활용한 피부건강 개선 소재 개발

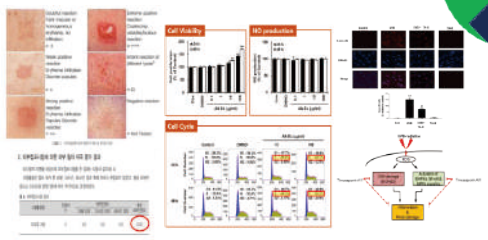
면역 조절 다중표적 스크리닝



표준화 및 대량 생산 공정 확립



안전성 확립 및 MoA 규명



인체 적용 시험 및 상용화

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한중 심포지엄 : KIOM-CACMS 국제공동연구 기획

[한의약융합연구부]

Discovery of New Cosmetic Ingredients Using Herbal Medicine
利用韩药材料发现化妆品新材料的研究

2024.10.30
한국한의학연구원

CONTENTS

한국한의학연구원
KOREA INSTITUTE OF ORIENTAL MEDICINE

Discovery of New Cosmetic Ingredients Using Herbal Medicine

- Taesoo KIM I KIOM

INTRODUCTION

한국한의학연구원 KOREA INSTITUTE OF ORIENTAL MEDICINE

基于天然材料的化妆品

基于天然材料的化妆品定义

» **천연화장품(Natural Cosmetics)**에 대한 정의와 기준은 국가마다 다르나 통상적으로는 식물, 동물, 미생물, 광물 등 **천연자원에서 얻어지는 소재** 자체로부터 얻거나, 물리· 화학·생물학적 공정에 따라 **가공한 천연유래 화장품**을 의미

» 천연화장품에 대한 중요성은 세계 공통으로 커지고 있으나, 이에 대한 규정 및 인증 취득 절차는 국가별·지역별로 상이

- 국가별로 '**오가닉**', '**유기농**', '**천연'화장품**' 등에 대한 개별적 규정 및 범위를 정하여 엄격한 요건 요구
- 천연화장품 인증 및 레이블 취득에 대한 요구가 강화되는 추세에 맞춰, 국가별 맞춤형 인증취득 필수

[천연화장품의 소재 워드클라우드]

天然化妆品产业及材料开发趋势

» **화학물질에 대한 우려**로 **유기농** 및 **천연유래** 화장품에 대한 관심이 고조되고, **동물권리의 보호, 친환경** 등의 사회적 이슈까지 더해져 인체와 사회, 환경에 모두 안전한 천연화장품의 산업 전망 이슈 증가

» 화장품 성분 이외에도 제조공정, 유통과정 등에서 **동물 임상실험 금지**, **탄소배출량 감소**, **생분해성 원료개발**(미세플라스틱 사용금지)의 확대 등 기업윤리와 환경적 책임을 요구하는 친환경 경영요구가 확대되며, 이를 소비성향에 반영하려는 움직임이 활발함.

[국가별 천연화장품 인증마크]

INTRODUCTION

한국한의학연구원 KOREA INSTITUTE OF ORIENTAL MEDICINE

基于韩药材料的化妆品 > 韩方化妆品

韩方化妆品的定义

» **「대한약전」, 「대약약전외한약(생약)규격집」 및 「기존 한약서에 대한 잠정 규정」**에 따른 기존 한약서에 수재된 생약 또는 한약재를 일정 기준 이상 제조 시 사용한 화장품

» 식품의약품안전청에서는 "한방화장품은 동의보감을 포함한 11대 한의학서적(본초강목, 향약집성방, 방약합편, 제중신표, 사상의학, 수세보원, 경약전서, 의약입문, 광제비급, 약성가)에 언급한 한약재를 활유한 화장품

韩国韩方化妆品的开发动向

» **(1997) 설화수** : (주)태평양과 경희대 한의대가 공동연구개발, 여성의 음기를 보해주는 자음단 처방의 한방원리에 따라 개발

» **(2000) 한방미인** : (주)코리아나화장품와 경희대 한의대가 공동개발, 사상의학에 근거하여 개발

» **(2001) 산심** : (주)한국화장품과 경희대 동서의학대학원이 공동개발, 산삼조직 배양 추출물을 함유한 화장품 개발

» **(2003) 수려한** : (주)LG 생활건강과 **한국한의학연구원** 공동개발, 경옥고와 비연목란단을 주성분으로 한방화장품 개발

INTRODUCTION

한국한의학연구원 KOREA INSTITUTE OF ORIENTAL MEDICINE

基于天然材料的化妆品全球市场动向

天然化妆品产业及市场持续增长的趋势

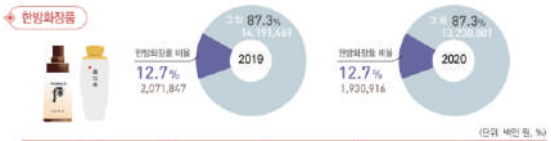
» 세계 천연화장품의 시장규모는 2022년 435억 달러에서 향후 5년간(2023-2028년) **6.15%의 CAGR(연평균성장률)**로 성장하여 610억 달러에 달할 것으로 예측 (Global Natural Cosmetics Market Outlook 2028, `23.05)

» 글로벌 천연화장품 시장은 2023년 486억 달러 수준에서 향후 10년간(2023-2033년) **CAGR 5.1%로 성장**하여 2033년에는 796억 달러까지 확대될 것으로 전망 (FMI(Future Market Insights))

韩国韩方化妆品生产占有率从2016年的7.1%增加至2020年的12.7%，增加了5.6%P

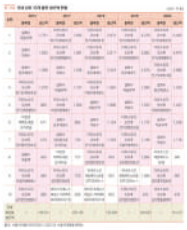
» 2020년 국내 화장품 생산 **상위 10개 품목 중 9개**가 한방 화장품이 차지

» 한방 화장품 생산 점유율은 2016년 7.1%, 2017년 6.7%, 2018년 10.2%, 2019년 12.7%, 2020년 12.7%로 매년 증가 추세



(단위: 백만 원, %)

구분	2019	2020
전체 화장품 생산액	16,263,316	15,161,717
한방화장품 생산액(상위10위)	2,071,847 (12.7)	1,930,916 (12.7)



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한국한의학연구원 KOREA INSTITUTE OF ORIENTAL MEDICINE

基于天然材料的化妆品全球专利动向

全球天然化妆品领域的专利申请持续增加

» 지난 반세기 동안(1974~2022) 화장품 관련 글로벌 특허출원은 연평균증가율(CAGR) 8% 성장하고 있으며, **천연화장품의 경우 11%**에 달해 일반화장품에 비해 더 높은 증가 추세

» **중국**은 천연화장품에 있어서 2012년 이후 최고점을 보인 **2018년까지** 연평균증가율 **43%**의 가파른 증가세를 보이다가 **최근 10년간은 17%의 높은 증가세**를 나타냄 (전세계 천연화장품 특허의 51%에 해당(46,569건)

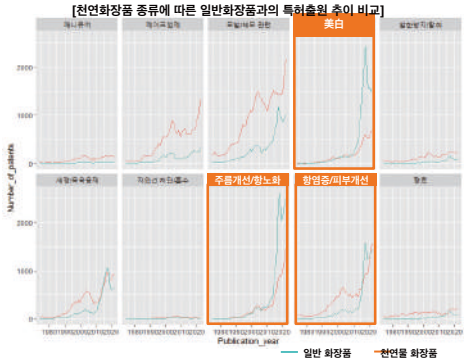
» 특허출원 점유율에 있어서 **중국, 일본**에 이어 미국을 제치고 **한국**이 16%의 점유율로 3위에 자리함으로써 자연친화적 기술의 천연화장품 분야는 **아시아 3국이 84%로 압도적 우위**로 나타남

以植物衍生材料为中心，美白功能领域最多，最近皱纹改善/老化领域剧增，抗炎症/皮肤改善领域有所增加

» 천연화장품의 종류에 따른 특허출원 추이를 일반화장품 종류와 비교해 본 결과 **미백, 주름개선/항노화, 항염증/피부개선** 분야에서 일반화장품에 비해 천연화장품의 비중이 확연히 높은 것으로 나타남

» 천연화장품의 원천소재 부분에 있어서 **식물유래 화장품이 대부분**을 차지하고 타 유래 분야(미생물, 동물 등)는 미미한 실정

[천연화장품 종류에 따른 일반화장품과의 특허출원 추이 비교]



Discovery of New Cosmetic Ingredients Using Herbal Medicine

- Taesoo KIM I KIOM

INTRODUCTION

한국한의학연구원 KOREA INSTITUTE OF ORIENTAL MEDICINE

基于天然材料的化妆品功能性研究动向

随着生命工程技术的发展，以机制为中心的功能性材料开发研究增加

» **생명공학기술**의 발달로 **피부세포의 분화** 및 **노화현상의 규명**, 세포배양, 면역학 및 분자생물학적 기반기술 등 피부과학 분야 연구가 급진전하면서 미백과 보습, 자외선 차단과 흡수, 유해산소 제거 등 항산화작용, 콜라겐 합성, 주름방지 등 항노화작용, 항염증작용을 포함한 피부장벽 개선 등 피부(모발 포함)에 다양한 효능·효과를 제공하는 **기능성화장품 소재 개발이 꾸준하게 증가**

» 특히 최근에는 과학기술의 진보에 따른 **다양한 메커니즘의 규명**으로 **선택적으로 작용하는 효능·효과를 지닌 소재 발굴**의 움직임이 활발함

[Anti-wrinkle Mechanism and Some Representative Active Materials]

Mechanism	Examples	Remark
Control of differentiation of epidermal cell	Retinoids, α-Hydroxy acids, Mevalonolacton, Niacinamide	Stimulating skin turnover
Control of ECM components	Silicic acid, N-Methyl-L-serine Isoflavonoids Dehydroepiendrosteron	Inhibition of collagen metabolism (MMP-1 inhibition)
	Paoniflorin, Prangenidin-77	Collagen synthesis
	Retinoic-d-δ-tocopherol, 3-methylcyclopentadecanone	Hyaluronic acid synthesis
Scavenging of ROS	Benzastatins, Inoscavin, Melanocins, Coenzyme Q10, Astaxanthin	Inhibition of lipid peroxidation
Anti-inflammation	Glycyrrizic acid derivatives	
UV protection DNA Repair	Creatin, Photolyase (Photosome) Candlebush ext	Protection of gene
Other	Acetyl hexapeptide	Reduction of muscular motion

기능성화장품 연구개발 동향 (2010, KIC News, Volume 13)

[Healthy Skin and Skin Aging]

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한국한의학연구원 KOREA INSTITUTE OF ORIENTAL MEDICINE

基于天然材料的化妆品功能性研究动向

来自皮肤基础研究的材料开发

» 화장품 소재 개발에 있어서 이미 활발하게 연구가 진행되고 있는 **genomics 등 다양한 ~Omics 기술을 활용한 제품, 타겟 유전자를 제어하는 기술을 활용이 활발히 진행 중**

» **피부의 노화 기전을 규명**하여 노화를 늦추는 것에서 더 나아가 보호, 치유 등 피부를 건강하게 유지하기 위한 기전을 찾는 다양한 **기초연구**가 진행 중

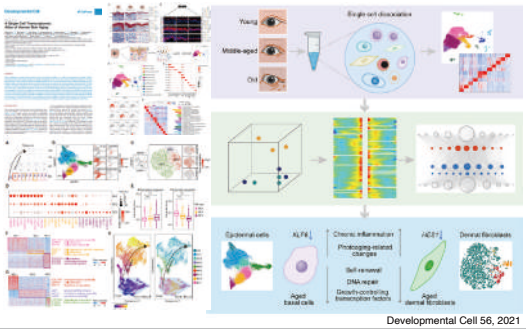
» 건강한 피부에 대한 연구뿐만 아니라 질환 등 문제를 안고 있는 피부에 대한 연구, 내부적 요인 뿐만 아니라 외부적 피부기전의 과학적 근거를 찾기 위한 연구가 활발히 진행되고 있으며 과학적인 분자 수준의 기전 연구를 바탕으로 한 근거 중심의 효능 연구 및 소재개발의 체인이 형성

通过单细胞转录组分析，分析人体皮肤衰老细胞

- **Single-cell transcriptional** landscapes of human skin aging
- Dysregulation of cell-type-specific transcriptional networks during skin aging
- Cell-type-specific downregulation of **HES1** or **KLF6** accelerates senescence
- **Quercetin** promotes the rejuvenation of aged dermal fibroblasts

✓ Chronic inflammation
✓ Photoaging-related changes

✓ Self-renewal
✓ DNA repair
✓ Growth-controlling transcription factors

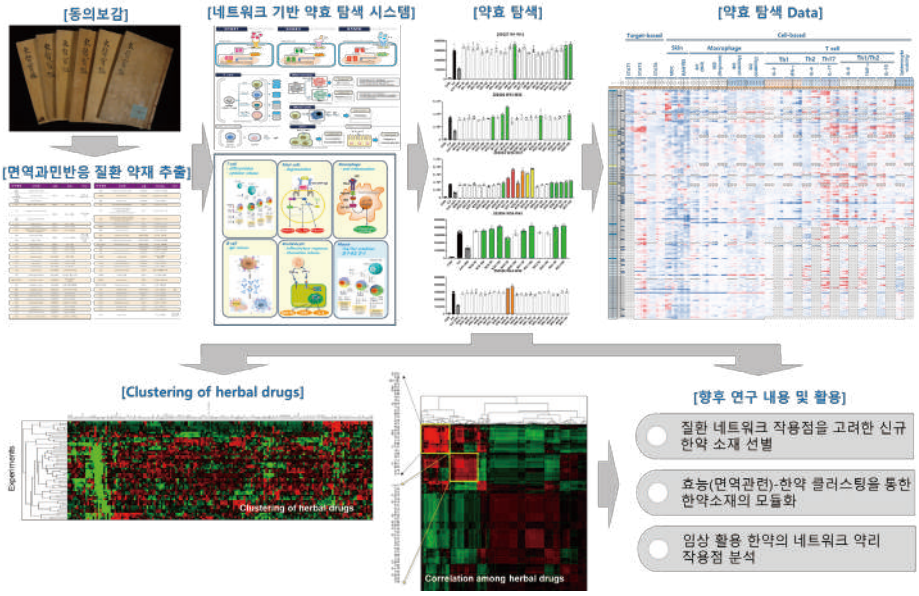


Developmental Cell 56, 2021

RESULTS

한국한의학연구원 KOREA INSTITUTE OF ORIENTAL MEDICINE

疾病网络控制多靶点药理作用点与药效研究

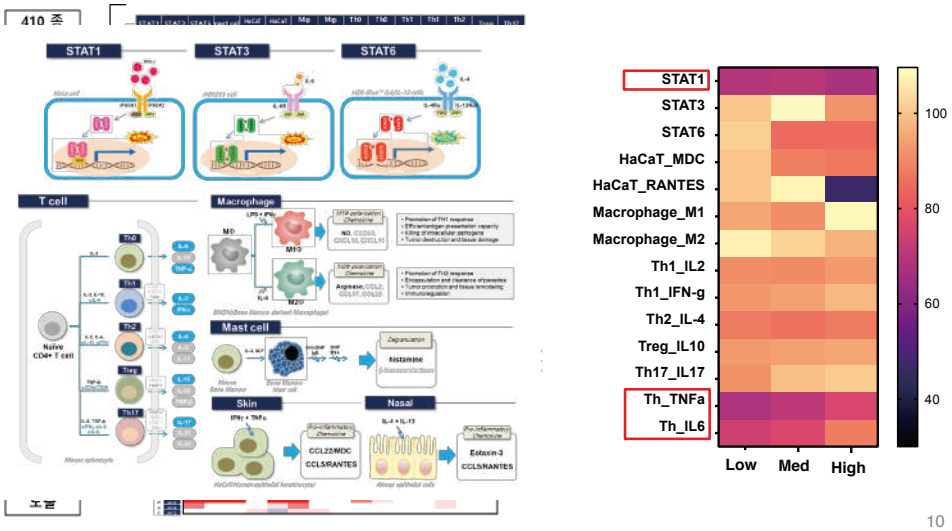


RESULTS

한국한의학연구원 KOREA INSTITUTE OF ORIENTAL MEDICINE

免疫网络控制多靶点药理作用点及功效

知母的免疫调节功效 : 抑制STAT1 & inflammatory cytokine(TNFa, IL-6)



RESULTS

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使用知母（Anemarrhena asphodeloides）材料开发改善皮肤健康材料

知母的特征及起源

과 : 백합과 Liliaceae

학명 : Anemarrhena asphodeloides

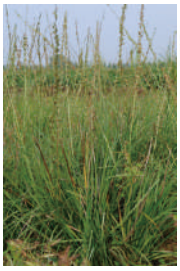
분포 : 한국, 중국(간쑤, 구이저우, 네이멍구, 랴오닝, 산둥 등), 타이완, 몽골

약용부위 : 뿌리줄기

공정서 : 대한민국약전외한약(생약)규격집(KHP)

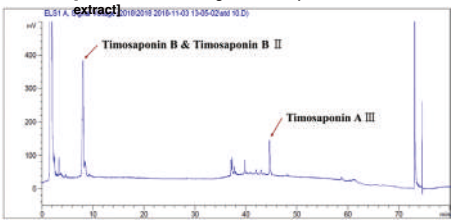
향기 / 맛 : 특유한 냄새가 있고, 약간 달고 뒷맛이 씀

전통적 사용 : 갈증, 두통, 천식, 토혈(코피)/방광 · 간 · 신의 습열을 제거/허리와 다리가 붓고 아픈 증상



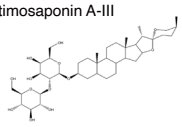
知母的构成成分

[HPLC-ELSD chromatogram of *A. asphodeloides* extract]

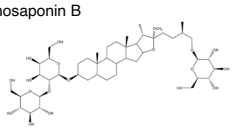


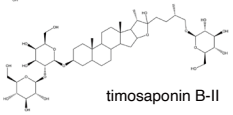
Biomedicine & Pharmacotherapy 133 (2021)

timosaponin A-III



timosaponin B





timosaponin B-II

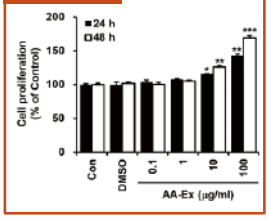
RESULTS

한국한의학연구원 KOREA INSTITUTE OF ORIENTAL MEDICINE

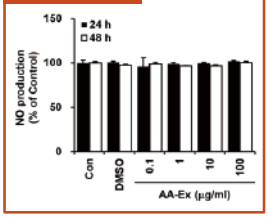
使用知母（Anemarrhena asphodeloides）材料开发改善皮肤健康材料

知母的免疫强化功效：促进免疫细胞（macrophage）增殖

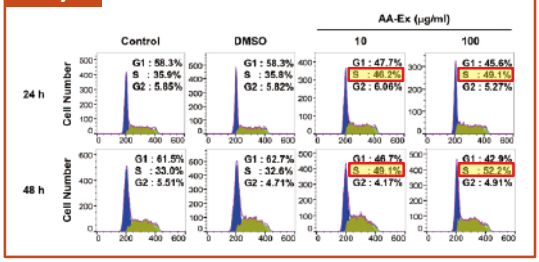
Cell Viability



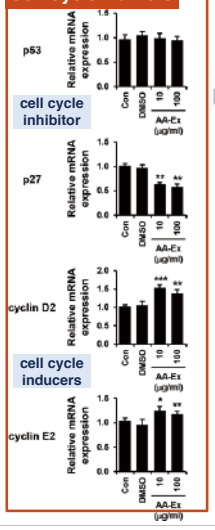
NO production

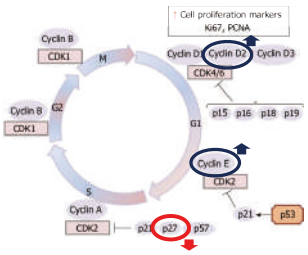


Cell Cycle



Cell Cycle markers





Phytomedicine 59 (2019)

The enhancing immune response and anti-inflammatory effects of *Anemarrhena asphodeloides* extract in RAW 264.7 cells

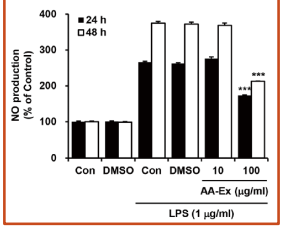
RESULTS

한국한의학연구원 KOREA INSTITUTE OF ORIENTAL MEDICINE

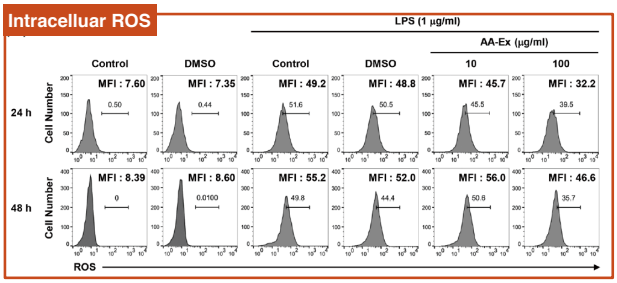
使用知母（Anemarrhena asphodeloides）材料开发改善皮肤健康材料

知母的抗炎功效：抑制NO、iROS和inflammatory cytokine生成

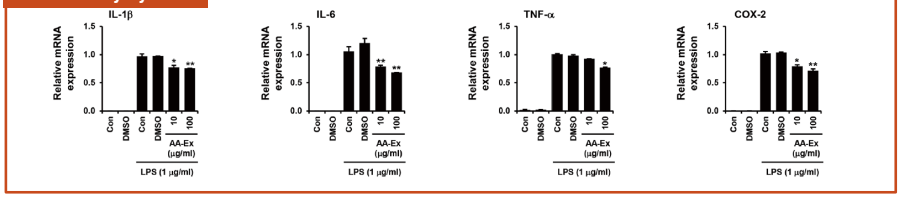
NO inhibition



Intracelluar ROS



Inflammatory cytokine



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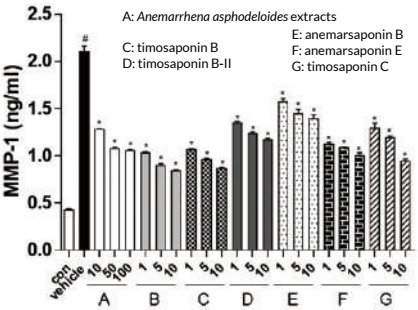
한국한의학연구원 KOREA INSTITUTE OF ORIENTAL MEDICINE

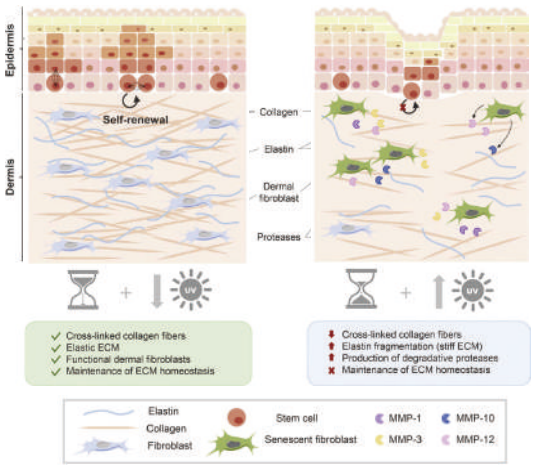
使用知母（Anemarrhena asphodeloides）材料开发改善皮肤健康材料

知母成分，timosaponin A-III的抑制皱纹功效：抑制MMP-1生成

MMP-1(collaganase-1)

- Control of physiological collagen turnover
- Initiation of **collagen fragmentation** in human aged skin
- **Increased expression** upon transiently **UV** irradiation and TNF-α induction
- Up-regulated expression in human cornea upon UVB irradiation





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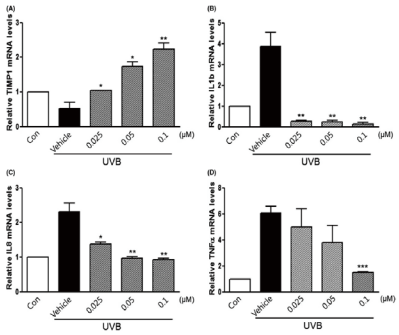
한국한의학연구원 KOREA INSTITUTE OF ORIENTAL MEDICINE

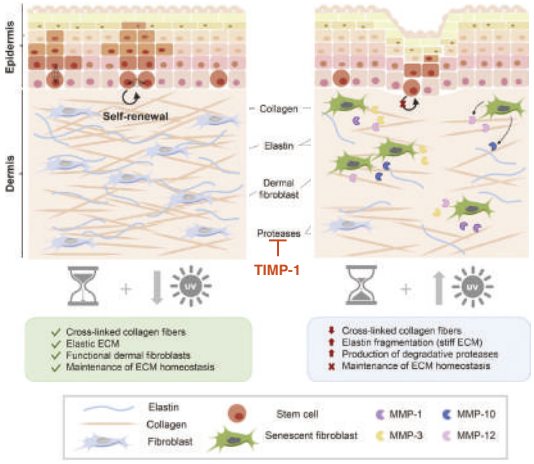
使用知母（Anemarrhena asphodeloides）材料开发改善皮肤健康材料

知母成分，timosaponin A-III的抑制皱纹功效：抑制TIMP1及inflammatory cytokine生成

≫ TIMP-1(Tissue Inhibitor Of Metalloproteinase 1)

- Natural inhibitor of the matrix metalloproteinases (MMPs)
- Regulates cell differentiation, migration and cell death and activates cellular signaling cascades
- Down-regulation of TIMP-1 in aged human skin and transiently UV irradiation





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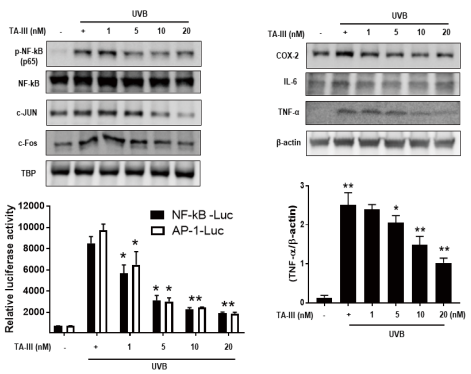
한국한의학연구원 KOREA INSTITUTE OF ORIENTAL MEDICINE

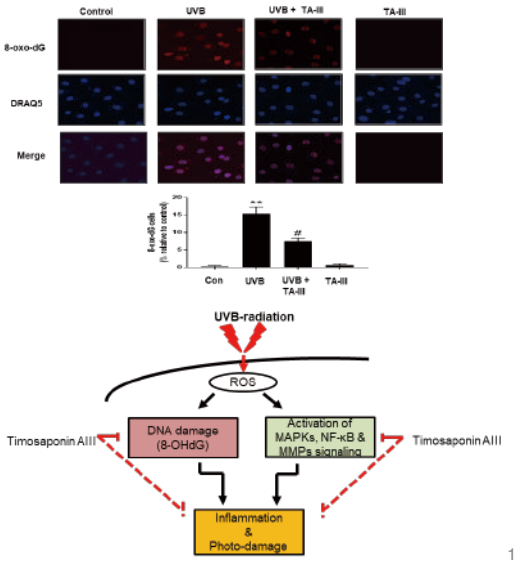
使用知母（Anemarrhena asphodeloides）材料开发改善皮肤健康材料

知母成分，timosaponin A-III的药理机制

≫ TA-III의 전사인자 및 염증인자 억제효능

- Inhibition of UVB induced transcription factors (pNF-kB, c-Jun, c-Fos)
- Inhibition of UVB induced COX-2, IL-6 and TNF-a)
- Inhibition of UVB induced DNA damage





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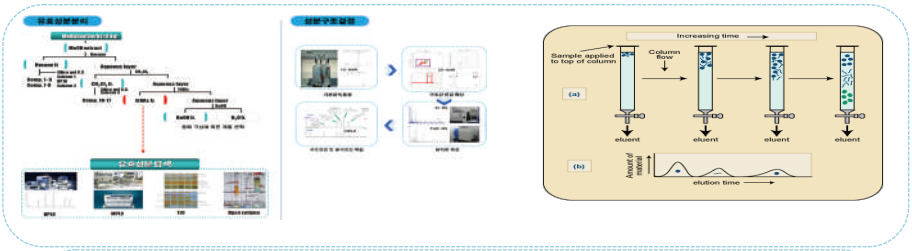
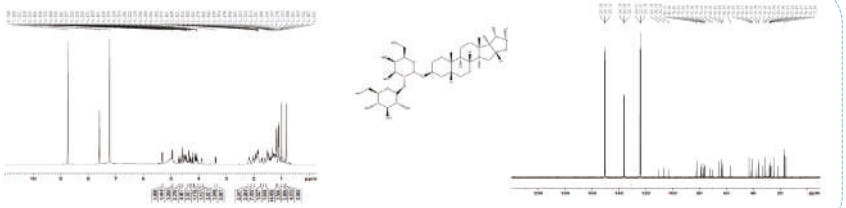
한국한의학연구원 KOREA INSTITUTE OF ORIENTAL MEDICINE

使用知母（Anemarrhena asphodeloides）材料开发改善皮肤健康材料

大量确保知母提取物由来功效成分以及决定结构

» 효능성분 분리를 위한 공정도





<¹H-NMR Spectrum> <Timosaponin A-III> <¹³H-NMR Spectrum>

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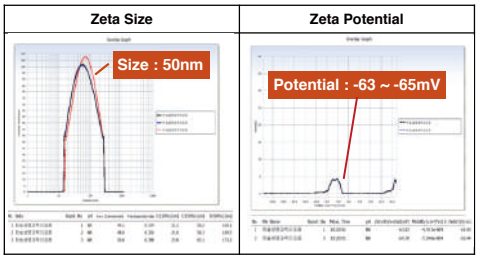
使用知母（Anemarrhena asphodeloides）材料开发改善皮肤健康材料

Timosaponin A-III（TA-III）脂质体剂型开发

[TA-III(0.5% 함유) 리포좀 제조 및 구성 원료]

상	원료명	함량
A	DI-Water	To 100
	Glycerin	2.5
	Butyrospermum parkii(Shea) Butter	2.5
	Squalane	0.5
	Caprylic/Capric Triglyceride	7.5
	Hydrogenated Phosphatidylcholine	7.5
	Ceramide NP	0.1
	Pentylene Glycol	2.5
	Timosaponin A3	0.5

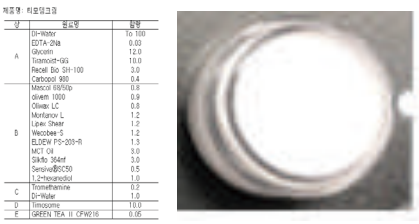
[TA-III(0.5% 함유) 리포좀 Size/Potential 측정]



※ Timosaponin A-III 리포좀은 피부 층 침투가 용이 할 것으로 판단되며 사이즈가 균일하며, Potential 결과도 안정한 값을 보임.

确认含有TA-III脂质体的面霜剂型稳定性

[TA-III(0.5% 함유) 리포좀 함유 크림]



[TA-III(0.5% 함유) 리포좀 함유 크림 안정성 시험]

※ Timosaponin A-III 리포좀 10% 함유 크림은 실온, 일광, 4도, 48도에서 장기간 안정함

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한국한의학연구원
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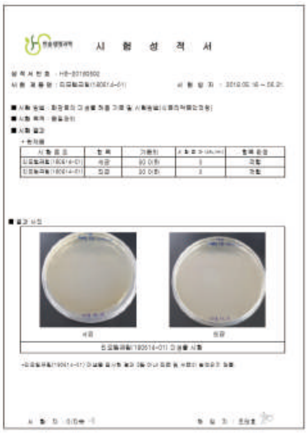
使用知母（Anemarrhena asphodeloides）材料开发改善皮肤健康材料

面霜剂型稳定性评价

- Timosaponin A-III 리포좀 함유 크림 제형은 **균주 측정** 결과 안전함
- Timosaponin A-III 리포좀 함유 크림 제형은 **방부력 시험** 결과 안전함



<Timosaponin A-III 리포좀 함유 크림 제형 미생물 시험 성적서>

방 부 력 시 험 성 적 서

결재	작성	검토	승인
	18.06.14		18.06.14

시험의뢰 업체	한솔생명과학	시험의뢰 부서	연구소
의뢰자	정재욱	의뢰일	2018.05.14
검체명	티모템크림	검체량	80g
시험자	이지숙	시험기간	2018.05.17. ~ 2018.06.14
시험목적	시간에 따른 항균력 확인	시험방법	자사 미생물 시험방법 표준서 HBQM-511에 따른다
특이사항	*티모템크림 (180514-01)		

시 험 결 과

■ 시험 균주

Staphylococcus aureus(KCTC 2513)
Escherichia Coli(KCTC 2571)
Pseudomonas aeruginosa (KCTC 2513)
Aspergillus brasiliensis (KCTC 6317)
Candida albicans (KCTC 7965)

■ 시험 결과

실험군 \ 생균수		Aerobic plate count (CFU/ml) after						종합판정
		초기균	0day	7day	14day	21day	28day	
티모템크림	Bac.	5.1×10^6	4.2×10^6	0	0	0	0	적 합
	Y/M	5.4×10^6	4.2×10^6	0	0	0	0	

■ 시험 소견

균수 측정 결과 7일 이내 99.9% 사멸도를 확인하였으므로 본 제품의 항균력을 증명함

<Timosaponin A-III 리포좀 함유 크림 제형 방부력 시험 성적서>

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한국한의학연구원
KOREA INSTITUTE OF ORIENTAL MEDICINE

使用知母（Anemarrhena asphodeloides）材料开发改善皮肤健康材料

临床用试制品面霜剂型开发

- Timosaponin A-III 리포좀 함유 크림 제형은 내부 품평(20대~50대)과 객관적인 피부진단기 측정을 통해 티모사포닌 A-III의 효능을 극대화 하며 사용감 좋은 제형으로 개발 하였음.

Timosaponin A-III 리포좀 함유 크림 실험군 대조군 품평테스트

제품명: 대조군

상	원료명	함량
A	DI-Water	To 100
	EDTA-2Na	0.03
	Glycerin	12.0
	Tiramoist-GG	10.0
	Recell Bio SH-100	3.0
	Carbopol 980	0.4
B	Mascol 68/50p	0.8
	olivem 1000	0.9
	Oliwax LC	0.8
	Montanov L	1.2
	Lipex Shear	1.2
	Wecobee-S	1.2
	ELDEW PS-203-R	1.3
	MCT Oil	3.0
	Silkflo 364nf	3.0
	Sensiva®SC50	0.5
	1,2-hexanediol	1.0
C	Tromethamine	0.2
	Di-Water	3.0
D	GREEN TEA II CFW216	0.05

제품명:실험군

상	원료명	함량
A	DI-Water	To 100
	EDTA-2Na	0.03
	Glycerin	12.0
	Tiramoist-GG	10.0
	Recell Bio SH-100	3.0
	Carbopol 980	0.4
B	Mascol 68/50p	0.8
	olivem 1000	0.9
	Oliwax LC	0.8
	Montanov L	1.2
	Lipex Shear	1.2
	Wecobee-S	1.2
	ELDEW PS-203-R	1.3
	MCT Oil	3.0
	Silkflo 364nf	3.0
	Sensiva®SC50	0.5
	1,2-hexanediol	1.0
C	Tromethamine	0.2
	Di-Water	1.0
D	Timosome	10.0
E	GREEN TEA II CFW216	0.05

티모템크림 품평 결과서

분류	척도 (1 나쁨 – 보통 – 10 좋음)	의견
사용감 평균 7.4점	1 2 3 4 5 6 7 8 9 10 / 나쁨 보통 좋음	자극 및 끈적임 無. 유분감 多
발림성 평균 7.6점	1 2 3 4 5 6 7 8 9 10 / 나쁨 보통 좋음	잘 발리고 흡수 빠름. 유분감 多. 번거로움
끈적임 평균 7.8점	1 2 3 4 5 6 7 8 9 10 / 나쁨 보통 좋음	끈적임 無. 건성피부에 적합
향 평균 4.9점	1 2 3 4 5 6 7 8 9 10 / 나쁨 보통 좋음	향에 대한 거부감 베이스취가 남. 산뜻한 취 원함.
기타 의견	전체적으로 만족하지만 향취가 강하고 미끈거림. 향이 유아용 같음(성인 취향의 향 원함) 약간의 백탁 현상이 남성에게는 적당하지 않은 것 같음.	

성별	남	여	연령대	20대	30대	40대	50대
	4	8		2	7	2	1

총 12명에게 설문한 결과임.
2018.10.08. 허경민 연구원

<Timosaponin A-III 리포좀 함유 크림 제형 품평 결과서>

<Timosaponin A-III 리포좀 함유 크림 제형 피부진단기 측정>

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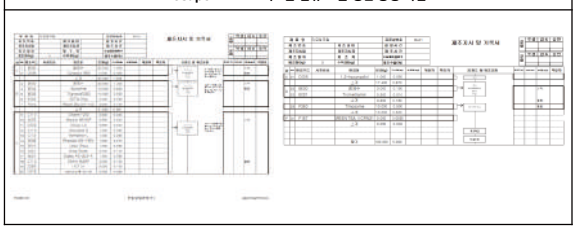
한국한의학연구원 KOREA INSTITUTE OF ORIENTAL MEDICINE

使用知母（Anemarrhena asphodeloides）材料开发改善皮肤健康材料

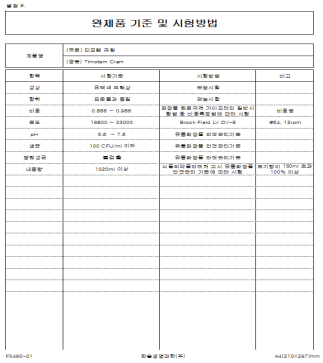
临床试制品制造及成品开发

- Timosaponin A-III 리포좀 함유 크림 제형의 대량생산 공정 확립 및 시제품 개발 완료함

Timosaponin A-III 리포좀 함유 크림 생산 공정 확립



<Timosaponin A-III 리포좀 함유 크림 시제품>



완제품 기준 및 시험방법

〈Timosaponin A-III 리포좀 함유 크림 시제품 성적서〉

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使用知母（Anemarrhena asphodeloides）材料开发改善皮肤健康材料

因皮肤斑贴引起的皮肤原发性刺激人体应用试验

- 피시험자 33명을 대상으로 피부첩포시험 결과 30분, 24시간, 48시간 경과후 자극이 관찰되지 않음
- 평균 피부반응도는 0.00으로 판정기준에 따라 **무자극으로 판정**

1) 시험물질 정보

(1) 시험물질명 : 티모탱 크림

(2) 시험물질 관리번호 : M-KOS-AQJP0Y-HSS

(3) 의뢰기관 : 한솔생명과학(주)

(4) 제형 : 미색의 불투명한 크림타입

(5) 전성분 : 별첨 2 참조

2) 시험물질의 용법 · 용량

(1) 시험담당자가 시험부위인 피시험자의 등부위를 70% 에탄올로 닦아내고 건조시켰다.

(2) 시험물질 20 ㎕를 직경 8 ㎜의 Finn Chamber에 적하하고 시험부위에 부착하여 고정하였다.

(3) 첩포는 24시간 경과 후 제거하였다.

표 3. 피시험자 기본정보

등록 피시험자	33명
최종 완료 피시험자	33명
성별	여성
평균연령	45.61세
표준편차	6.76

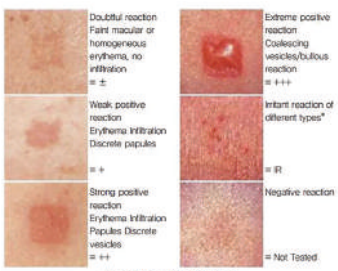
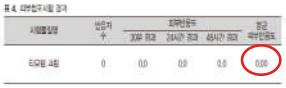
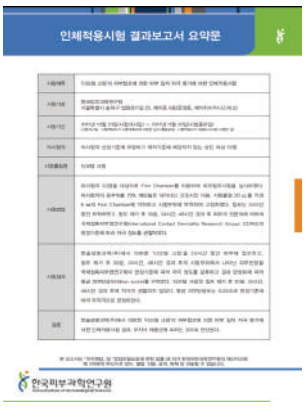


그림 1. 국제접촉피부염연구회의 판정기준.

2. 피부첩포시험에 의한 피부 일차 자극 평가 결과





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使用知母（Anemarrhena asphodeloides）材料开发改善皮肤健康材料

进行人体皮肤皱纹改善临床试验

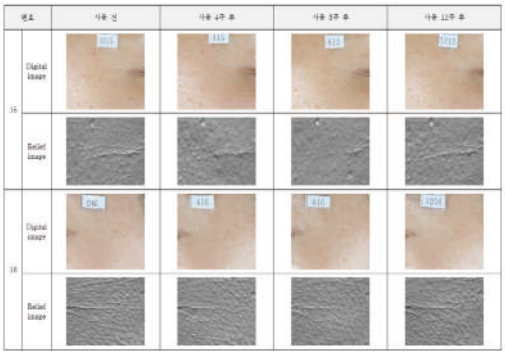
2. 시험 제품

2-1. 제품명: TAIII-0.05
(1) 시험군: Timosaponin AIII 0.05% 함유 크림(Lot No. TAIII-0.05(2018))
(2) 대조군: Timosaponin AIII 미함유 크림
2-2. 제품의 성상: 크림
2-3. 제품의 보관: 실온 보관
2-4. 제품의 유효성분: Timosaponin AIII 0.05%
2-5. 제품의 사용방법
12주 동안 1일 2회(아침, 저녁) 세안 후 스킨, 로션 다음단계에서 시험제품과 대조제품을 이중맹검 상태로 지급하고, 블록무작위배정(block randomization)에 따라 안면 과, 우측 경해진 부위에 사용하도록 하였다.

3. 시험 방법

시험제품 관리자는 시험제품을 피험자가 내용물의 차이를 인식할 수 없도록 동일한 제형, 동일한 용기에 제공받은 후 무림적으로 시험제품 관리실에서 시험코드 라벨 작업을 수행하였으며, 시험자는 블라인드 상태로 시험제품 관리자로부터 시험제품을 제공받아 피험자에게 지급하여 이중맹검으로 수행되었다.
또한, 블록 무작위 배정(Block Randomization) 방법을 이용하였으며, DDFP, DFDP, DFPD, FFDD, FDPD, FDDP인 블록 무작위 배정표를 생성하여 피험자에게 제공, 선택하도록 하여 시험제품 D 또는 F를 12주간 사용하도록 하였다.
모든 피험자는 방문 시마다 시험부위를 세척한 다음에 항온항습실(22±2℃, 50±5%)에 입실하였으며 30분 동안 안정을 취한 후 시험에 참여하였다.
평가는 제품 사용 전과 사용 후 각 시점(4주, 8주 및 12주)에서 육안평가, 피부주름 파라미터 측정, 피험자에 의한 설문평가 및 시험자의 관찰과 문진을 통해 피부 이상반응을 평가하였다.

평가지표	- 피부주름의 육안평가 - 레플리카를 이용한 주름 파리미터 평가 - 사진 촬영 (안면 피부 촬영장치) - 설문평가 - 피부 이상 평가



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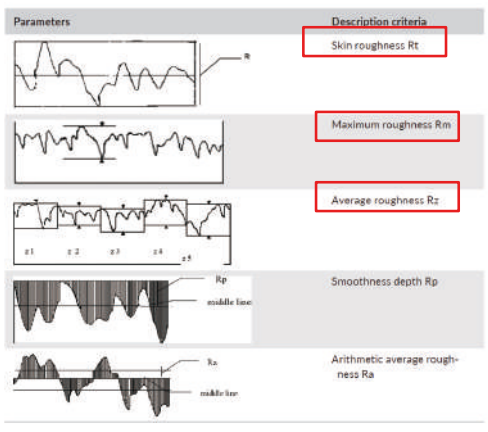
RESULTS

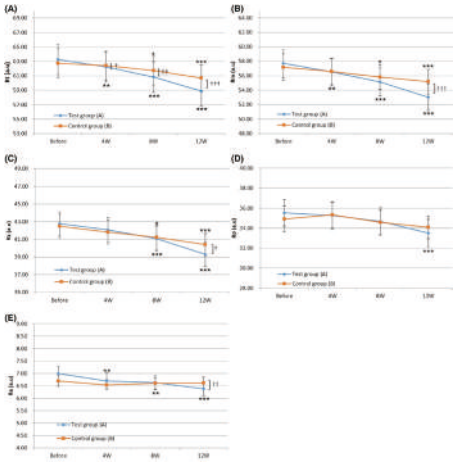
한국한의학연구원 KOREA INSTITUTE OF ORIENTAL MEDICINE

使用知母（Anemarrhena asphodeloides）材料开发改善皮肤健康材料

人体皮肤皱纹改善临床试验

- 피부주름 개선효과 평가 결과 육안평가 및 3종의 주름 파라메타 (skin roughness, Maximum roughness, Average roughness) 에서 유의한 개선 효능을 확인하였고, 모든 피험자에게서 피부 이상반응은 나타나지 않음



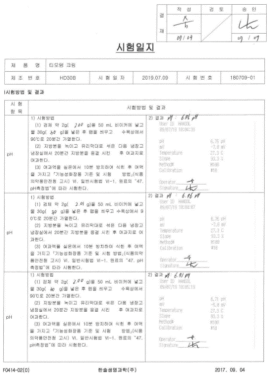


RESULTS

한국한의학연구원 KOREA INSTITUTE OF ORIENTAL MEDICINE

使用知母（Anemarrhena asphodeloides）材料开发改善皮肤健康材料

食药处功能性资料：含胸腺皂苷A-III脂质体面霜（TIMOTEM霜）制剂提交食品药品安全处的附件文件


시험일지


HANSOLBIO CO., LTD.

Certificate of Analysis


시 험 성 적 서

<Timosaponin A-III 리포좀 함유 크림 시험일지>

<Timosaponin A-III 리포좀 함유 크림 성적서>

<Timosaponin A-III 리포좀 함유 크림 기준 및 시험법 확립>

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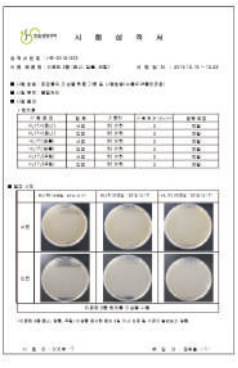
RESULTS

한국한의학연구원 KOREA INSTITUTE OF ORIENTAL MEDICINE

使用知母（Anemarrhena asphodeloides）材料开发改善皮肤健康材料

成品上市与商业化：产品名-CELLEANSER ARHEN 3件套

<아르헨 3종 세트 완제품>



<아르헨 3종 세트 미생물 시험성적서>

<아르헨 3종 세트 방부력 시험성적서>

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Discovery of New Cosmetic Ingredients Using Herbal Medicine

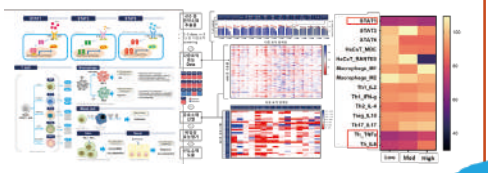
- Taesoo KIM I KIOM

SUMMARY

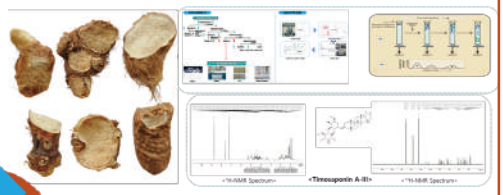
한국한의학연구원
KOREA INSTITUTE OF ORIENTAL MEDICINE

使用知母（Anemarrhena asphodeloides）材料开发改善皮肤健康材料

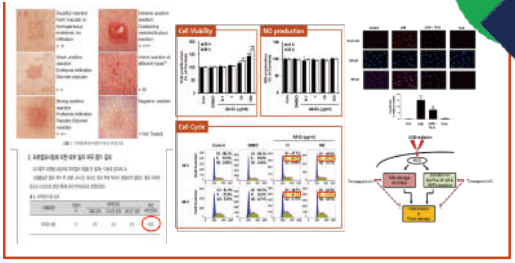
免疫调节多靶点筛选



确立标准化和批量生产工艺



确立安全性及查明MoA



人体应用试验及商用化

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PRESENTATION

Yu ZHOU
CACMS

STUDY ON THE APPLICATION OF ACUPUNCTURE AND MOXIBUSTION IN SLEEP HEALTH MANAGEMENT AND INTERNATIONAL DISSEMINATION

针灸在睡眠健康管理中的应用与国际推广研究

Study on the Application of Acupuncture and Moxibustion in Sleep Health Management and International Dissemination

讲 者：周宇
Speaker: Yu Zhou

中国中医科学院针灸研究所
Institute of Acupuncture & Moxibustion, China Academy of Chinese Medical Sciences

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系统检索
Systematic retrieval

以“针灸疗法”和“睡眠障碍”为检索词，在Pubmed检索到相关研究474篇，在CNKI检索到相关研究1669篇。

With *acupuncture therapy* and *sleep disorder* as the search terms, 474 related studies were retrieved in Pubmed and 1669 related studies were retrieved in CNKI.

1. 针灸治疗睡眠障碍的临床研究

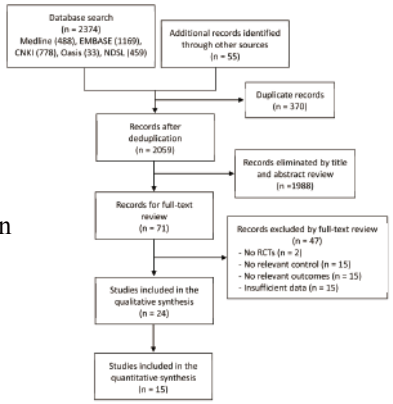
15项随机对照试验的荟萃分析显示，与药物治疗相比，至少3周的针刺治疗在改善睡眠质量和失眠严重程度方面效果更为显著。然而，治疗失眠的有效穴位和针灸类型有待进一步研究。

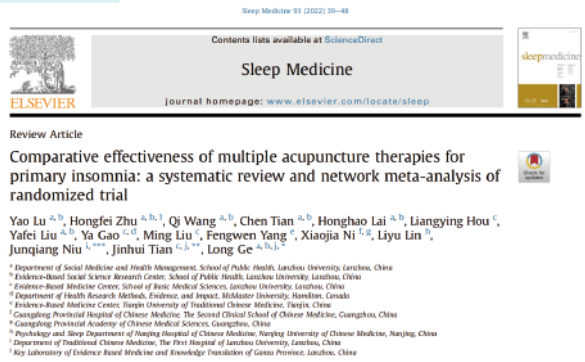
The meta analysis of 15 randomized controlled trials showed that acupuncture treatment for at least 3 weeks was more effective than medication in improving sleep quality and insomnia severity. However, the effective acupuncture points and types of acupuncture for insomnia need to be further studied.

The American Journal of Chinese Medicine, Vol. 49, No. 5, 1–16

Institute for Advanced Research in Asian Science and Medicine
DOI: 10.1142/S0192415X21500543

Efficacy of Acupuncture for Insomnia: A Systematic Review and Meta-Analysis




Sleep Medicine 93 (2022) 39–48
Contents lists available at ScienceDirect
Sleep Medicine
journal homepage: www.elsevier.com/locate/sleep
ELSEVIER
Review Article

Comparative effectiveness of multiple acupuncture therapies for primary insomnia: a systematic review and network meta-analysis of randomized trial

Yao Lu [a, b], Hongfei Zhu [a, b, 1], Qi Wang [a, b], Chen Tian [a, b], Honghao Lai [a, b], Liangying Hou [c], Yafei Liu [a, b], Ya Gao [c, d], Ming Liu [c], Fengwen Yang [e], Xiaojia Ni [f, g], Liyu Lin [h], Junqiang Niu [i, ***], Jinhui Tian [c, j, **], Long Ge [a, b, j, *]

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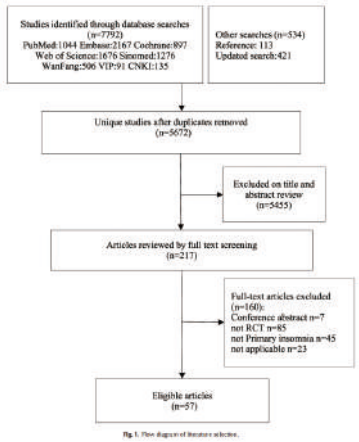
[h] Psychology and Sleep Department of Nanjing Hospital of Chinese Medicine, Nanjing University of Chinese Medicine, Nanjing, China
[i] Department of Traditional Chinese Medicine, The First Hospital of Lanzhou University, Lanzhou, China
[j] Key Laboratory of Evidence Based Medicine and Knowledge Translation of Gansu Province, Lanzhou, China



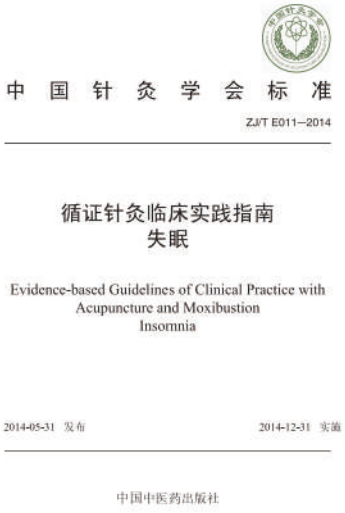
针灸疗法治疗原发性失眠的系统评价提示：

多种针灸疗法能够有效改善睡眠质量，特别是毫针刺法联合耳穴压丸、穴位埋线、电针联合穴位贴敷。

目前证据主要为中低质量，且研究间的异质性较大。

Systematic review of acupuncture therapy for primary insomnia:
A variety of acupuncture therapy can effectively improve the quality of sleep, especially the acupuncture combined with auricular point pressure pill, acupoint burying thread, electroacupuncture combined with acupoint application. At present, the evidence is mainly of low to medium quality, and the heterogeneity between studies is large.

2.针灸治疗失眠的临床实践指南研制



中 国 针 灸 学 会 标 准

ZJ/T E011—2014

循证针灸临床实践指南
失眠

Evidence-based Guidelines of Clinical Practice with Acupuncture and Moxibustion Insomnia

2014-05-31 发布　　2014-12-31 实施

中国中医药出版社

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针灸治疗失眠应在脏腑辨证的基础上，按患者主诉症状进行针对性治疗。以整体睡眠质量、睡眠时间、日间觉醒状态为主要障碍的失眠，针灸治疗以头部局部取穴为主，配合远端取穴；以入睡、觉醒、深睡眠质量为主要障碍的失眠，针灸治疗以远端及背部取穴为主。针对特殊类型的失眠，可在上述治疗的基础上配合特殊疗法进行治疗。

Acupuncture treatment of insomnia should be based on the differentiation of zang-fu organs and targeted treatment according to the patient's complaint symptoms. For insomnia with overall sleep quality, sleep time and daytime wakefulness as the main obstacles, acupuncture treatment is mainly based on local head point selection, combined with remote point selection; The main obstacle of insomnia is the quality of falling asleep, awakening and deep sleep. Acupuncture treatment is mainly based on remote

推荐意见 Recommendations	推荐级别 Strength
（1）在改善失眠患者整体睡眠质量，尤其是日间觉醒状态方面，应使用结合脏腑辨证的毫针刺法。 In order to improve the overall sleep quality of insomnia patients, especially the daytime awakening state, the acupuncture method combined with zang fu syndrome differentiation should be used.	强推荐 Strong recommendation
（2）在改善失眠患者睡眠时间和睡眠质量方面，可使用耳穴压丸疗法。其中，慢性失眠可将其作为毫针刺法的补充疗法，急性或亚急性失眠建议单独使用。 In improving the sleep time and sleep quality of insomnia patients, auricular point pressure pill therapy can be used. Among them, chronic insomnia can be used as a supplementary therapy of the acupuncture method. It is recommended to use alone in acute or subacute insomnia patients.	弱推荐 Weak recommendation

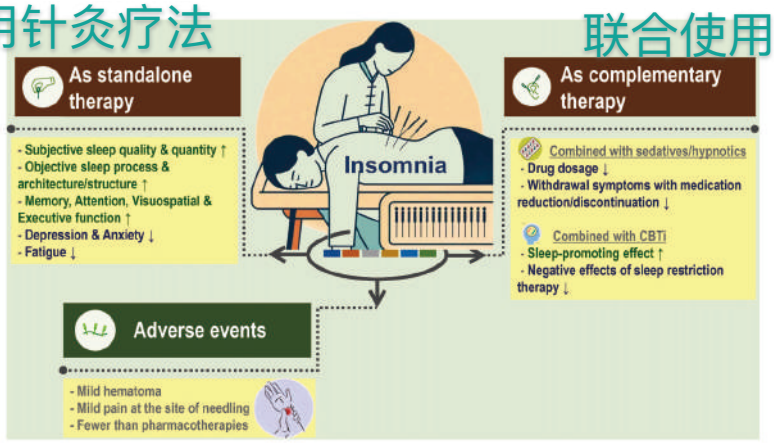
推荐意见 Recommendations	推荐级别 Strength
（3）伴有日间功能障碍的失眠患者，可使用以头部安神腧穴透刺法为主，兼顾脏腑辨证的毫针刺法。 Patients with insomnia accompanied by daytime dysfunction can use the penetrating acupuncture method on the head acupoints with the effect of mental relaxation, together with the filiform needling based on zang-fu syndrome differentiation.	弱推荐 Weak recommendation
（4）在改善入睡困难、觉醒问题及深睡眠缺少方面，可使用跷脉补泻法，身体虚弱及惧怕针刺的失眠患者建议使用本法。 In order to improve the difficulty of falling asleep, awakening problems and lack of deep sleep, Qiao meridian supplementing and draining method can be use, and it is recommended for insomnia patients who are weak and afraid of acupuncture.	弱推荐 Weak recommendation

推荐意见 **Recommendations**	推荐级别 **Strength**
（5）在改善失眠患者人睡困难方面，可使用膀胱经及督脉皮肤针疗法，也可作为毫针刺法的配合疗法。 In the improvement of insomnia patients sleep difficulty, the dermal needling on the bladder meridian and governor vessel can be used. It can also be used togethered with filiform needling.	弱推荐 Weak recommendation
（6）顽固性失眠可配合使用维生素B12注射液穴位注射。 For intractable insomnia, acupoint injection of vitamin B12 can be use as a supplementary therapy.	弱推荐 Weak recommendation

睡眠障碍相关临床实践指南推荐针灸疗法

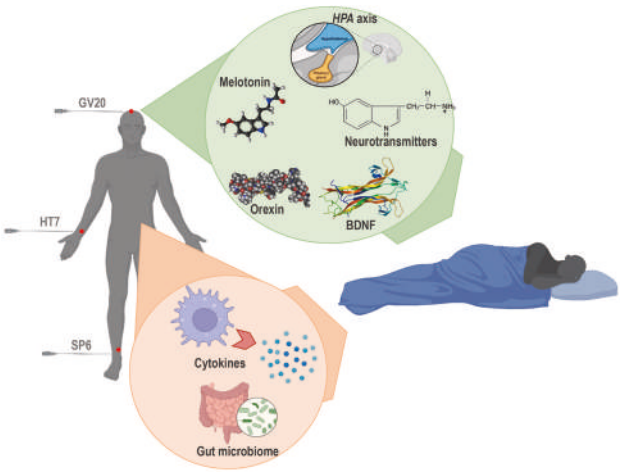
Clinical practice guidelines for sleep disorders recommend acupuncture

单独使用针灸疗法　　联合使用针灸疗法



中华医学会神经病学分会睡眠障碍学组. 中国成人失眠诊断与治疗指南(2023版)[J]. 中华神经科杂志,2024,57(6):560-584.

3. 针灸治疗睡眠障碍的基础研究



针灸缓解失眠的确切机制尚不清楚。

可能抑制过度活跃的HPA轴，调节炎症细胞因子、神经递质、食欲素-A神经元、褪黑素和脑源性神经营养因子(BDNF)及其相关通路，调节时钟基因的表达，或改变肠道微生物群。

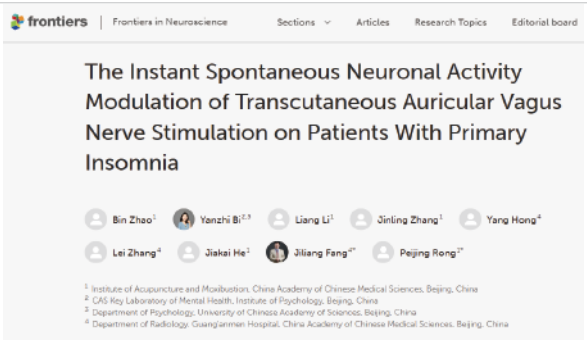
The precise mechanism by which acupuncture relieves insomnia remains unclear.
Acupuncture may inhibit the hyperactive hypothalamic-pituitary-adrenal (HPA) axis, regulate inflammatory cytokines, neurotransmitters, orexin-A neurons, melatonin and its related pathways, and brain-derived neurotrophic factor (BDNF) and its related pathways, modulate the expression of clock genes, or alter gut microbiota.

Zhao, F.-Y., et al. (2024). "Acupuncture for primary insomnia: Effectiveness, safety, mechanisms and recommendations for clinical practice." Sleep Medicine Reviews 74: 101892.


BRAIN STIMULATION

Articles Publish Multimedia About Contact

Transcutaneous auricular vagus nerve stimulation in treating post-stroke insomnia monitored by resting-state fMRI: The first case report


frontiers | Frontiers in Neuroscience

The Instant Spontaneous Neuronal Activity Modulation of Transcutaneous Auricular Vagus Nerve Stimulation on Patients With Primary Insomnia


BRAIN STIMULATION

Articles Publish Multimedia About Contact

Transcutaneous electrical cranial-auricular acupoints stimulation (TECAS) for treatment of the depressive disorder with insomnia as the complaint (DDI): A case series

前期，我们所围绕耳迷走神经电刺激治疗不同患者群体（卒中后患者、抑郁障碍患者等）失眠症状的脑效应机制进行了系列研究。

Previously, our institute conducted a series of studies on the brain effec mechanism of auricular vagus nerve electrical stimulation in treating insomnia symptoms in different patient groups (post-stroke patients, patients with depression disorders, etc.).

目录
Contents

1. 流行病学研究
Epidemiologic study

收集和分析中韩两国睡眠障碍的流行病学数据，比较不同人群的发病率和风险因素。
The epidemiological data of sleep disorders in China and South Korea were collected and analyzed to compare the incidence and risk factors of different populations.

类型（Type）	相关内容（Contents）
研究设计 Study design	横断面研究，通过问卷调查和数据收集来评估当前的睡眠障碍流行情况。 A cross-sectional study using questionnaires and data collection to assess the current prevalence of sleep disorders.
样本选择 Sample	20岁以上的成年人（考虑不同的年龄段进行亚组分析，如青年、中年和老年）。 Adults over the age of 20 (consider different age groups for subgroup analysis, such as young adults, middle age, and older adults)

类型（Type）	相关内容（Contents）
数据收集方法 Data collection	问卷调查（PSQI、ESS）、人口学信息、生活方式、心理健康、既往病史。 Questionnaire (PSQI, ESS), demographic information, lifestyle, mental health, past medical history.
数据来源 Source	已有的公开流行病学数据库（如中国健康与营养调查，CHNS）、KNHANES等。 Existing public epidemiological databases (such as China Health and Nutrition Survey, CHNS), KNHANES, etc
数据分析 Date analysis	发病率计算、风险因素分析（多变量逻辑回归分析）、组间比较；使用卡方检验（Chi-squared test）比较两国不同人群的发病率。通过Cox回归模型估算风险比（Hazard Ratio, HR），评估各因素对睡眠障碍的影响。使用t检验或Mann-Whitney U检验比较两国的平均PSQI得分。 Incidence calculation, risk factor analysis (multivariate logistic regression analysis), comparison between groups; Chi-squared test was used to compare the incidence of different populations in the two countries. Hazard Ratio (HR) was estimated by Cox regression model to assess the influence of each factor on sleep disorders. The average PSQI scores of the two countries were compared using the T-test or the Mann-Whitney U test.

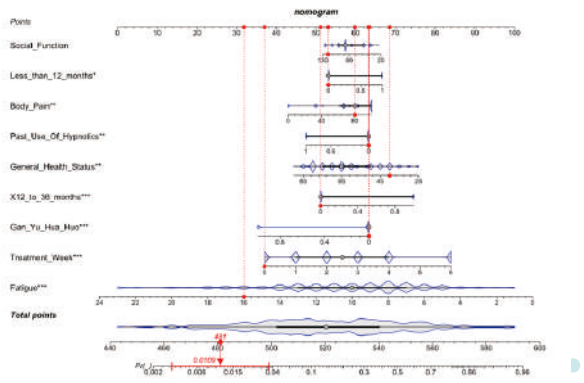
2. 睡眠障碍相关风险模型及针灸疗效预测研究

Risk model related to sleep disorders and prediction of acupuncture efficacy

既往研究
Previous Studies

采用回顾性队列研究方法，收集2019年6月至2020年6月于中国中医科学院针灸医院、丰体时代社区卫生服务站2个中心接受穴位贴敷疗法治疗的64例**ID**患者0周、1周、2周、3周、4周、6周的临床资料（2例剔除，共372例数据）。

A retrospective cohort study was used to collect clinical data of 64 patients with ID who received acupoint application therapy at 2 centers of Acupuncture Hospital of China Academy of Chinese Medical Sciences and Fengtitimes Community Health Service Station from June 2019 to June 2020 for 0, 1, 2, 3, 4 and 6 weeks (2 cases were excluded, a total of 372 cases of data).



类型（Type）	相关内容（Contents）
研究背景与目的	背景：中韩两国由于文化、生活方式、医疗体系等差异，睡眠障碍的风险因素和针灸疗效可能有所不同。因此，有必要构建适合中韩两国不同人群的风险预测模型，并比较其适用性。 目的：设计多个预测模型，针对中韩人群分别进行风险因素分析和针灸疗效预测，通过比较筛选出最优模型。
Research background and purpose	Background: Due to differences in culture, lifestyle and medical system between China and South Korea, the risk factors for sleep disorders and the efficacy of acupuncture and moxibustion may be different. Therefore, it is necessary to construct risk prediction models suitable for different populations in China and South Korea and compare their applicability. Purpose: to design multiple prediction model, in view of China and South Korea people analysis of risk factors and acupuncture curative effect predicted respectively, by comparing the optimum selection model.

类型（Type）	相关内容（Contents）
数据分层与模型设计	中韩分层分析：将中韩人群作为两个独立的数据子集，分别进行模型设计与评估。 独立模型构建：分别为中国人群和韩国人群设计风险预测模型，考察其各自的风险因素和针灸疗效预测能力。 合并模型构建：也可以通过添加国家（中/韩）作为一个协变量，构建一个综合预测模型，探讨国家对睡眠障碍风险及针灸疗效的调节作用。
Data layering and model design	Chinese and Korean stratified analysis: The Chinese and Korean population were taken as two independent data subsets for model design and evaluation. Independent model construction: respectively designed for Chinese people and Korean people risk prediction model, and investigate their respective risk factors and acupuncture curative effect prediction ability. Merger model construction: can also by adding countries (China/South Korea) as a collaborators variable, build a comprehensive prediction model, about the risk of sleep disturbance and the curative effect of acupuncture and moxibustion.

3. 中医针灸及韩医在睡眠障碍诊疗的应用情况调研

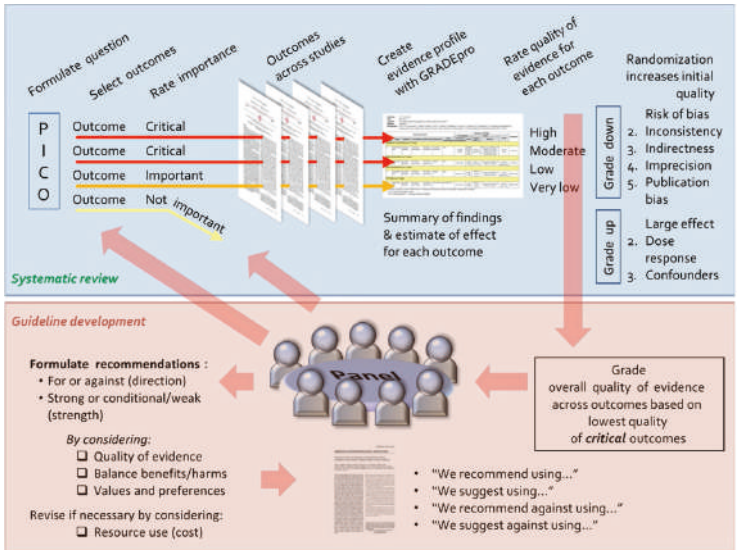
Investigation on the application of TCM acupuncture and Korean medicine in the diagnosis and treatment of sleep disorders

4. 中医针灸治疗睡眠障碍的临床试验

Clinical trial of acupuncture and moxibustion in treatment of sleep disorders

5. 循证针灸临床实践指南的研制

Development of evidence-based acupuncture and moxibustion clinical practice guidelines



采用国际公认的GRADE循证临床实践指南研制方法学，研制一部面向国际目标使用人群的失眠针灸临床实践指南，并在中韩及全球推广。

Using internationally recognized GRADE evidence-based clinical practice guideline development methodology, a clinical practice guideline for insomnia acupuncture and moxibustion for international target users was developed and promoted in China, Korea and the world.

目录

Contents

- 科技论文（**Academic publications**）

  在国际学术期刊上发表高质量的研究论文。

  Publish high quality research papers in international academic journals.

- 临床实践指南（**Clinical practice guidelines**）

  制定或更新中医针灸/韩医治疗睡眠障碍的相关临床实践指南，指导临床诊疗。

  Develop or update the relevant clinical practice guidelines of TCM acupuncture/Korean medicine in the treatment of sleep disorders to guide clinical diagnosis and treatment.

- 公众教育（**Public education**）

  通过科普宣传和教育活动，提高公众对睡眠障碍的认识和预防意识。

  Promote public awareness and prevention of sleep disorders through popular science publicity and education activities.

谢谢！

PRESENTATION

Jieun PARK
KIOM

THE IMPACT OF SLEEP DURATION, SLEEP QUALITY AND SLEEP PATTERN ON COGNITIVE DISORDERS

수면시간, 수면의 질, 수면패턴이 인지기능장애에 미치는 영향

2024.10.30.

한국한의학연구원

박지은

연구배경

- 수면시간과 인지기능의 관계.
  - 적정수면시간보다 짧거나 긴 수면시간은 인지기능 감소와 관련있음.
- Chrotnoytpe(아침형/저녁형)과 인지기능 간의 관계는 서로 상충하는 연구결과.

  - 아침형은 인지기능과 부정적인 관계가 있으나, 학업성취와는 긍정적인 상관관계는 나타냄. (Preckelet al., 2011)

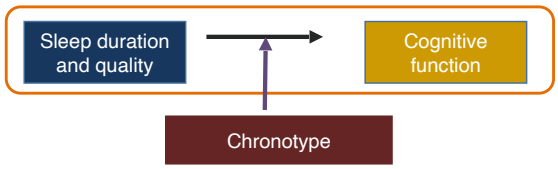
  - Shimura et al.은 저녁형이 수면 방해와 낮 동안의 졸림을 통해 학업 성취에 영향을 미친다고 설명. (Shimuraet al., 2022)

- 수면 시간과 인지 기능 간의 관계를 조사하기 위해서는 Chronotype(아침형/저녁형)을 고려하는 것이 중요.

2

연구목적

- 가설: 수면과 인지기능 간의 관련성은 chronotype (아침형/저녁형)에 따라 달라질 것이다.



한국한의학연구원	Imperial College London
Chronoytype 에 따른 수면시간과 인지기능 변화의 관계	Chronoytype 에 따른 수면시간과 인지기능의 관계

3

한국연구 – 연구목적

- 수면 시간과 인지 기능 변화 간의 관계를 규명하고, chronotype(아침형/저녁형)이 관계에 영향을 미치는지를 살펴보는 것

4

한국연구 – 연구방법

- 2018년 지역사회 건강조사 데이터 이용
  - 만 19세 이상 성인 대상으로, 전국적으로 분포한 254개 보건소에서 수행
  - 인지기능 변화를 평가하기 위해, '최근 1년 동안 점점 더 자주 또는 더 심하게 정신이 혼란스럽거나 기억력이 떨어지는 것을 경험한 적이 있는지' 를 대상자에게 물음

- 수면시간과 수면의 질을 평가하기 위해, 한국어판 Pittsburgh Sleep Quality Index (PSQI-K)를 이용함.

5

한국연구 – 연구방법

- 아침형/저녁형을 구분하기 위해 Wirz-Justice et al.의 선행연구에서 보고된 기준을 이용함.
- Wirz-Justice et al. (2012)은 취침시간 및 기상시간을 기준으로 5개 그룹으로 분류함(완전저녁형, 저녁형, 중간형, 아침형, 완전아침형).

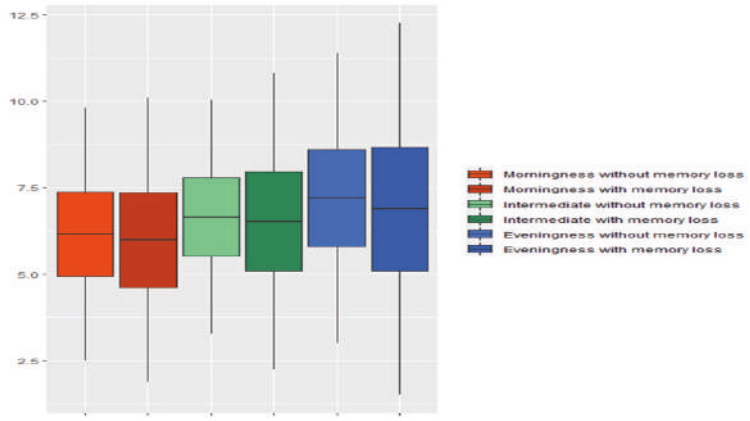
Modified criteria for morningness and eveningness based on Wirz-Justice el al. (Wirz-Justice and Terman, 2012).

Morningness-eveningness score	Morningness-eveningness type	Sleep onset	Wake-up
	None		0–4:00 AM
70–86	Definite morningness	9–9:30 PM	4:00–5:00 AM
59–69	Moderate morningness	9:30–10:45 PM	5:00–6:30 AM
42–58	Intermediate	10:45 PM-12:45 AM	6:30–8:30 AM
31–41	Moderate eveningness	12:45–2:00 AM	8:30–10:00 AM
16–30	Definite eveningness	2:00–3:00 AM	10:00–11:30 AM

6

한국연구 – 연구결과

- 아침형과 중간형, 저녁형 모두에서 기억력저하군의 평균수면시간이 기억력 유지군의 평균수면시간보다 짧았음



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Korean study – Results

- 수면의 질을 보정하지 않은 경우,
  - 아침형에 비해, 중간형과 저녁형에서 인지기능 저하의 위험도가 높음
  - 인지기능저하의 위험도는 7-9시간 수면하는 사람들에서 가장 낮음

- 수면의 질을 보정하는 경우,
  - 인지기능 저하의 위험도가 가장 낮은 수면시간은 아침형과 중간형, 저녁형에서 다르게 나타남.
  - 인지기능 저하 위험도가 가장 낮은 수면시간은 아침형에서 5-6시간으로 가장 짧고, 저녁형에서 7-8시간으로 가장 길었음.

8

Table 3
Association of sleep hours and the change in cognitive function without considering sleep quality as a covariate.

Variables		Total (n = 224,714)		Morningness (n = 124,906)		Intermediate (n = 79,400)		Eveningness (n = 11,297)	
		Estimate	OR (95 % CI)	Estimate	OR (95 % CI)	Estimate	OR (95 % CI)	Estimate	OR (95 % CI)
Intercept		−3.50	0.03 (0.03,0.03)***	−3.40	0.03 (0.03, 0.04)***	−3.69	0.03 (0.02, 0.03)***	−2.79	0.06 (0.04, 0.10)***
Sex (ref: male)		0.33	1.39 (1.35,1.43)***	0.26	1.30 (1.26, 1.35)***	0.46	1.59 (1.51, 1.68)***	0.32	1.38 (1.20, 1.58)***
Age (ref: < 30 years)	30-39	0.53	1.70 (1.57,1.83)***	0.48	1.62 (1.55, 1.94)***	0.54	1.72 (1.55, 1.91)***	0.47	1.61 (1.30, 1.98)***
	40-49	0.90	2.46 (2.26, 2.65)***	0.90	2.46 (2.09, 2.92)***	0.89	2.43 (2.19, 2.69)***	0.81	2.24 (1.79, 2.79)***
	50-59	1.30	3.66 (3.40, 3.92)***	1.27	3.57 (3.03, 4.22)***	1.31	3.69 (3.33, 4.09)***	1.30	3.66 (2.96, 4.53)***
	60-69	1.56	4.76 (4.43, 5.11)***	1.53	4.64 (3.95, 5.49)***	1.55	4.79 (4.21, 5.24)***	1.49	4.43 (3.44, 5.70)***
	70-79	1.90	6.72 (6.25, 7.23)***	1.86	6.46 (5.46, 7.64)***	1.99	7.31 (6.48, 8.25)***	1.81	6.14 (4.43, 8.46)***
	≥ 80	2.23	9.26 (8.57, 10.01)***	2.18	8.83 (7.49, 10.49)***	2.34	10.35 (9.03, 11.87)***	2.46	11.68 (7.05, 17.38)***
Occupation (ref: administrator, desk job)	Sales, service industry	0.06	1.06 (1.03, 1.14)**	0.11	1.12 (1.05, 1.20)**	0.00	1.00 (1.01, 1.13)*	−0.29	0.75 (0.61, 0.92)**
	Agriculture, manual work	0.11	1.11 (1.06, 1.16)***	0.17	1.19 (1.12, 1.27)***	0.04	1.05 (0.97, 1.13)	−0.27	0.76 (0.58, 0.98)*
	Students, housewives	0.15	1.16 (1.11, 1.21)***	0.24	1.27 (1.19, 1.36)***	0.07	1.07 (0.99, 1.14)	−0.19	0.83 (0.67, 1.02)
	No occupation	0.30	1.35 (1.29, 1.42)***	0.37	1.44 (1.34, 1.54)***	0.27	1.31 (1.21, 1.43)***	−0.04	0.97 (0.78, 1.20)
Living area (ref: city)		−0.08	0.92 (0.90, 0.95)***	−0.09	0.92 (0.89, 0.94)***	−0.06	0.94 (0.89, 0.99)**	−0.04	0.96 (0.83, 1.11)
Education (ref: primary)	High school or lower	−0.13	0.88 (0.86, 0.91)***	−0.11	0.89 (0.86, 0.93)***	−0.10	0.91 (0.78, 0.90)***	−0.39	0.68 (0.53, 0.87)**
	College or higher	−0.23	0.79 (0.76, 0.83)***	−0.25	0.78 (0.73, 0.82)***	−0.23	0.79 (0.73, 0.85)***	−0.52	0.59 (0.45, 0.78)***
Marriage status (ref: married)	Divorced/separated/ Widowed/not married	−0.11	0.89 (0.87, 0.92)***	−0.09	0.92 (0.89, 0.95)***	−0.16	0.85 (0.81, 0.90)***	−0.29	0.75 (0.65, 0.87)***
Controlled hypertension		0.20	1.22 (1.18, 1.31)***	0.20	1.22 (1.12, 1.33)***	0.12	1.13 (0.95, 1.34)	0.36	1.43 (0.86, 2.36)
Controlled diabetes		0.33	1.39 (1.29, 1.51)***	0.35	1.42 (1.26, 1.56)***	0.26	1.30 (1.09, 1.54)**	0.59	1.80 (1.16, 2.77)**
Depressive symptoms		1.20	3.32 (3.19, 3.45)***	1.11	3.04 (2.86, 3.20)***	1.31	3.69 (3.43, 3.96)***	1.41	4.09 (3.44, 4.85)***
Sleep hours(ref: 7-8 h)	< 5 h	0.52	1.68 (1.62, 1.75)***	0.46	1.59 (1.52, 1.67)***	0.70	2.02 (1.85, 2.20)***	0.70	2.01 (1.55, 2.60)***
	5-6 h	0.31	1.36 (1.32, 1.41)***	0.25	1.29 (1.23, 1.34)***	0.46	1.59 (1.48, 1.71)***	0.61	1.85 (1.49, 2.29)***
	6-7 h	0.12	1.13 (1.09, 1.16)***	0.09	1.10 (1.06, 1.14)***	0.16	1.17 (1.11, 1.24)***	0.28	1.33 (1.10, 1.60)**
	8-9 h	−0.01	0.98 (0.94, 1.02)	−0.04	0.96 (1.91, 1.01)	0.03	1.03 (0.96, 1.10)	−0.06	0.94 (0.79, 1.13)
	≥ 9 h	0.19	1.21 (1.13, 1.30)***	0.12	1.12 (1.00, 1.26)*	0.24	1.27 (1.14, 1.42)***	0.17	1.19 (0.95, 1.47)
Morningness-eveningness type (ref: morningness)	Intermediate	0.07	1.07 (1.04, 1.10)***	–	–	–	–	–	–
	Eveningness	0.20	1.22 (1.14, 1.31)***	–	–	–	–	–	–
	None	−0.01	0.99 (0.98, 1.04)	–	–	–	–	–	–

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한국연구 – 결론

KIOM

- 인지기능 저하의 위험도를 낮추는 적정수면시간은 아침형과 저녁형에서 다를 수 있음.

- 적정수면시간에 대한 향후 연구들은 수면패턴이나 아침형/저녁형에 대한 고려가 필요함.

10

영국연구 – 연구목적

- 인지기능에 대한 수면시간과 수면의 지리, chronotype의 영향과 관례를 분석하기 위함

11

영국연구 - 연구방법

- 본 연구는 영국 의학 연구 위원회와 Wellcome Trust재단이 설립한 인구 기반의 전향적 연구인 UK Biobank 데이터를 이용함.
- 인지기능은 cohort1에서 4개, cohort2에서 2개 테스트를 통해 평가됨
  - 유연한 지능(Fluid intelligence), 짝 맞추기(Pairs matching), 반응시간(Reaction time), 전향적 기억(Prospective memory).
- 수면과 관련된 세 가지 변수, 즉 수면시간, 수면의 질, chronotype의 영향을 연구함.

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영국연구 - 연구결과

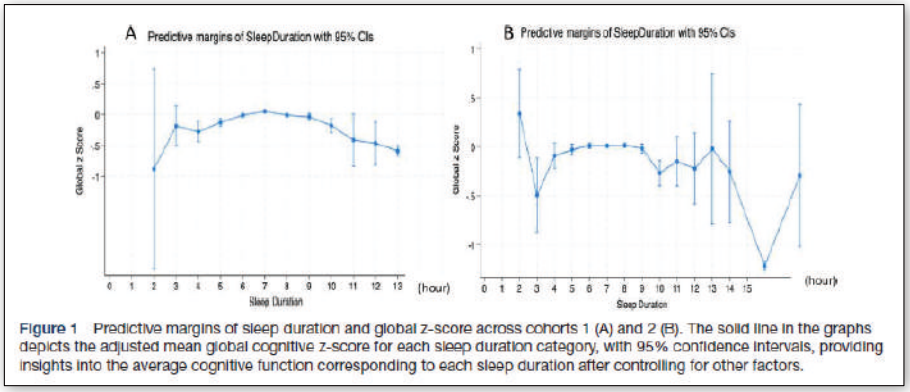

Figure 1 Predictive margins of sleep duration and global z-score across cohorts 1 (A) and 2 (B). The solid line in the graphs depicts the adjusted mean global cognitive z-score for each sleep duration category, with 95% confidence intervals, providing insights into the average cognitive function corresponding to each sleep duration after controlling for other factors.

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영국연구 - 연구결과

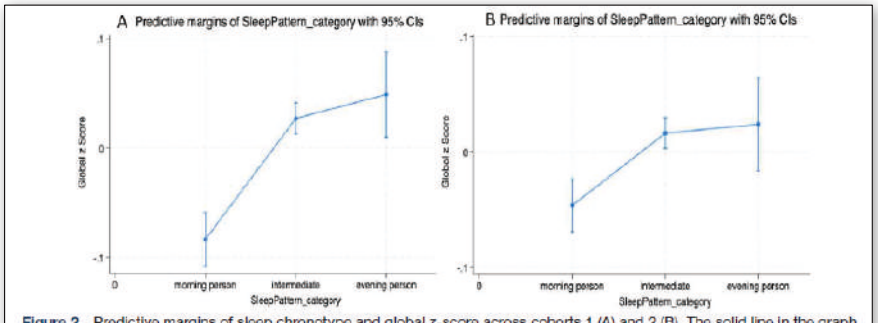

Figure 2 Predictive margins of sleep chronotype and global z-score across cohorts 1 (A) and 2 (B). The solid line in the graph depicts the adjusted mean global cognitive z-score for each sleep chronotype, with 95% confidence intervals, providing insights into the average cognitive function corresponding to each sleep chronotype after controlling for other factors.

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영국연구 - 연구결과

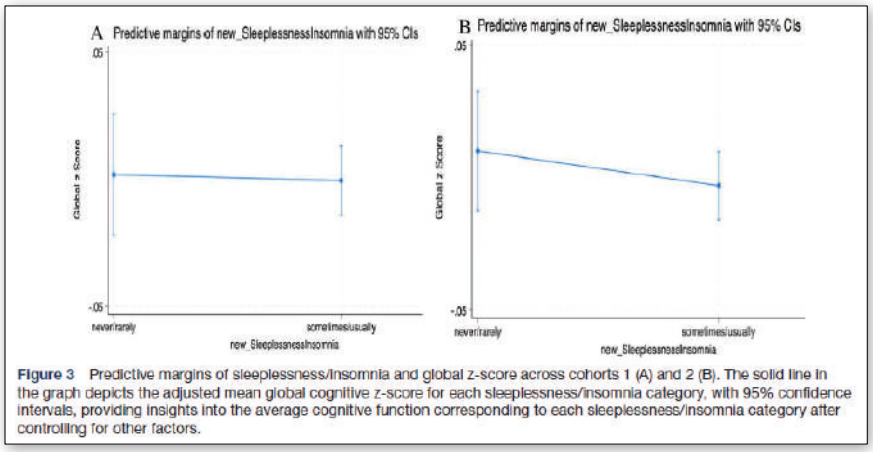

Figure 3 Predictive margins of sleeplessness/insomnia and global z-score across cohorts 1 (A) and 2 (B). The solid line in the graph depicts the adjusted mean global cognitive z-score for each sleeplessness/insomnia category, with 95% confidence intervals, providing insights into the average cognitive function corresponding to each sleeplessness/insomnia category after controlling for other factors.

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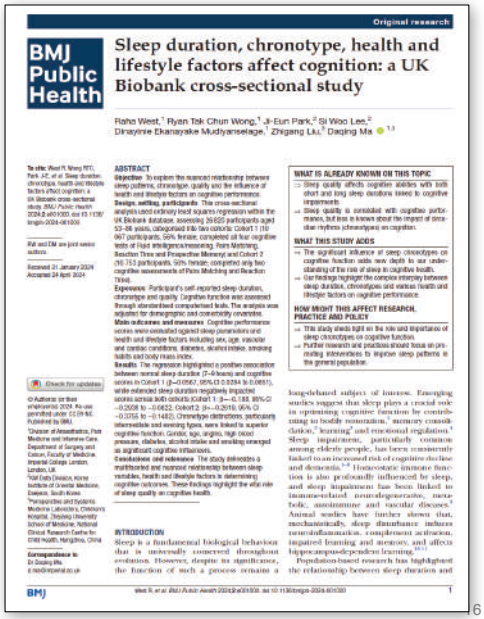
게재논문

Journal of Affective Disorders

Research paper

Association between sleep hours and changes in cognitive function according to the morningness-eveningness type: A population-based study



Original research

BMJ Public Health

Sleep duration, chronotype, health and lifestyle factors affect cognition: a UK Biobank cross-sectional study

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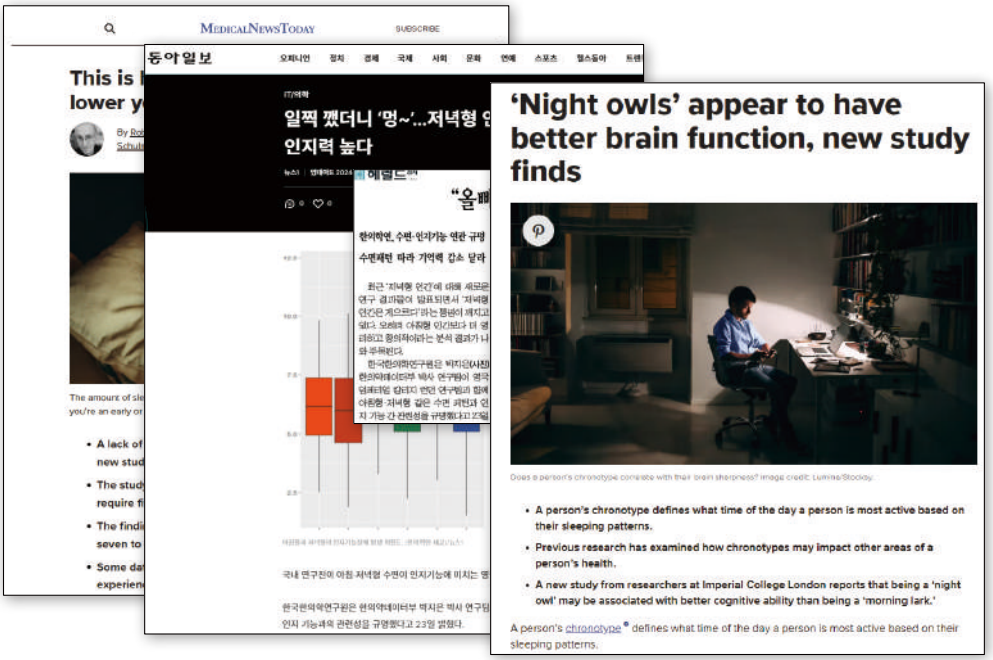
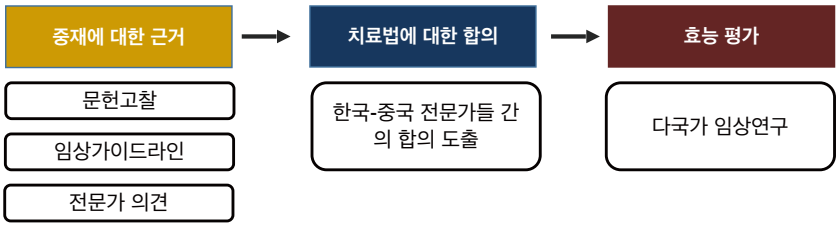
신문기사 및 뉴스레터



한국-중국 공동 수면연구

- 연구목적
  - 수면장애에 대한 한의학/중의학의 치료효과 연구



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KIOM

감사합니다!

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睡眠时间，睡眠质量，睡眠模式

对认知功能障碍的影响

2024.10.30.

韩国韩医学研究院

Park Ji-eun

研究背景

- 睡眠时间与认知功能的关系

  - 睡眠时间比最佳睡眠时间短或长都与认知功能下降有关

- 研究结果显示，Chrotnoytpe（清晨型/夜晚型）与认知功能之间的关系相互矛盾

  - 清晨型与认知功能呈负相关，但与学业成绩呈正相关 (Preckelet al., 2011)

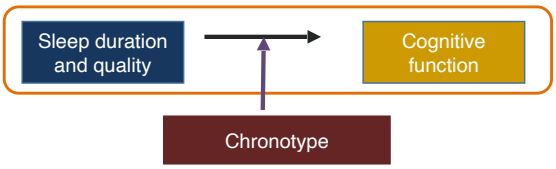
  - Shimura etal.解释说，夜晚型因妨碍睡眠和白天犯困影响学业成就 (Shimuraet al., 2022)

- 为了研究睡眠时间与认知功能之间的关系，考虑Chronotype（清晨型/夜晚型）至关重要

2

研究目的

- 假设：睡眠和认知功能之间的关联性将取决于Chronotype（清晨型/夜晚型）



한국한의학연구원 KOREA INSTITUTE OF ORIENTAL MEDICINE	Imperial College London
根据Chronoytype的睡眠时间与认知功能变化的关系	根据Chronoytype的睡眠时间与认知功能的关系

3

韩国研究 – 研究目的

- 阐明睡眠时间与认知功能之间变化的关系，观察chronotype（清晨型/夜晚型）是否对此关系产生影响

4

韩国研究 – 研究方法

- 使用2018年社区健康调查数据
  - 以19周岁以上的成年人为对象，在全韩国分布的254个保健所执行
  - 为了评估认知功能的变化，询问受试者“在过去的一年里，你是否更频繁或更严重地经历过精神混乱或记忆力下降？”
- 为了评价睡眠时间和睡眠质量，使用韩语版Pittsburgh Sleep Quality Index (PSQI-K)

5

韩国研究 – 研究方法

- 为了区分清晨型/夜晚型的类型，使用了 Wirz-Justice et al.等人之前研究报告中的标准
- Wirz-Justice et al.（2012）根据睡觉时间和起床时间将睡眠类型分为五组（完全夜晚型、夜晚型、中间型、清晨型和完全清晨型）

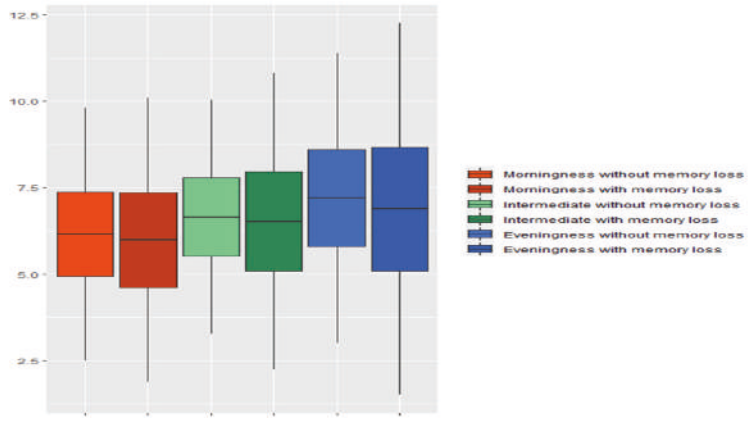
Modified criteria for morningness and eveningness based on Wirz-Justice el al. (Wirz-Justice and Terman, 2012).

Morningness-eveningness score	Morningness-eveningness type	Sleep onset	Wake-up
	None		0–4:00 AM
70–86	Definite morningness	9–9:30 PM	4:00–5:00 AM
59–69	Moderate morningness	9:30–10:45 PM	5:00–6:30 AM
42–58	Intermediate	10:45 PM-12:45 AM	6:30–8:30 AM
31–41	Moderate eveningness	12:45–2:00 AM	8:30–10:00 AM
16–30	Definite eveningness	2:00–3:00 AM	10:00–11:30 AM

6

韩国研究 – 研究结果

- 在清晨型、中间型和夜晚型中，记忆力低下组的平均睡眠时间都比记忆力维持组的平均睡眠时间短



7

Korean study – Results

- 如果睡眠质量不得到纠正，
  - 与清晨型相比，中间型和夜晚型认知功能低下的危险度更高
  - 认知功能低下的危险度在睡眠7-9小时的人群中最低

- 在纠正睡眠质量时，
  - 认知功能低下危险度最低的睡眠时间在清晨型、中间型、夜晚型有所不同
  - 认知功能低下危险度最低的睡眠时间在清晨型为5-6小时，在夜晚型为7-8小时，时间最长

8

Table 3
Association of sleep hours and the change in cognitive function without considering sleep quality as a covariate.

Variables		Total (n = 224,714)		Morningness (n = 124,906)		Intermediate (n = 79,400)		Eveningness (n = 11,297)	
		Estimate	OR (95 % CI)	Estimate	OR (95 % CI)	Estimate	OR (95 % CI)	Estimate	OR (95 % CI)
Intercept		−3.50	0.03 (0.03,0.03)***	−3.40	0.03 (0.03, 0.04)***	−3.69	0.03 (0.02, 0.03)***	−2.79	0.06 (0.04, 0.10)***
Sex (ref: male)		0.33	1.39 (1.35,1.43)***	0.26	1.30 (1.26, 1.35)***	0.46	1.59 (1.51, 1.68)***	0.32	1.38 (1.20, 1.58)***
Age (ref: < 30 years)	30-39	0.53	1.70 (1.57,1.83)***	0.48	1.62 (1.55, 1.94)***	0.54	1.72 (1.55, 1.91)***	0.47	1.61 (1.30, 1.98)***
	40-49	0.90	2.46 (2.26, 2.65)***	0.90	2.46 (2.09, 2.92)***	0.89	2.43 (2.19, 2.69)***	0.81	2.24 (1.79, 2.79)***
	50-59	1.30	3.66 (3.40, 3.92)***	1.27	3.57 (3.03, 4.22)***	1.31	3.69 (3.33, 4.09)***	1.30	3.66 (2.96, 4.53)***
	60-69	1.56	4.76 (4.43, 5.11)***	1.53	4.64 (3.95, 5.49)***	1.55	4.79 (4.21, 5.24)***	1.49	4.43 (3.44, 5.70)***
	70-79	1.90	6.72 (6.25, 7.23)***	1.86	6.46 (5.46, 7.64)***	1.99	7.31 (6.48, 8.25)***	1.81	6.14 (4.43, 8.46)***
	≥ 80	2.23	9.26 (8.57, 10.01)***	2.18	8.83 (7.49, 10.49)***	2.34	10.35 (9.03, 11.87)***	2.46	11.68 (7.05, 17.38)***
Occupation (ref: administrator, desk job)	Sales, service industry	0.06	1.06 (1.03, 1.14)**	0.11	1.12 (1.05, 1.20)**	0.00	1.00 (1.01, 1.13)*	−0.29	0.75 (0.61, 0.92)**
	Agriculture, manual work	0.11	1.11 (1.06, 1.16)***	0.17	1.19 (1.12, 1.27)***	0.04	1.05 (0.97, 1.13)	−0.27	0.76 (0.58, 0.98)*
	Students, housewives	0.15	1.16 (1.11, 1.21)***	0.24	1.27 (1.19, 1.36)***	0.07	1.07 (0.99, 1.14)	−0.19	0.83 (0.67, 1.02)
	No occupation	0.30	1.35 (1.29, 1.42)***	0.37	1.44 (1.34, 1.54)***	0.27	1.31 (1.21, 1.43)***	−0.04	0.97 (0.78, 1.20)
Living area (ref: city)		−0.08	0.92 (0.90, 0.95)***	−0.09	0.92 (0.89, 0.94)***	−0.06	0.94 (0.89, 0.99)**	−0.04	0.96 (0.83, 1.11)
Education (ref: primary)	High school or lower	−0.13	0.88 (0.86, 0.91)***	−0.11	0.89 (0.86, 0.93)***	−0.10	0.91 (0.78, 0.90)***	−0.39	0.68 (0.53, 0.87)**
	College or higher	−0.23	0.79 (0.76, 0.83)***	−0.25	0.78 (0.73, 0.82)***	−0.23	0.79 (0.73, 0.85)***	−0.52	0.59 (0.45, 0.78)***
Marriage status (ref: married)	Divorced/separated/ Widowed/not married	−0.11	0.89 (0.87, 0.92)***	−0.09	0.92 (0.89, 0.95)***	−0.16	0.85 (0.81, 0.90)***	−0.29	0.75 (0.65, 0.87)***
Controlled hypertension		0.20	1.22 (1.18, 1.31)***	0.20	1.22 (1.12, 1.33)***	0.12	1.13 (0.95, 1.34)	0.36	1.43 (0.86, 2.36)
Controlled diabetes		0.33	1.39 (1.29, 1.51)***	0.35	1.42 (1.26, 1.56)***	0.26	1.30 (1.09, 1.54)**	0.59	1.80 (1.16, 2.77)**
Depressive symptoms		1.20	3.32 (3.19, 3.45)***	1.11	3.04 (2.86, 3.20)***	1.31	3.69 (3.43, 3.96)***	1.41	4.09 (3.44, 4.85)***
Sleep hours(ref: 7-8 h)	< 5 h	0.52	1.68 (1.62, 1.75)***	0.46	1.59 (1.52, 1.67)***	0.70	2.02 (1.85, 2.20)***	0.70	2.01 (1.55, 2.60)***
	5-6 h	0.31	1.36 (1.32, 1.41)***	0.25	1.29 (1.23, 1.34)***	0.46	1.59 (1.48, 1.71)***	0.61	1.85 (1.49, 2.29)***
	6-7 h	0.12	1.13 (1.09, 1.16)***	0.09	1.10 (1.06, 1.14)***	0.16	1.17 (1.11, 1.24)***	0.28	1.33 (1.10, 1.60)**
	8-9 h	−0.01	0.98 (0.94, 1.02)	−0.04	0.96 (1.91, 1.01)	0.03	1.03 (0.96, 1.10)	−0.06	0.94 (0.79, 1.13)
	≥ 9 h	0.19	1.21 (1.13, 1.30)***	0.12	1.12 (1.00, 1.26)*	0.24	1.27 (1.14, 1.42)***	0.17	1.19 (0.95, 1.47)
Morningness-eveningness type (ref: morningness)	Intermediate	0.07	1.07 (1.04, 1.10)***	–	–	–	–	–	–
	Eveningness	0.20	1.22 (1.14, 1.31)***	–	–	–	–	–	–
	None	−0.01	0.99 (0.98, 1.04)	–	–	–	–	–	–

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韩国研究-结论

KIOM

- 降低认知功能低下危险度的适当睡眠时间在早晚可能有所不同
- 关于适当睡眠时间的今后研究需要考虑睡眠模式或清晨型/夜晚型

10

英国研究 – 研究目的

- 分析睡眠时间、睡眠质量和chronotype对认知功能的影响和惯例

11

英国研究 - 研究方法

- 本研究利用英国医学研究委员会和Wellcome Trust财团设立的基于人口的前瞻性研究UK Biobank数据
- 认知功能通过队列1中的4项测试和队列2中的2项测试进行评估
  - 流体智力/推理(Fluid intelligence)、配对(Pairs matching)、反应时间(Reaction time)、前瞻性记忆(Prospective memory)
- 研究睡眠相关的3个变量，即睡眠时间、睡眠质量、chronotype的影响

12

英国研究 - 研究结果

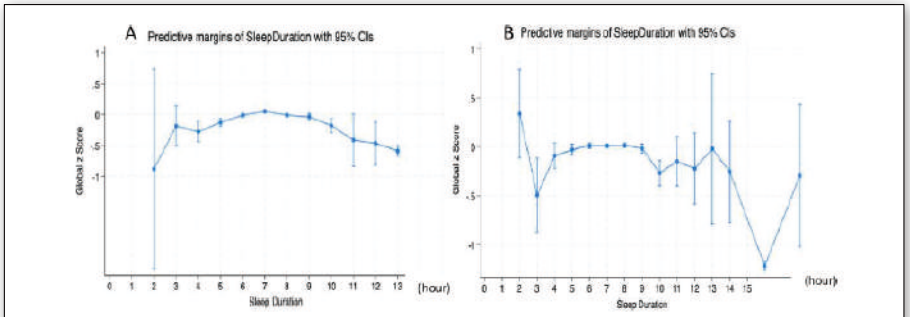

Figure 1 Predictive margins of sleep duration and global z-score across cohorts 1 (A) and 2 (B). The solid line in the graphs depicts the adjusted mean global cognitive z-score for each sleep duration category, with 95% confidence intervals, providing insights into the average cognitive function corresponding to each sleep duration after controlling for other factors.

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英国研究 - 研究结果

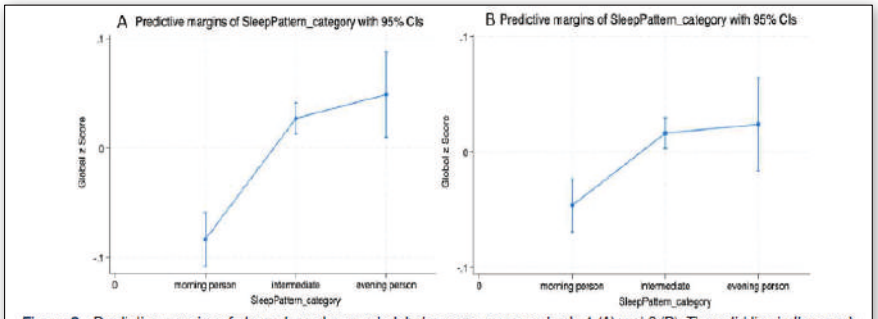

Figure 2 Predictive margins of sleep chronotype and global z-score across cohorts 1 (A) and 2 (B). The solid line in the graph depicts the adjusted mean global cognitive z-score for each sleep chronotype, with 95% confidence intervals, providing insights into the average cognitive function corresponding to each sleep chronotype after controlling for other factors.

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英国研究 - 研究结果

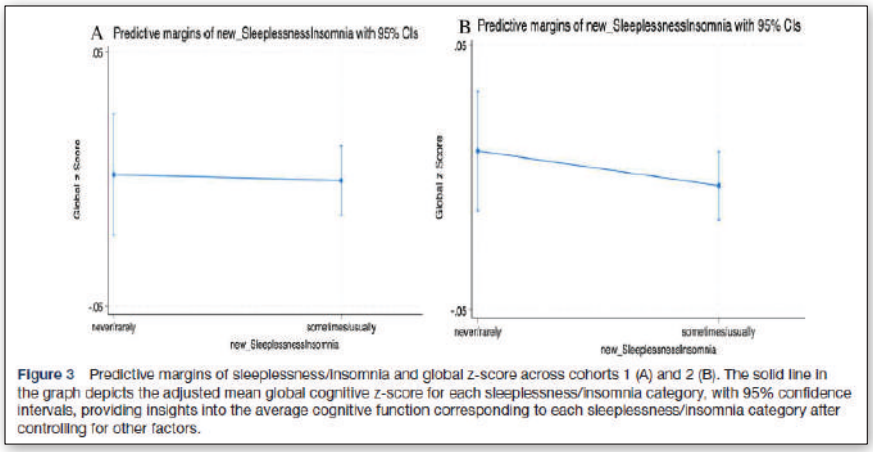

Figure 3 Predictive margins of sleeplessness/insomnia and global z-score across cohorts 1 (A) and 2 (B). The solid line in the graph depicts the adjusted mean global cognitive z-score for each sleeplessness/insomnia category, with 95% confidence intervals, providing insights into the average cognitive function corresponding to each sleeplessness/insomnia category after controlling for other factors.

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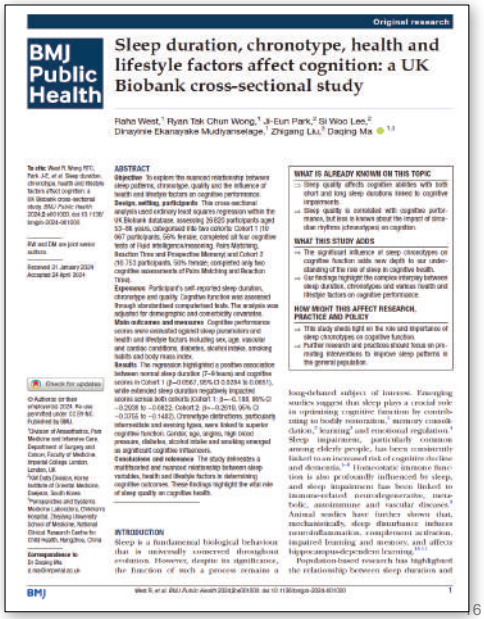
刊载论文

Journal of Affective Disorders

Research paper

Association between sleep hours and changes in cognitive function according to the morningness-eveningness type: A population-based study



Original research

BMJ Public Health

Sleep duration, chronotype, health and lifestyle factors affect cognition: a UK Biobank cross-sectional study

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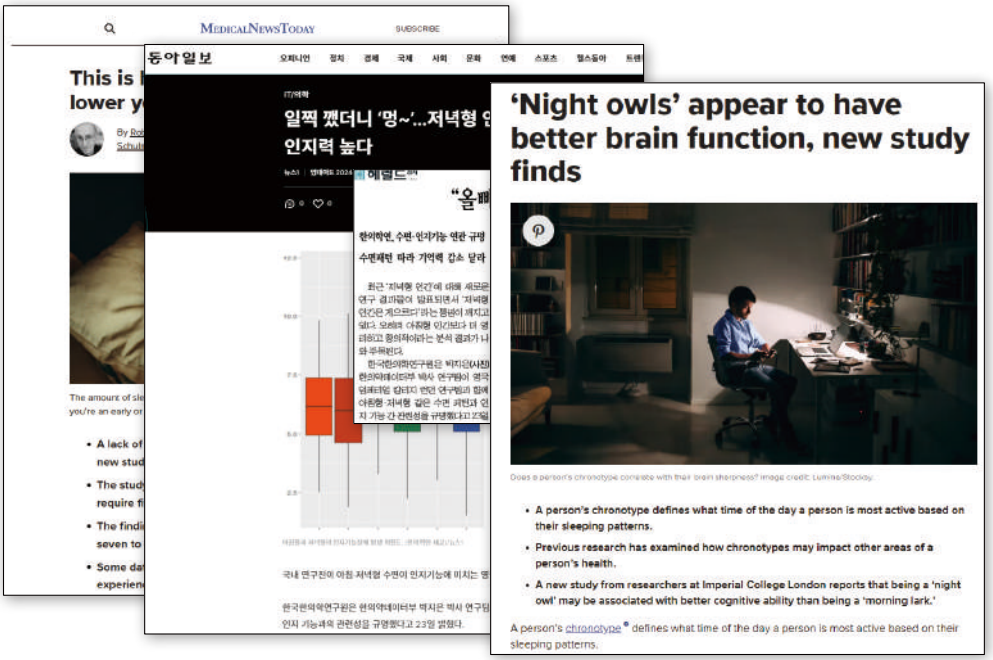
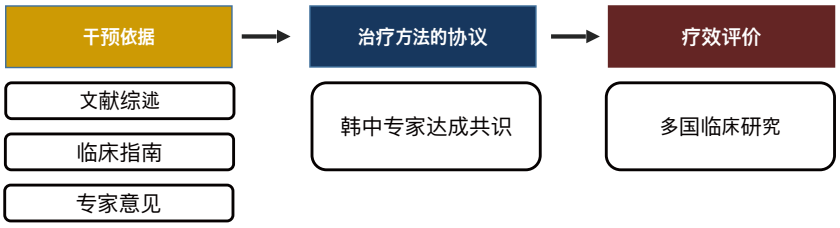
新闻报道及时事通讯



韩中联合睡眠研究

- 研究目的
  - 韩医学/中医学对睡眠障碍的治疗效果研究



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谢谢!

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KOREA INSTITUTE OF ORIENTAL MEDICINE
INTERNATIONAL SYMPOSIUM

PRESENTATION

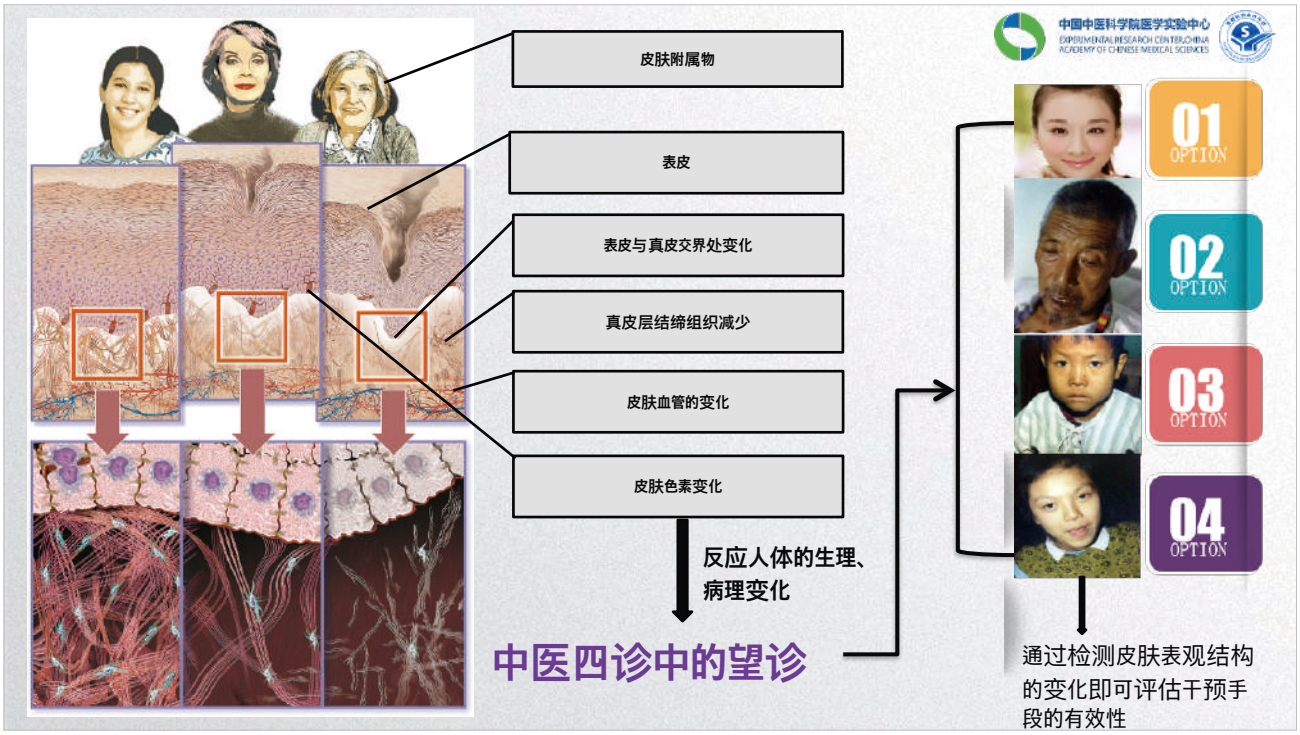
Yi WANG
CACMS

THE ESTABLISHMENT AND APPLICATION OF AN OPTICAL IMAGING METHOD FOR THE SKIN MANIFESTATION FOR THE EFFICACY OF TRADITIONAL CHINESE MEDICINE

PRESENTATION

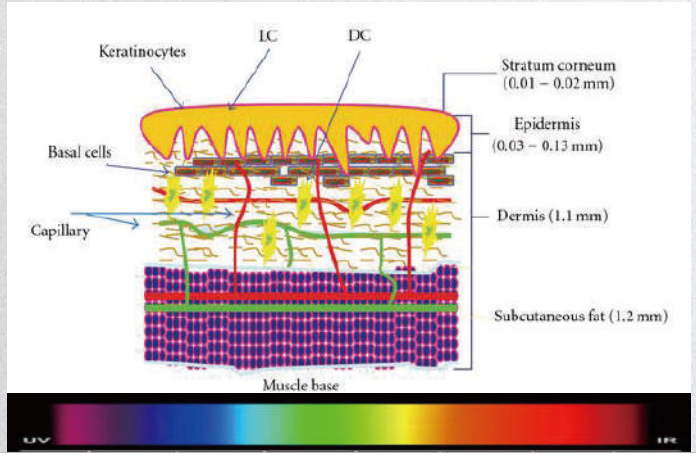
The Establishment and Application of an Optical Imaging Method for the Skin Manifestation for the Efficacy of Traditional Chinese Medicine

- Yi WANG I CACMS



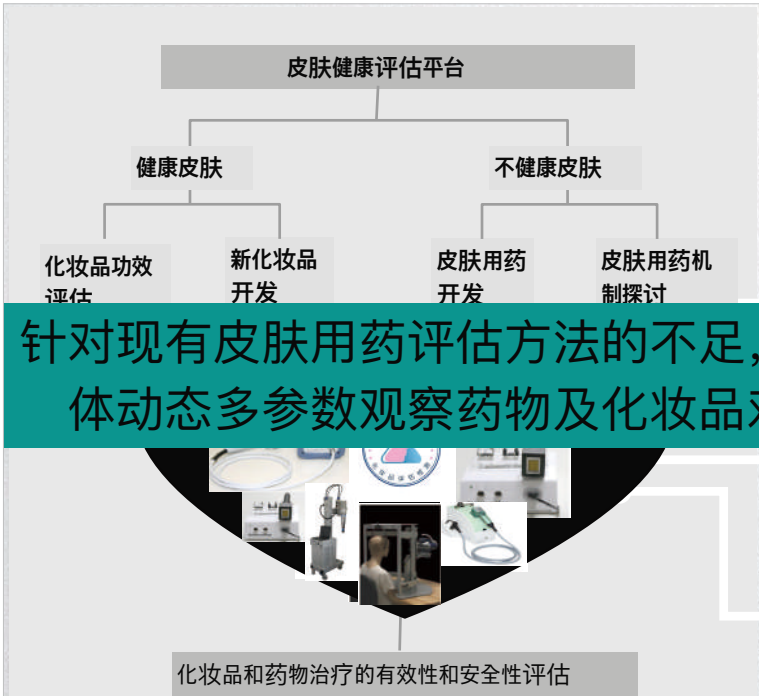
光学成像的优势使皮肤在体观测成为可能

皮肤是人体最大的器官，皮肤厚度随着部位不同而有差别。最薄的是眼睑部位，皮肤厚度约为0.5mm，面部皮肤平均厚度约为1～1.5mm，手足掌部最厚，可达4mm。



普通激光共聚焦显微镜穿透深50μm，双光子扫描显微镜可达1000μm。

充分利用光波的四个基本特征：光强、波长、相位和偏振，提取有效信息，探索皮肤表观特征



针对现有皮肤用药评估方法的不足，建立无损、非介入式活体动态多参数观察药物及化妆品对皮肤状态的功效评估

研究对象：口服及外用药品、化妆品
研究重点：新评估技术的开发与应用

细胞水平

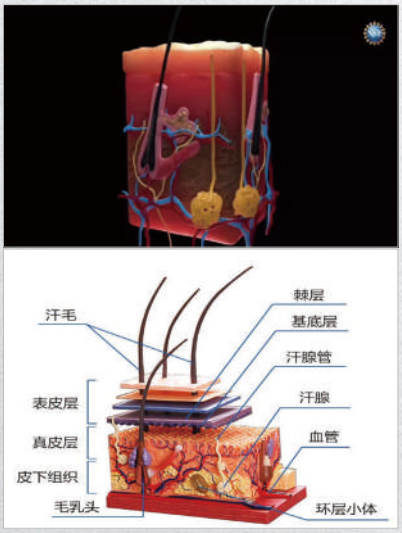
基于光学成像仪器，开发应用各种光学成像手段活体动态评估药物及日化产品的功效。

人体检测
应用可用于人体检测的仪器设备，对药物及日化产品进行人体的功效评价。

The Establishment and Application of an Optical Imaging Method for the Skin Manifestation for the Efficacy of Traditional Chinese Medicine

- Yi WANG I CACMS

皮肤微观结构



微观结构元素提取

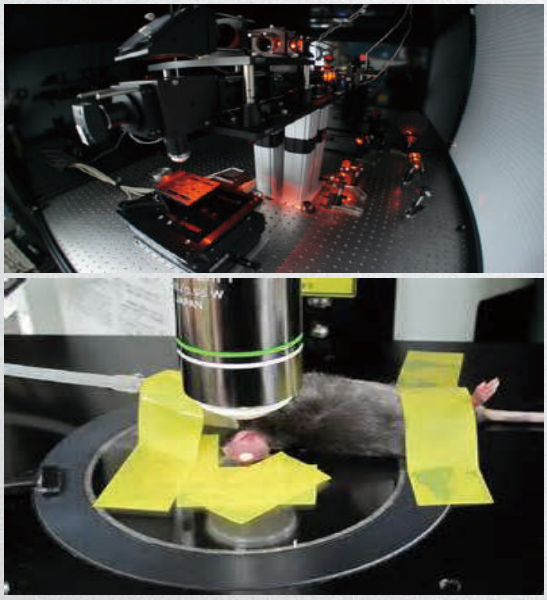
- 表皮各层细胞 → 1.光学相干断层扫描OCT 2.经皮失水
- 真皮胶原纤维 → 皮肤弹性检测仪
- 血管 → 散斑仪
- 黑色素 → RGB皮肤颜色测定
- 皮肤附属物 → 毛发、皮脂腺

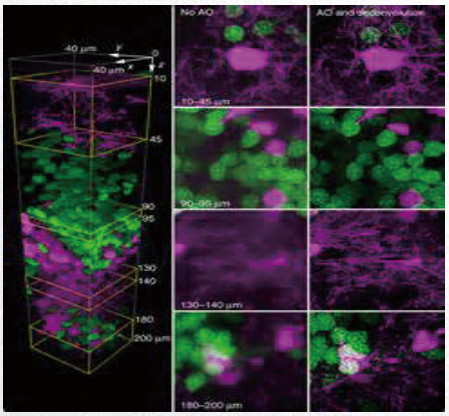
光疗对毛发及皮脂分泌影响可做为后期实验拓展方向

The Establishment and Application of an Optical Imaging Method for the Skin Manifestation for the Efficacy of Traditional Chinese Medicine

- Yi WANG I CACMS

新成像技术的开发应用





双光子成像、自发荧光、二次谐波成像技术、光学相干断层扫描、光声、偏振光成像技术

经典商品化测肤仪器的相辅相成

设备名称	功能
防晒指数测试系统	该系统主要应用于评估和筛选具有防晒功效的中草药活性物质，扩大中草药在皮肤防晒方面的应用，为防治紫外线引起皮肤红肿，脱皮，皱纹，甚至诱发皮肤癌的发生提供技术支撑。
皮肤快速成像分析系统	主要用于评估中草药作用于衰老皮肤后，皱纹、毛孔、皮纹、皮肤蜂窝等病理指标的改变。能进行皮肤三维快速成像，采用蓝色光源，快速完成测量。同时通过激光定位功能使其具有稳定的二次定位功能，高分辨率的镜头和条纹投影器可以进行非常好的调整和固定，使整个系统更加稳定、精确和可靠。
面部图像分析仪+皮肤图像分析VISIA-CR+FrameScan	15多种分析参数：皮肤亮度、美 白、ITA，斑点的大小、颜色、灰度，皱纹的面积，彩妆、口红稳定性、皮肤均匀度（色素、红斑）等 16分析模式：不少于6种
皮肤敏感度测试仪	毛细管形态和血细胞流动速度测量
皮肤生理性质分析仪器系列	：1.皮肤弹性测试探头；2.皮肤硬结测试；3.皮肤皮脂测试探头；4.皮肤角质层水分含量测试探头；5.皮下0.5mm水分含量测试探头；6.皮肤颜色测试探头；7.皮肤亮度测试探头
皮肤快速三维成像系统	有3D、2D模式可测皱纹、毛孔粗糙度、干燥度、防晒、老化、炎症、彩妆、头发、质地、粉刺、等功能
头发多功能测试仪器	主要评估中药及其他活性物质作用于问题毛发后，毛发摩擦特性、拉伸特性、柔顺特性、抗弯特性和梳理特性等的改变，为中药在毛发方面的应用提供技术支撑。

The Establishment and Application of an Optical Imaging Method for the Skin Manifestation for the Efficacy of Traditional Chinese Medicine

- Yi WANG I CACMS

Research Approach:

A	B	C
皮肤微观结构	光学成像方法	化妆品功效评估
表皮各层细胞	自发荧光	美白
真皮胶原纤维	双光子成像	祛痘
血管	二次谐波成像	抗光老化
毛囊	偏振光成像	抗炎
皮脂腺	激光血流散斑成像	防脱发等
黑色素	光学相干断层扫描	

针对皮肤微观结构特征的光学成像方法建立药物及化妆品功效的综合评价方法

Application:

应用概述

1.脓疱型痤疮动物模型的建立
2.脾胃湿热痤疮动物模型

器械：载药微针和电导微针
仪器：基于光学成像技术的面部荧光斑点生物学对应

透皮吸收活体观测方法
痤疮活体动态评估体系的建立

1.鹿茸提取物具有促进创伤愈合的作用
2.TRQ具有改善炎症性痤疮的药效作用；
改善痤疮形成过程中的脂质异常与炎症反应；
发现TRQ中核心成分的能有效降低脂质合成

10

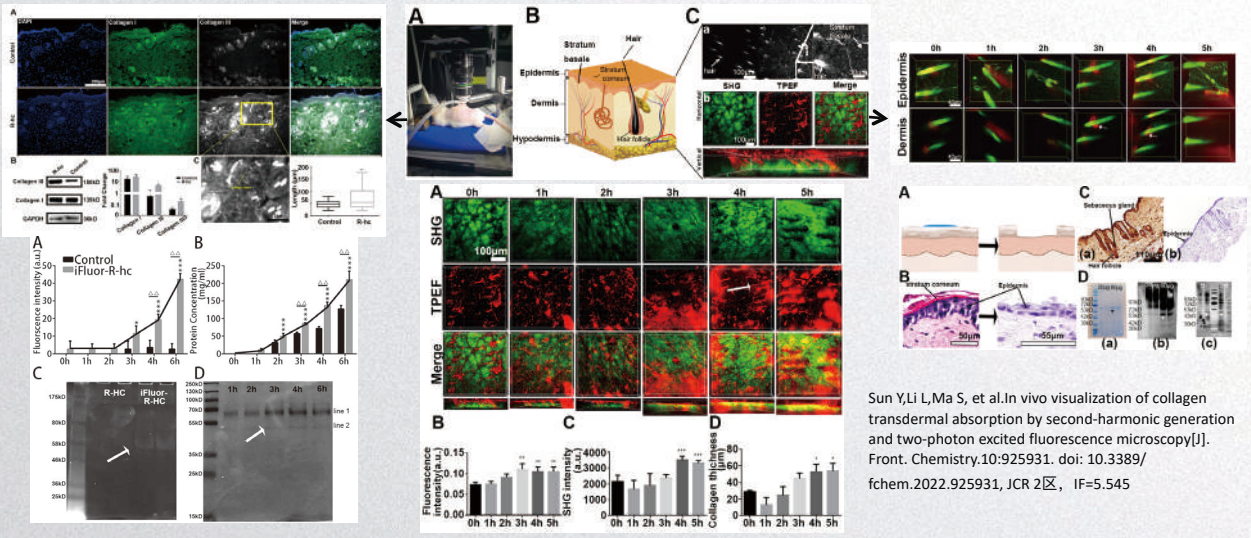
The Establishment and Application of an Optical Imaging Method for the Skin Manifestation for the Efficacy of Traditional Chinese Medicine

- Yi WANG I CACMS

Research progress: 观测方法

研究进展-透皮吸收活体观测方法

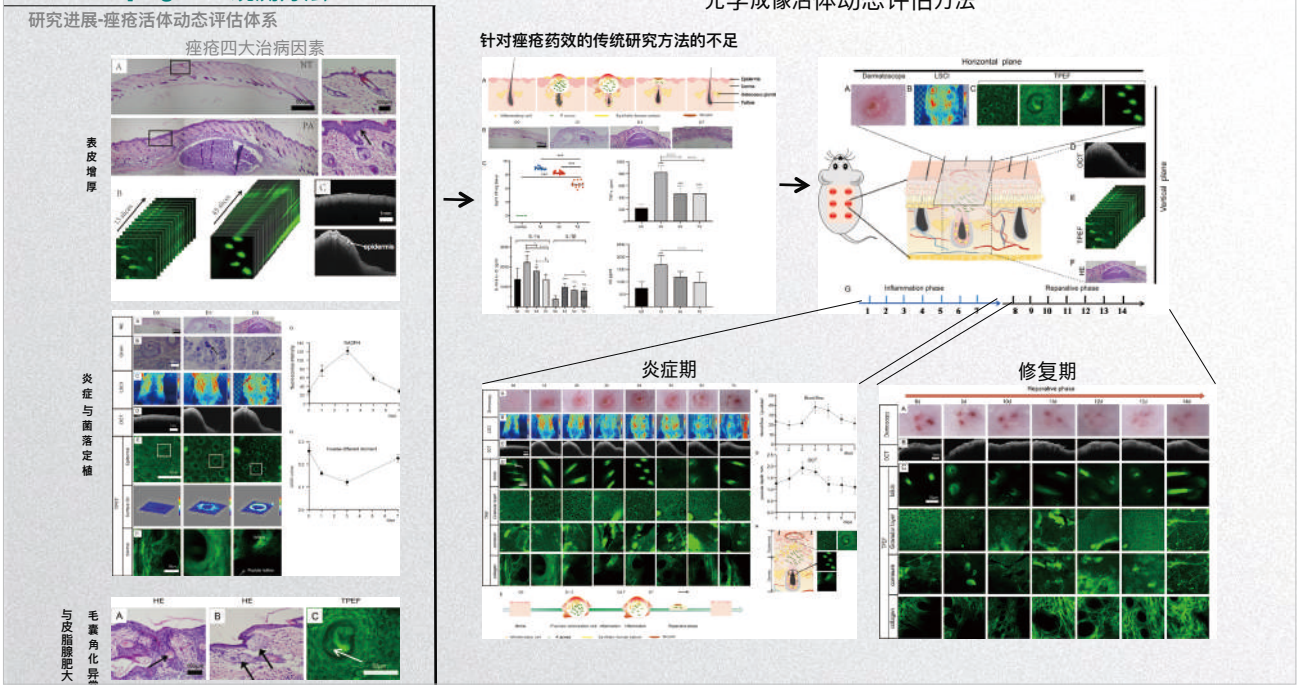
将二次谐波产生与双光子激发荧光相结合的新方法，以可视化体外胶原蛋白透皮吸收的动态过程。高分辨率图像显示，外源性重组人胶原蛋白通过毛囊渗透表皮和 皮脂腺到达真皮层，实时形成网状结构。



Sun Y,Li L,Ma S, et al.In vivo visualization of collagen transdermal absorption by second-harmonic generation and two-photon excited fluorescence microscopy[J]. Front. Chemistry.10:925931. doi: 10.3389/fchem.2022.925931, JCR 2区，IF=5.545

Research progress: 观测方法

研究进展-痤疮活体动态评估体系



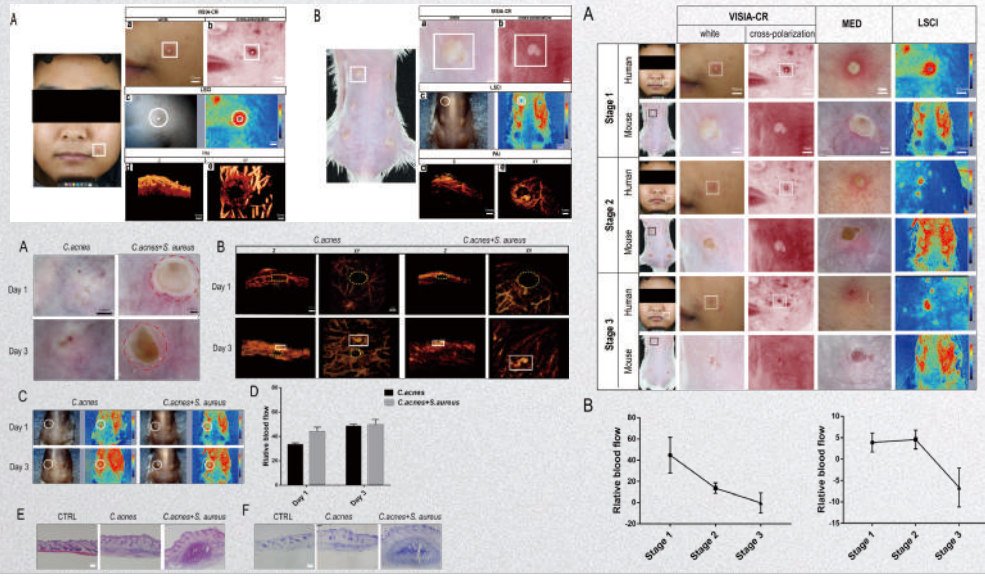
The Establishment and Application of an Optical Imaging Method for the Skin Manifestation for the Efficacy of Traditional Chinese Medicine

- Yi WANG I CACMS

Research progress: 动物模型的建立

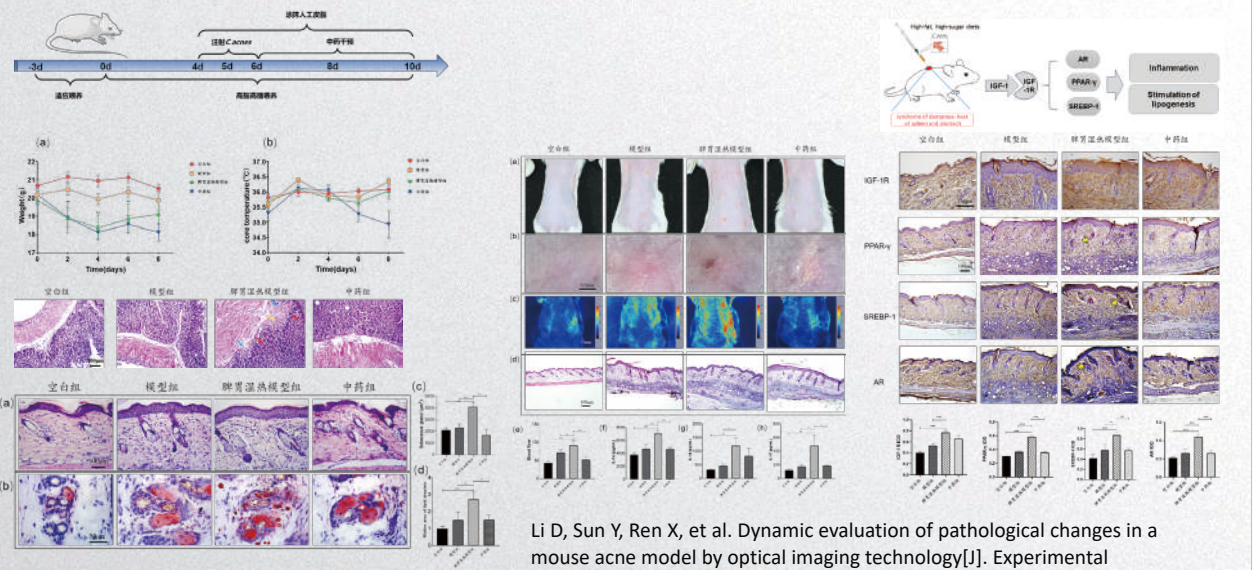
研究进展- 1.脓疱型痤疮动物模型的建立

为了更好的模拟人类脓疱型痤疮的动态演变过程，制备了一种痤疮混合菌动物模型，通过与人类脓疱型痤疮以及单菌感染动物模型比较，混合菌感染脓包无论是从外观形态还是炎症水平都与临床实际更为贴近。



Research progress: 动物模型的建立

研究进展-2.脾胃湿热痤疮动物模型



Li D, Sun Y, Ren X, et al. Dynamic evaluation of pathological changes in a mouse acne model by optical imaging technology[J]. Experimental Dermatology, 2023.JCR 1区， IF=3.6

The Establishment and Application of an Optical Imaging Method for the Skin Manifestation for the Efficacy of Traditional Chinese Medicine

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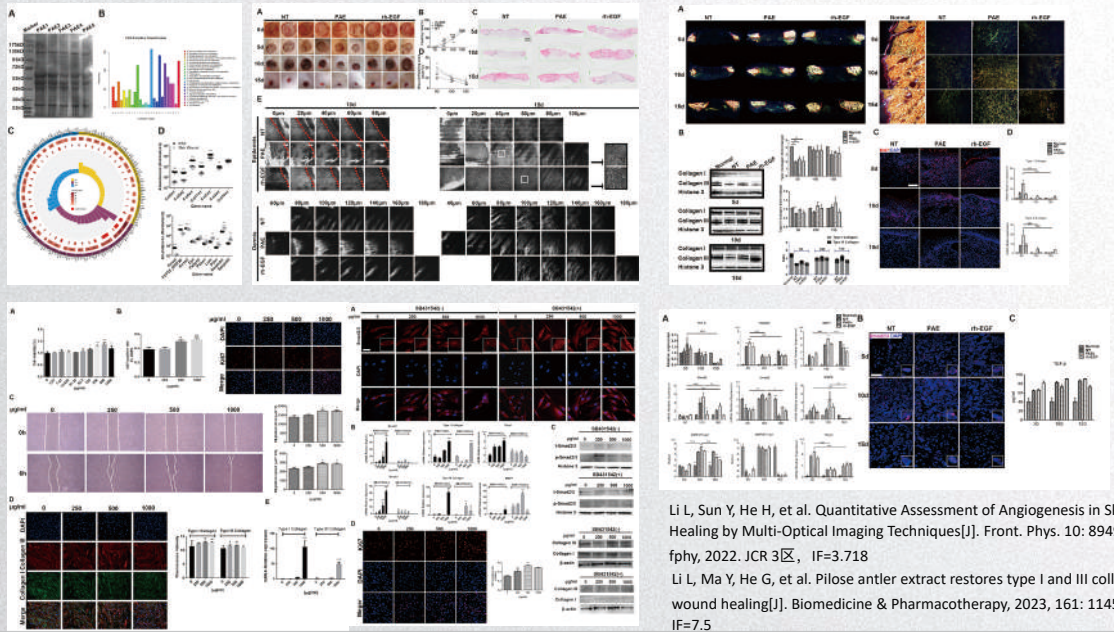
Research progress: 药效评估

研究进展-鹿茸提取物具有促进创伤愈合的作用

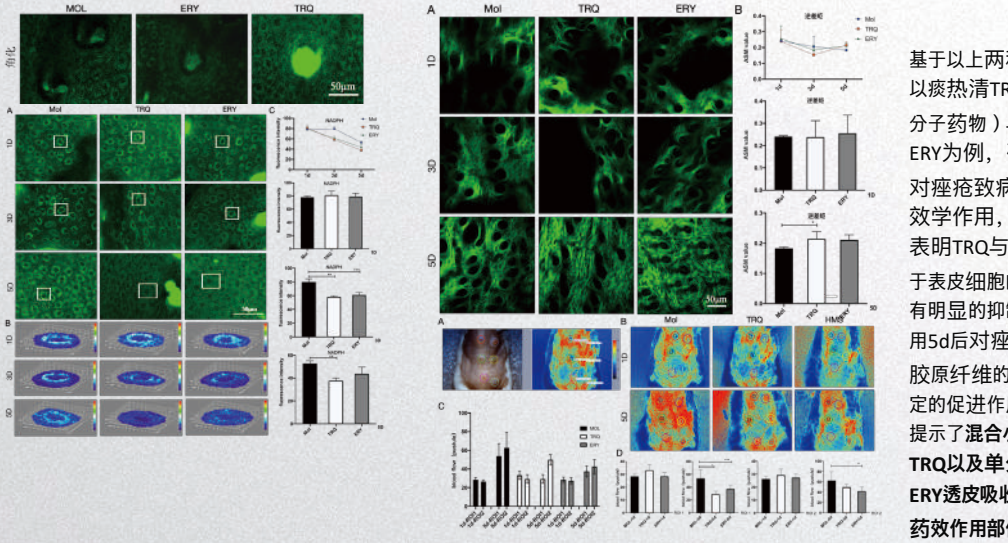


Li L, Sun Y, He H, et al. Quantitative Assessment of Angiogenesis in Skin Wound Healing by Multi-Optical Imaging Techniques[J]. Front. Phys. 10: 894901. doi: 10.3389/fphy, 2022. JCR 3区， IF=3.718

Li L, Ma Y, He G, et al. Pilose antler extract restores type I and III collagen to accelerate wound healing[J]. Biomedicine & Pharmacotherapy, 2023, 161: 114510.JCR 1区，IF=7.5

Research progress: 药效评估

研究进展-**TRQ**具有改善炎症性痤疮的药效作用

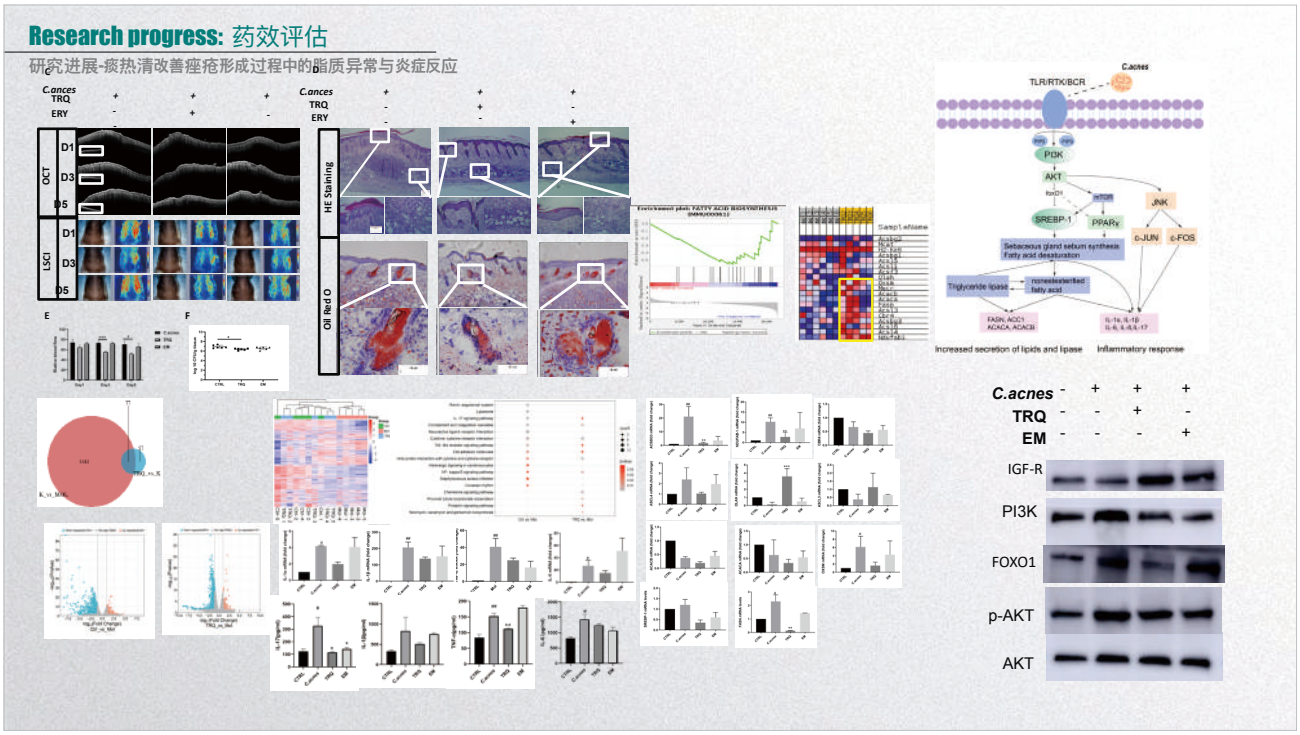


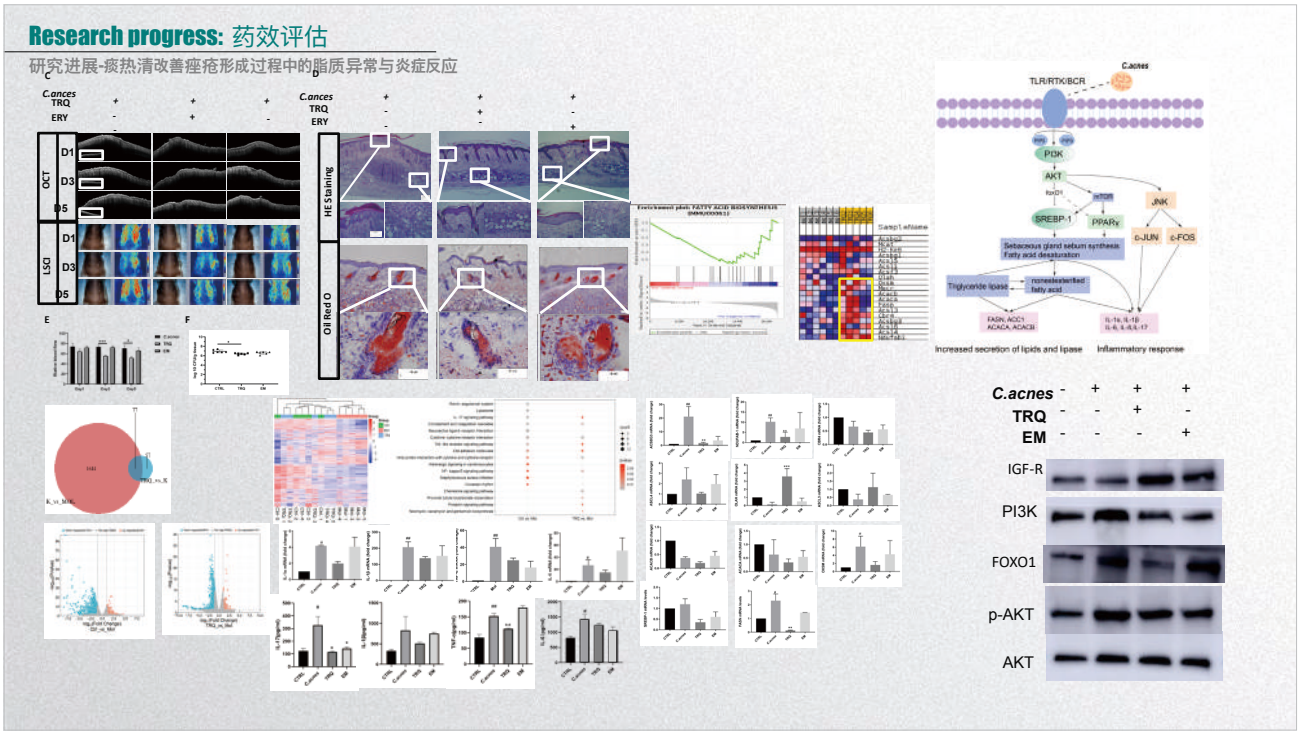
基于以上两种技术我们以痰热清TRQ（混合小分子药物）与红霉素ERY为例，研究了其对痤疮致病因素的药效学作用，研究结果表明TRQ与ERY不仅对于表皮细胞的炎症反应有明显的抑制作用，使用5d后对痤疮恢复期胶原纤维的恢复也有一定的促进作用，该结果提示了**混合小分子药物TRQ以及单分子药物ERY透皮吸收后的局部药效作用部位在表皮与真皮层。**

PRESENTATION

The Establishment and Application of an Optical Imaging Method for the Skin Manifestation for the Efficacy of Traditional Chinese Medicine

- Yi WANG I CACMS





The Establishment and Application of an Optical Imaging Method for the Skin Manifestation for the Efficacy of Traditional Chinese Medicine

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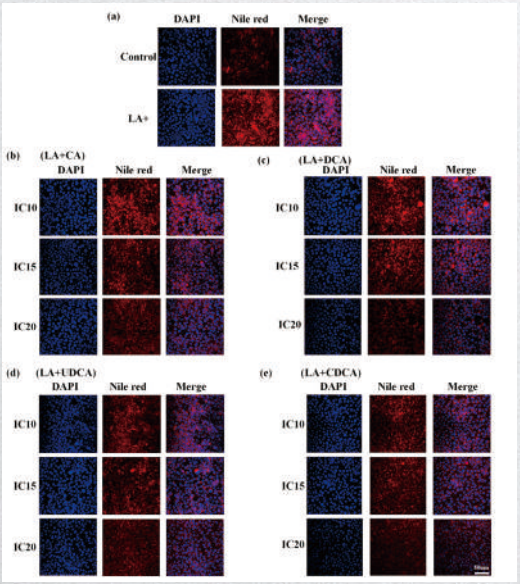
Research progress:

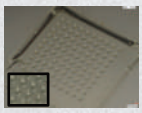
研究进展-发现瘀热清中核心成分的能有效降低脂质合成

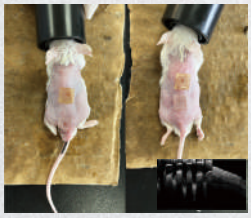


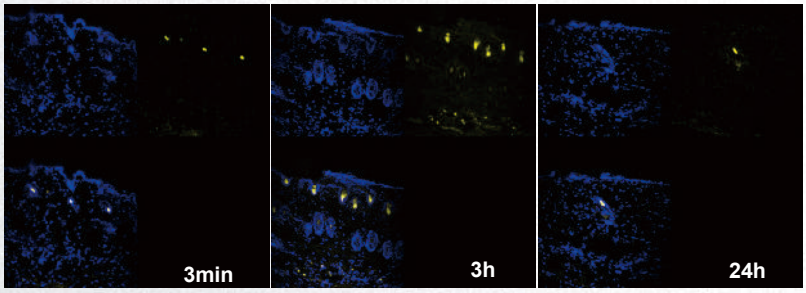
CDCA和UDCA对于脂质合成抑制作用最明显

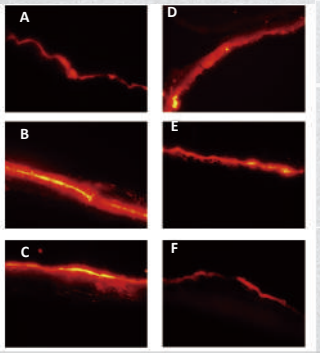
Research progress:

研究进展

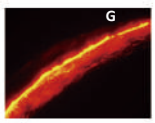


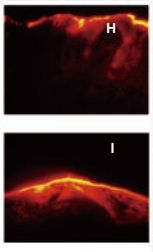






A	50v 0.5ms 99p 1sint	涂抹	D
B	100v 0.5ms 99p 1 sint	30v 0.5ms 99p 1sint+50v 0.5ms 99p 1sint	E
C	150v 5ms 10p 1sint+30v 0.5ms 99×2p 1sint	未处理	F





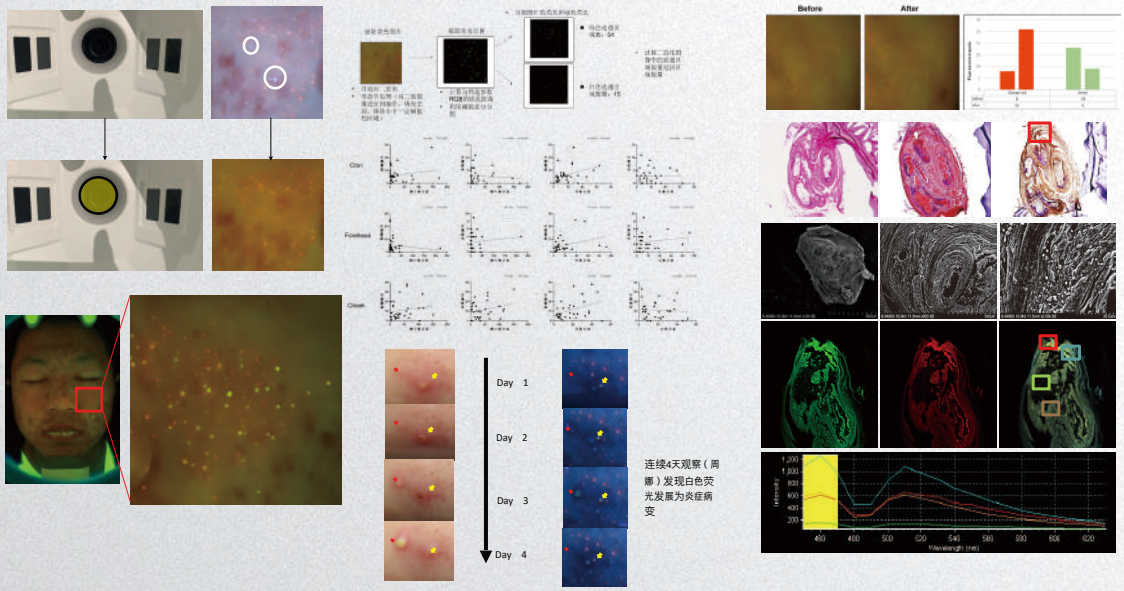
G	150v 5ms 10p 1sint+50v 0.5ms 99×2p 1sint
H	无孔微针 1500MN+敷
I	无孔微针 500MN+敷

The Establishment and Application of an Optical Imaging Method for the Skin Manifestation for the Efficacy of Traditional Chinese Medicine

- Yi WANG I CACMS

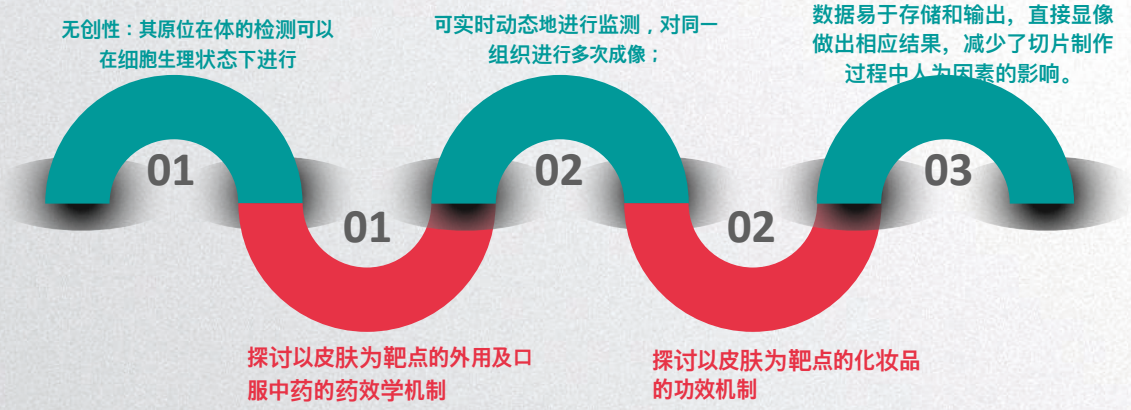
Research progress:

研究进展-基于多光学成像技术确定UVF光下面部不同颜色荧光斑点的物质基础



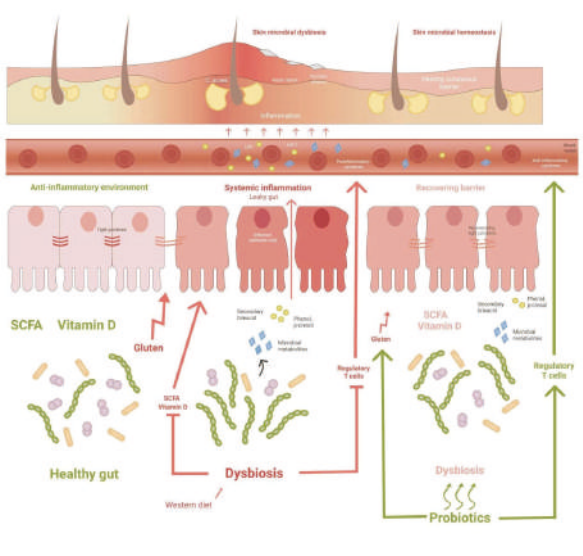
The Advantages of Optical Imaging Technology in Observing Skin Microstructure:

光学成像技术在皮肤微观结构观测中的优势：



22

Cooperation Intention with KIOM
合作意向：



gut-skin axis

研究计划：

1 共同探讨植物药或者肠内菌群调节剂通过gut-skin axis对皮肤状态的影响

2 共同开发改善皮肤健康的候选药材

请 多 指 教

PRESENTATION

Sunguk CHAE
KIOM

DEVELOPMENT OF SKIN HEALTH LAB-BASED ON GUT FUNCTION

Development of Skin Health LAB-based on Gut Function

- Sunguk CHAE I KIOM

한국한의학연구원
KOREA INSTITUTE OF ORIENTAL MEDICINE

'2024 symposium

Development of skin health lactic acid bacteria based on gut function

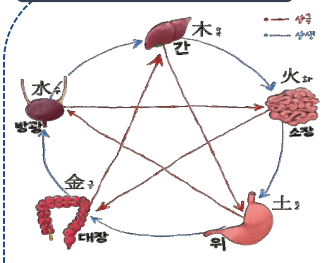
한의약융합연구부

채 성 욱

연구개발

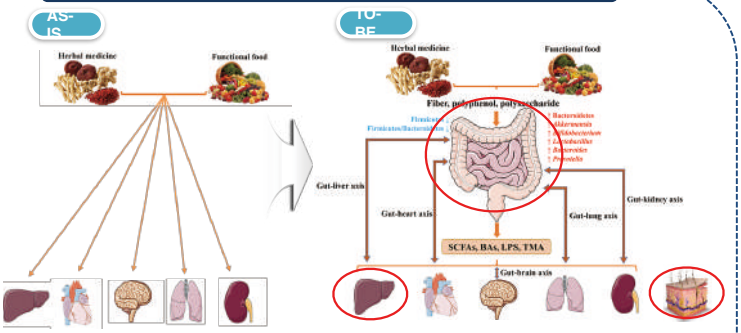
한국한의학연구원
KOREA INSTITUTE OF ORIENTAL MEDICINE

한의학 – '속'이 편해야 건강



<오행과 장기의 관계도>

현대 질환의 복합성으로 인한 도전적 연구로 질환 조절 약물 개발 필요



- ✓ 하나의 모델에 하나의 질환치료 연구
- ✓ 개별질환 약물 개발의 한계
- ✓ 만· 성난치성 질환의 지속적 증가
- ✓ 미충족 의료수요기술 분야

- ✓ 하나의 모델이 아닌 장-간-피부 축 질환치료로 접근
- ✓ 다양한 축 연구로 대사성, 뇌, 피부 질환 등의 연구로 확장
- ✓ 만· 성난치성 질환의 치료 패러다임 제시
- ✓ 미충족 의료수요기술 해결을 위한 해결책 제시

2

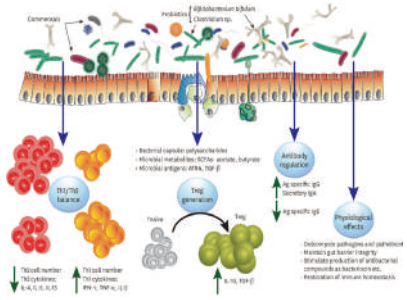
Development of Skin Health LAB-based on Gut Function

- Sunguk CHAE I KIOM

Pharmabiotics

한국한의학연구원 KOREA INSTITUTE OF ORIENTAL MEDICINE

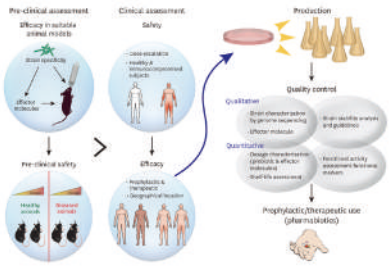
Pharmabiotics 의약을 뜻하는 '파마슈티컬(pharmaceuticals)'와 유익한 생균이라는 '프로바이오틱스(probiotics)'의 합성어



SCIENTIFIC REPORTS

OPEN

Prevention of respiratory syncytial virus infection with probiotic lactic acid bacterium *Lactobacillus gasseri* SBT2055



SCIENTIFIC REPORTS

OPEN

Heat-killed *Lactobacillus casei* confers broad protection against influenza A virus primary infection and develops heterosubtypic immunity against future secondary infection

3

Gut-Brain-liver-Skin axis

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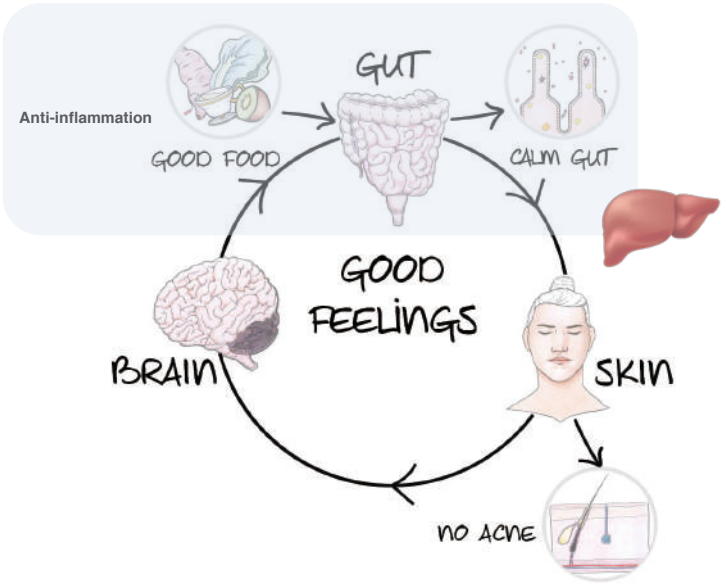

https://www.janinetait.co.nz/29/the-new-science-on-acne/

항염증 및 면역활성 효능평가

- ○ 면역세포주의 세포증식능 (in vitro)
- ○ 비장조직 분리 면역세포 변화 (in vivo)

염증성장질환 개선 효능평가

- ○ 염증성 장질환 효능평가
  - 체중변화 및 DAI 변화 측정
- ○ 면역세포들의 population 변화 평가
  - 비장조직 분리 면역세포 변화

피부건강 개선 효능평가

- ○ 피부조직을 이용한 효능평가
  - 표피두께, 콜라겐 변화 측정
  - 보습(경피수분증발량, 수분보유량)
- ○ 주름유발 관련 인자 평가

4

Development of Skin Health LAB-based on Gut Function

- Sunguk CHAE I KIOM

Inflammation

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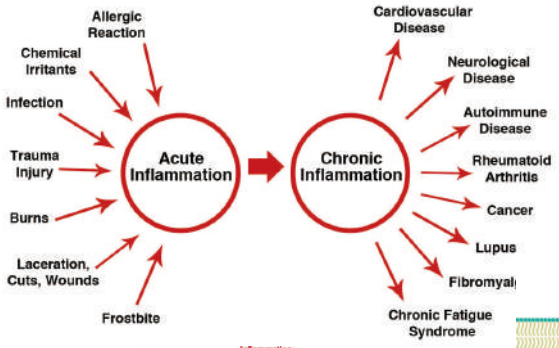
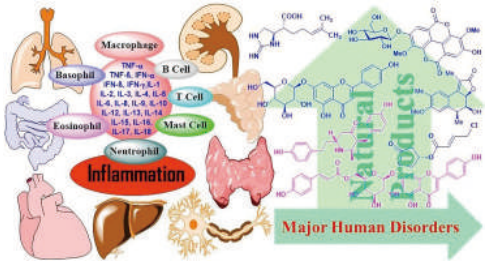
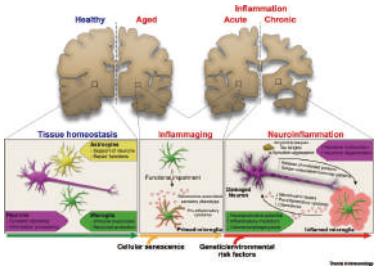
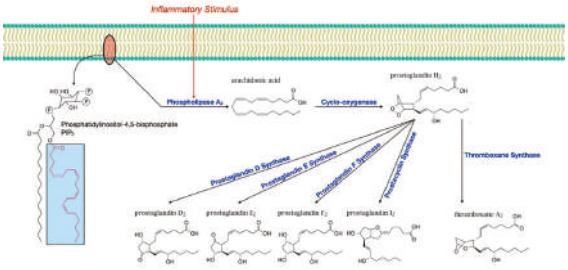
Acute Vs. Chronic Inflammation







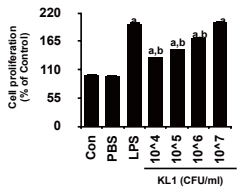


5

Immune enhance

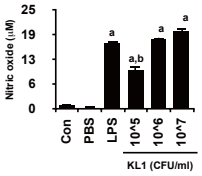
한국한의학연구원 KOREA INSTITUTE OF ORIENTAL MEDICINE

(A)

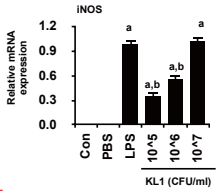


< Figure 1. Cell proliferation of RAW 264.7 cells (A) KL1 >

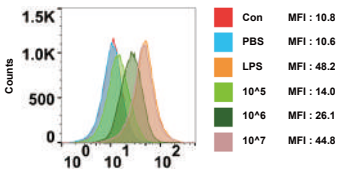
(A)



(B)

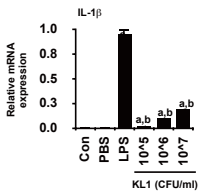


(C)

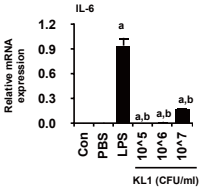


< Figure 2. The production of NO and ROS (A and B) KL1>

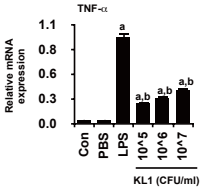
(A)



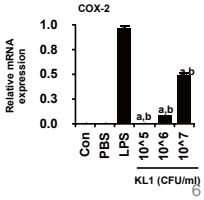
(B)



(C)



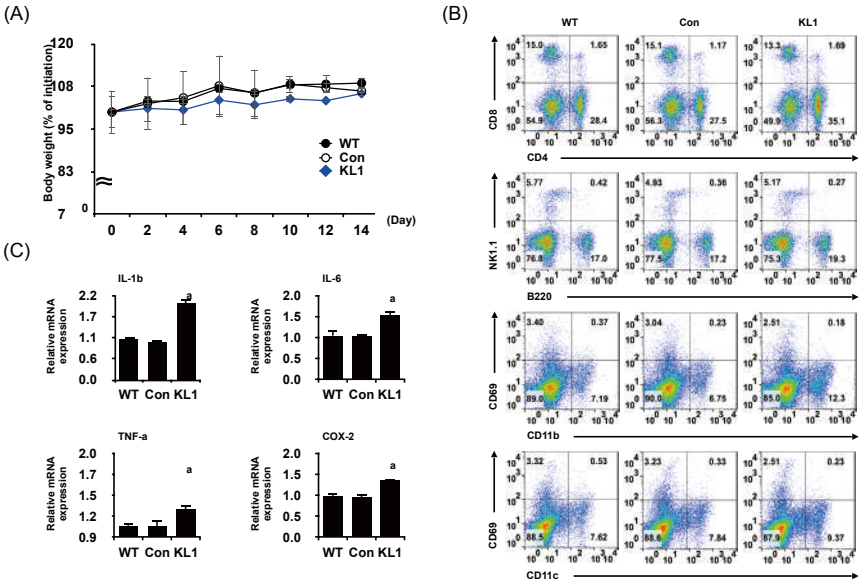
(D)



< Figure 3. The expression of inflammatory cytokines KL1>

6

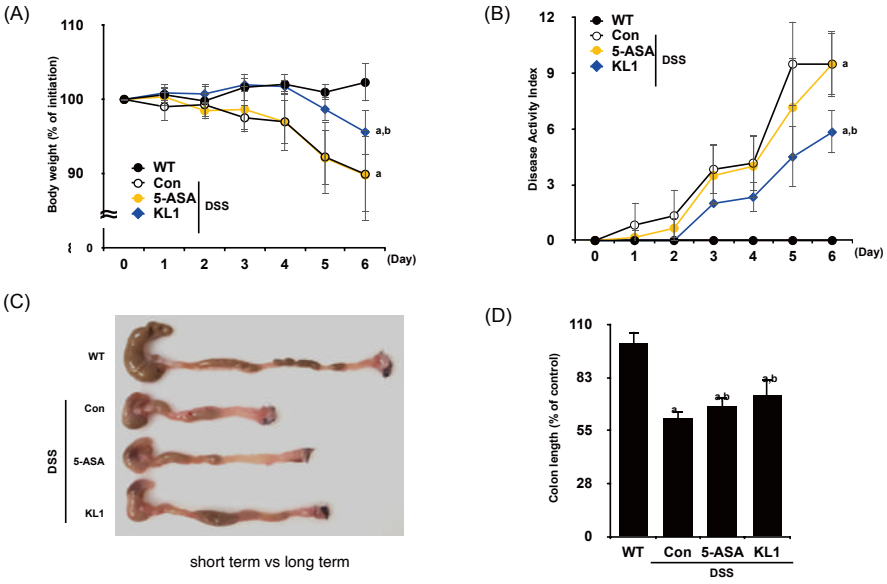
Immune enhance



< Figure 4. (A) Body weight (B) Immune cells population (C) Gene expression of inflammatory cytokines >

7

Inflammatory Bowel Disease



< Figure 5. Body weight DAI colon length>

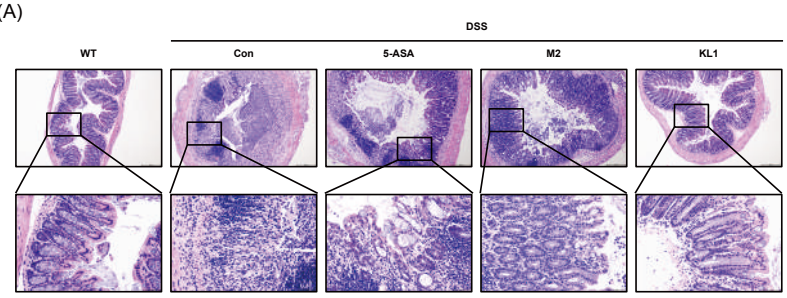
8

Inflammatory Bowel Disease

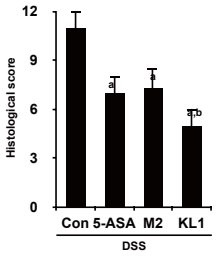
< Table 1. Disease activity index score >

Score	Weight loss	Stool consistency	Visible blood in rectal and feces
0	No weight loss	Well form pellets	No bleeding
1	1~5% weight loss		
2	5~10% weight loss	Loose stool	Slight bleeding
3	10~15% weight loss		
4	Over 15% weight loss	Diarrhoea	Gross bleeding

(A)



(B)



< Figure 6. Histology>

9

Inflammatory Bowel Disease

< Table 2. Histological score >

Histological feature	Score	Description
Loss of epithelium	**0**	**None**
	1	**0~5% loss of epithelium**
	2	**5~10% loss of epithelium**
	3	**Over 10% loss of epithelium**
Crypt damage	**0**	**None**
	1	**0~10% loss of crypt**
	2	**10~20% loss of crypt**
	3	**Over 20% loss of crypt**
Depletion of goblet cells	**0**	**None**
	1	**Mild**
	2	**Moderate**
	3	**Severe**
Infiltration of inflammatory cells	**0**	**None**
	1	**Mild**
	2	**Moderate**
	3	**Severe**

10

Inflammatory Bowel Disease

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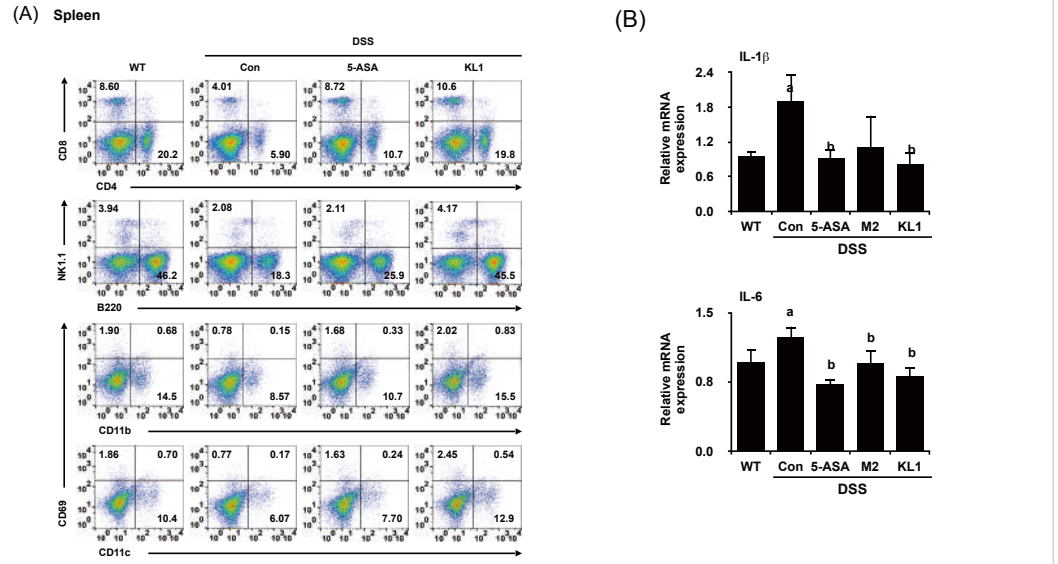

< Figure 7. Immune cell population and gene expression of inflammatory cytokines>

11

Gut-Brain-liver-Skin axis

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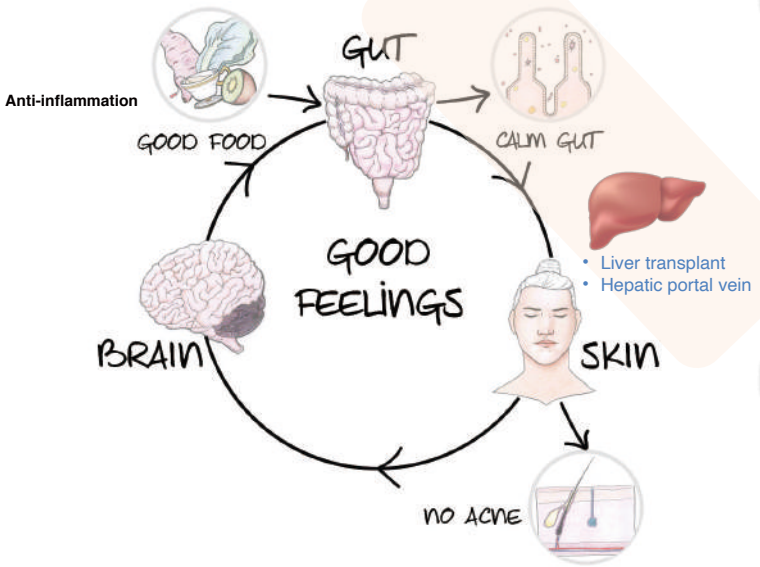


항염증 및 면역활성 효능평가

- ○ 면역세포주의 세포증식능 (in vitro)
- ○ 비장조직 분리 면역세포 변화 (in vivo)

염증성장질환 개선 효능평가

- ○ 염증성 장질환 효능평가
  - 체중변화 및 DAI 변화 측정
- ○ 면역세포들의 population 변화 평가
  - 비장조직 분리 면역세포 변화

피부건강 개선 효능평가

- ○ 피부조직을 이용한 효능평가
  - 표피두께, 콜라겐 변화 측정
- ○ 주름유발 관련 인자 평가

https://www.janinetait.co.nz/29/the-new-science-on-acne/

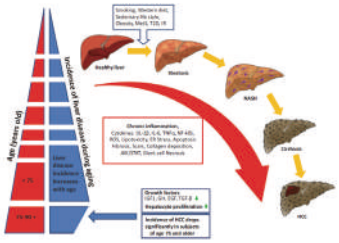
12

비알콜성지방간 (NAFLD)

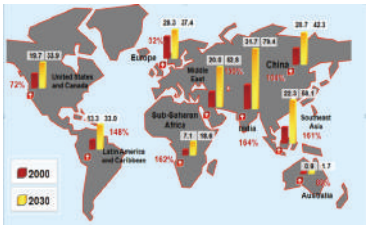
한국한의학연구원 KOREA INSTITUTE OF ORIENTAL MEDICINE

NAFLD 유병률

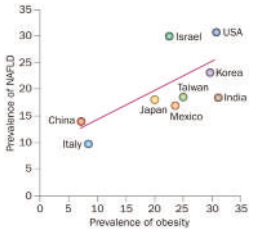
➢ Prevalence of NAFLD & Importance of NAFLD in Korean health care



< Liver disease proecess during aging>



<Worldwide prevalence of NAFLD>



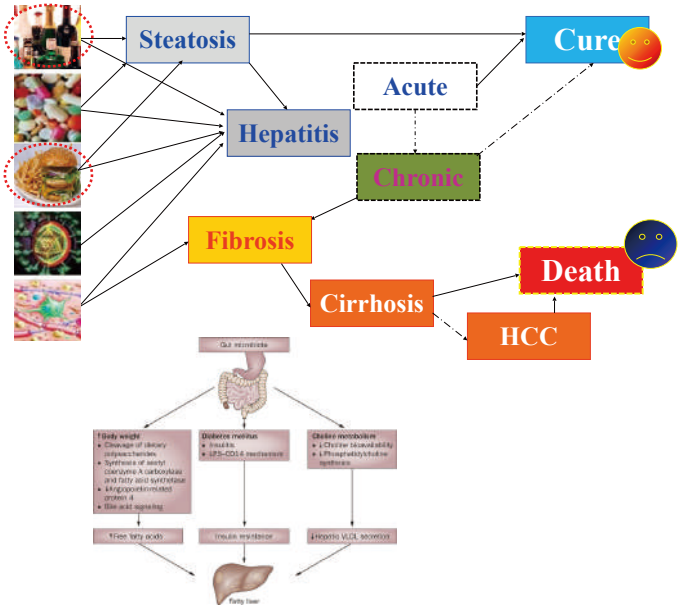
<The prevalence of NAFLD and obesity>

References:
Aging Cell, 2013, 950-954
NEJM, 2007, 356, 213-215
Nat. Rev. Gastroenterol. Hepatol. doi:10.1038/nrgastro.2013.171
Curren Gerontology and Geriatrics Research, 2011, 831536

비알콜성지방간 (NAFLD)

한국한의학연구원 KOREA INSTITUTE OF ORIENTAL MEDICINE

Complexity of Liver injury



비알콜성지방간 - unmet needs

C형 간염 - 완치율 90-100%

B형 간염 - 치료제 존재

사용되는 치료제
- Vitamin E : fibrosis는 개선되지 않음
  No.1 가이드라인
- Pioglitazone : 당뇨가 있는 경우 권고

개발되는 치료제
- FXR agonist (담즙산 유도체): LDL이 증가되는 단점
- PPAR-α/δ agonist
- Golden-505
- Aramchol

비알콜성지방간 (NAFLD)

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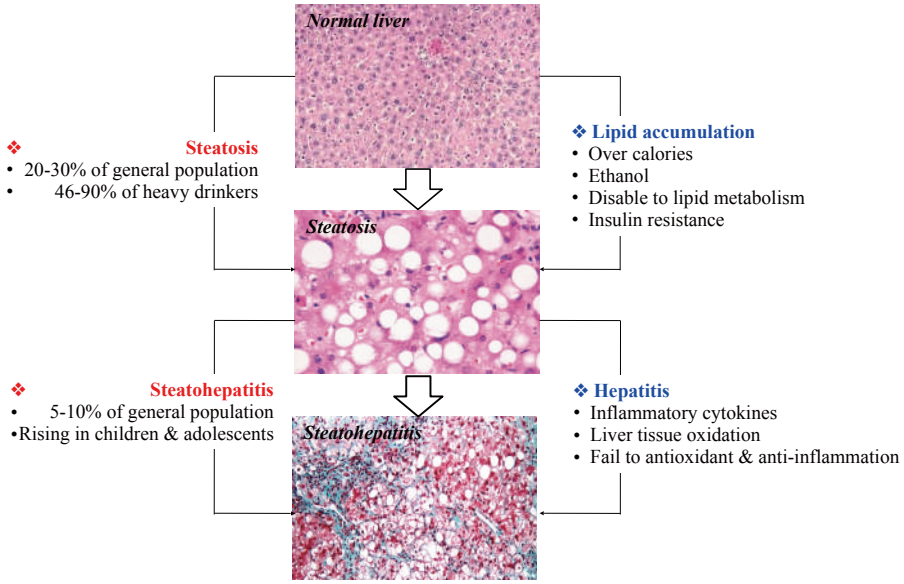
Distinguish between steatosis & steatohepatitis



Semin Liver Dis. 2007;27(2):173-193. [15]

비알콜성지방간 (NAFLD) 모델

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Various animal models for adapting NASH

Table 1 Biochemical and pathological characteristics of animal models of nonalcoholic fatty liver disease/nonalcoholic steatohepatitis

	Model	Obesity	Insulin resistance	Steatosis	Steatohepatitis	Fibrosis
Genetic models	SREBP-1c transgenic mice	No (decreased adiposity)	Yes	Yes	Yes	Yes
	Ob/ob mice	Yes	Yes	Yes	No (does not develop spontaneously)	No (resistant to fibrosis)
	Db/db mice	Yes	Yes	Yes	No (does not develop spontaneously)	No (does not develop spontaneously)
	KK-A^y mice	Yes	Yes	Yes	No (does not develop spontaneously)	No (does not develop spontaneously)
	PTEN null mice	No	No	Yes	Yes	Yes
	PPAR-α knockout mice	No	No	No (steatosis occurs in the starved state)	No	No
	AOX null mice	No	No	Yes	Yes	No
	MAT1A null mice	No	No	Yes	Yes	Yes
Diet models	Methionine and choline deficiency	No (decreased weight and adiposity)	Hepatic insulin resistance	Yes	Yes (severe)	Yes
	High fat	Yes	Yes	Yes	Yes (mild)	Yes
	Cholesterol and cholate (atherogenic diet)	No (decreased weight)	Hepatic insulin resistance	Yes	Yes	Yes
	Fructose	No	Yes	Yes	No/Yes	No

SREBP: Sterol regulatory element binding protein; PTEN: Phosphatase and tensin homologue deleted on chromosome 10; AOX: Acyl-coenzyme A oxidase; MAT1A: Methionine adenosyltransferase-1A; PPAR: Peroxisome proliferator-activated receptor.

World J Gastroenterol 2012 21; 18(19): 2300-2308

16

Development of Skin Health LAB-based on Gut Function

- Sunguk CHAE I KIOM

In vivo experiment

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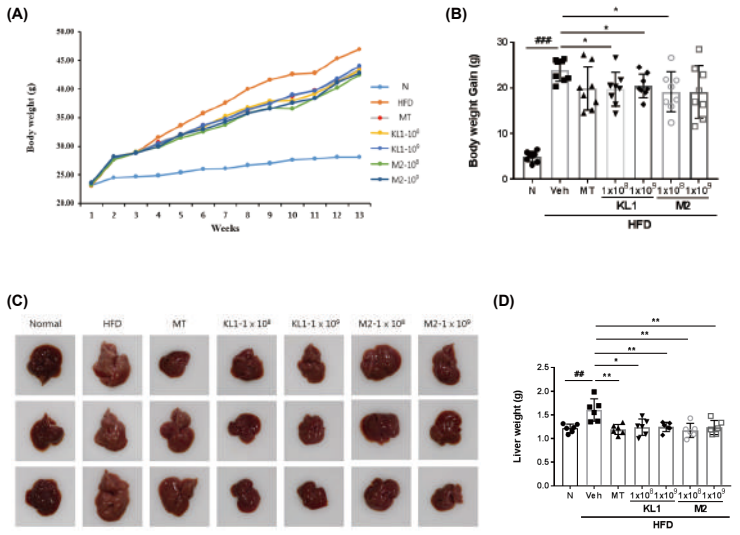

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Gut-Brain-liver-Skin axis

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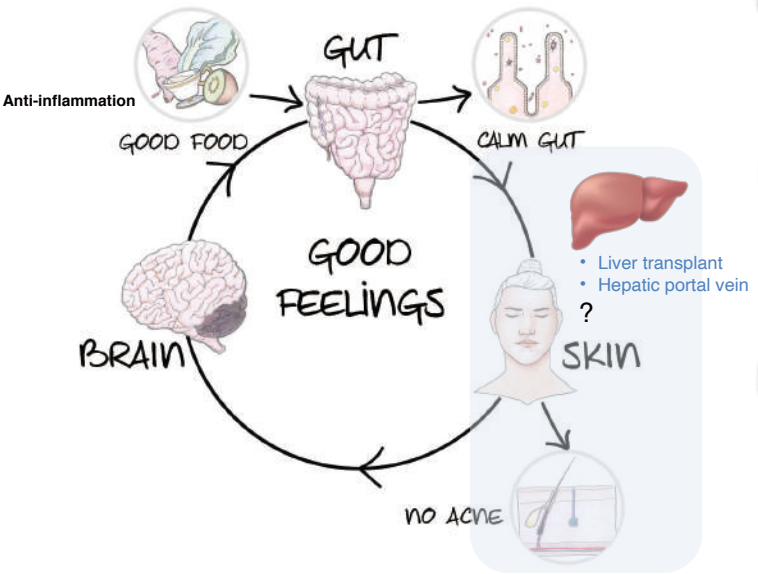

항염증 및 면역활성 효능평가

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- ○ 주름유발 관련 인자 평가

https://www.janinetait.co.nz/29/the-new-science-on-acne/

18

UVB induced photodamage or skin aging

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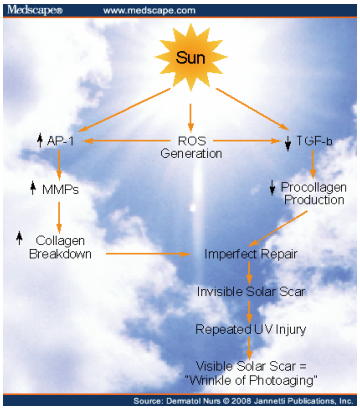
This man was a trucker for 28 years... guess which side of his face was next to the window

Google + 0 Recommend 20 Tweet 0

Read More: No tags for this article

06/03/2012 12:08.00 Lena Sullivan / Dailymail



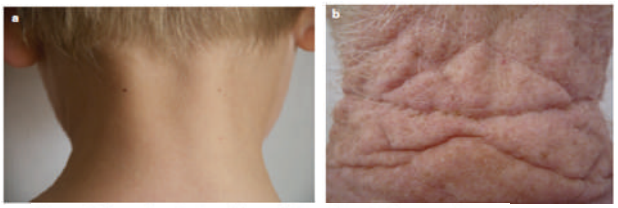


Figure 1 The neck region is readily, and often unknowingly, exposed to sunlight and is a primary site of photoaging. (a) Nonphotodamaged, youthful skin is smooth and elastic. (b) Elderly, photoaged skin is rough, mottled, rigid, and wrinkled.

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In vitro experiment

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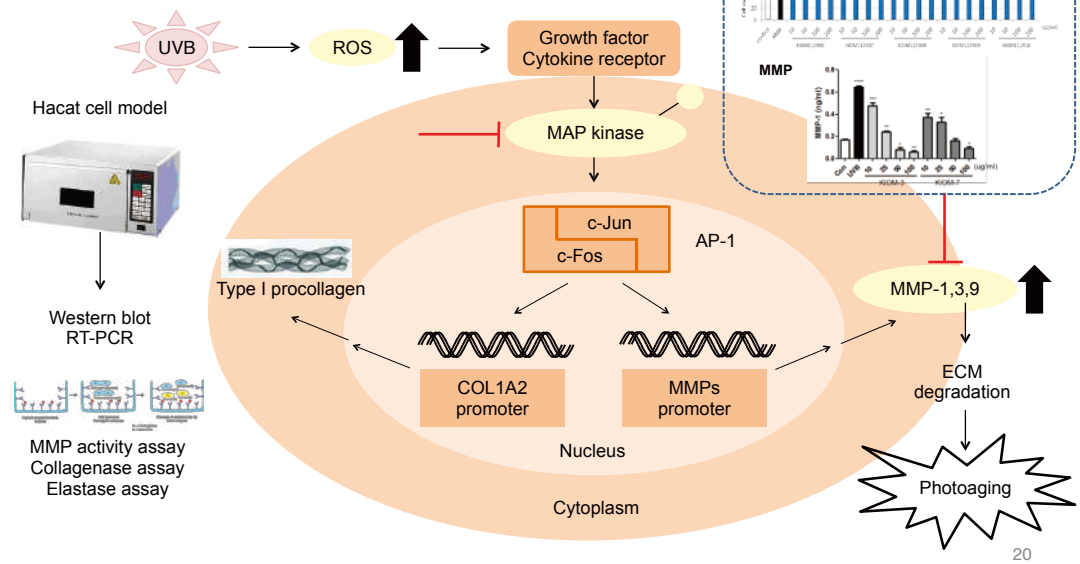
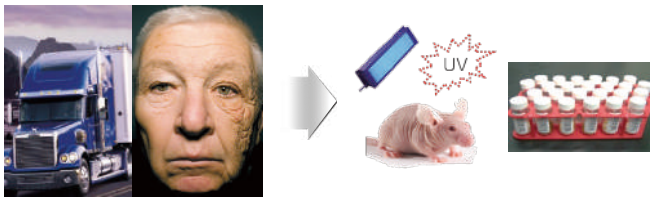


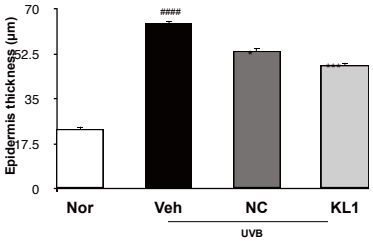
20

Development of Skin Health LAB-based on Gut Function

- Sunguk CHAE I KIOM

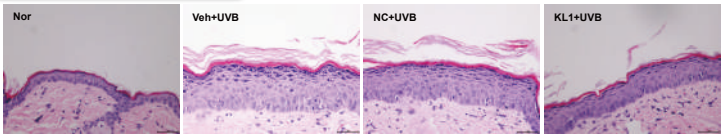
In vivo experiment



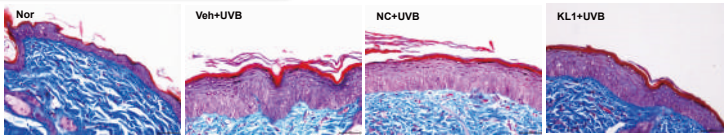


- UVB was applied three times a week for 12wks
- 60mJ/cm² at wk 1→ 90mJ/cm² at wk7

H & E staining



Masson's trichome staining



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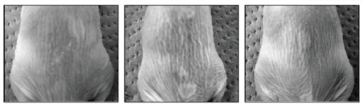
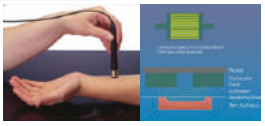
Skin barrier function

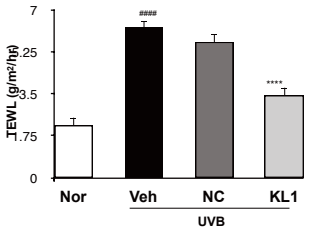


- UVB was applied three times a week
- Hairless mice
- Fillaggrin, involucrin, loricrin
- TM 300(C&K, Cologne, Germany)

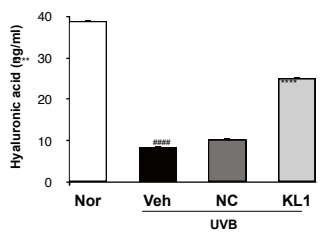
Tewameter

Corneometer

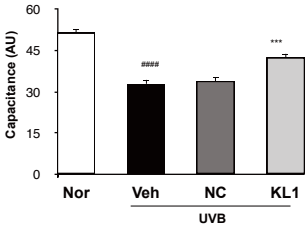




####: significantly different from normal (P<0.0001).
****: significantly different from UV (P<0.0001).



####: significantly different from normal (P<0.0001).
****: significantly different from UV (P<0.0001).



####: significantly different from control (P<0.0001).
***: significantly different from UV (P<0.001).

22

In vivo experiment

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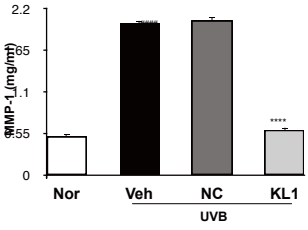
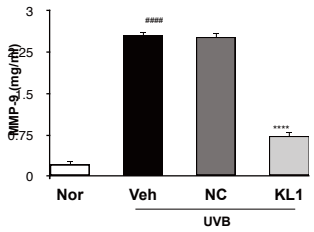
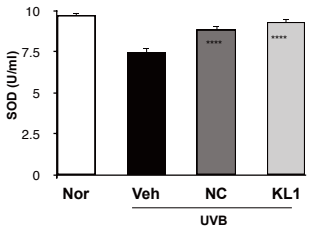
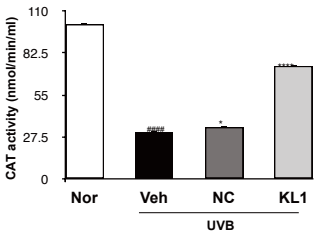
주름관련인자





항산화결과





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RNA-seq

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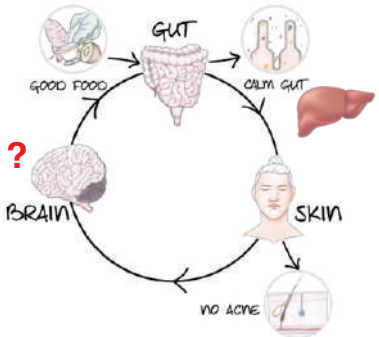
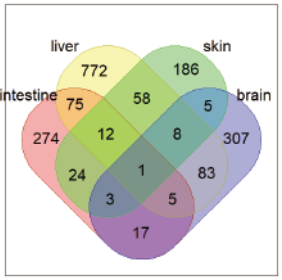
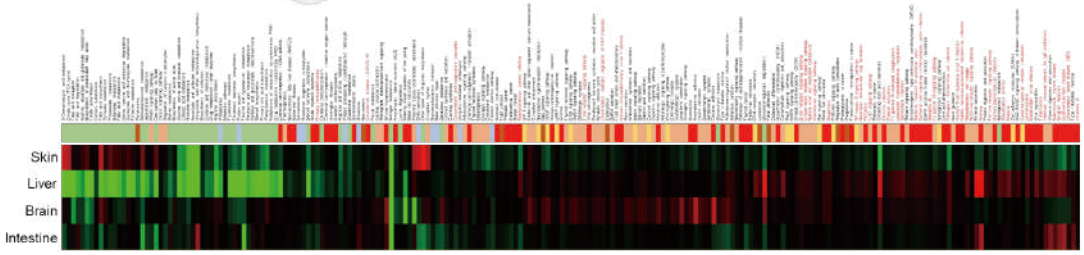




	Intest	Liver	Skin	Br
Intest	2.921607	2.976151	3.006677	3.017026
Liver	2.976151	2.990348	3.048058	3.047496
Skin	3.006677	3.048058	3.071026	3.080604
Br	3.017026	3.047496	3.080604	3.045651

1. Metabolism
2. Genetic Information Processing
3. Environmental Information Processing
4. Cellular Processes
5. Organismal Systems
6. Human Diseases



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Development of Skin Health LAB-based on Gut Function

- Sunguk CHAE I KIOM

Conclusion

한국한의학연구원 KOREA INSTITUTE OF ORIENTAL MEDICINE

비알콜성지방간 개선

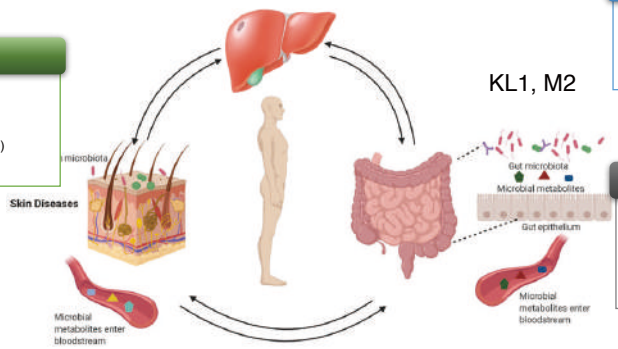
- ○ 간조직 및 무게 변화 측정
  - 지방조직, 혈액인자, 체중, 간 무게 측정
- ○ 조직염색 및 관련 인자 평가

항염증 및 면역활성

- ○ 면역세포주의 세포증식능 (in vitro)
- ○ 비장조직 분리 면역세포 변화 (in vivo)

피부건강 개선

- ○ 피부조직을 이용한 효능평가
  - 표피두께, 콜라겐 변화 측정
  - 보습인자 평가(TEWL, capacitance)
- ○ 주름유발 관련 인자 평가



염증성장질환 개선

- ○ 염증성 장질환 효능평가
  - 체중변화 및 DAI 변화 측정
- ○ 면역세포들의 population 변화 평가
  - 비장조직 분리 면역세포 변화

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Thank you for your attention

26

한국한의학연구원 KOREA INSTITUTE OF ORIENTAL MEDICINE

'2024 symposium

Development of skin health lactic acid bacteria based on gut function

韩医药融合研究部

Chae Seong-wook

研究开发

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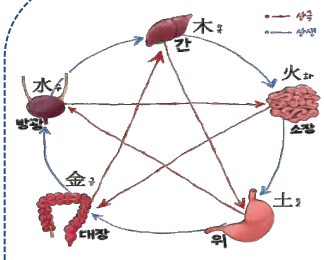
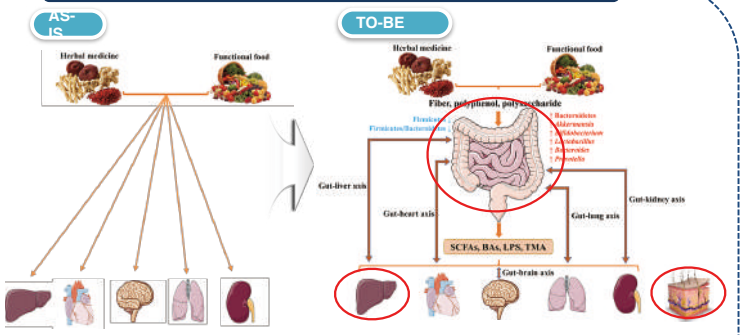
韩医学 – 五脏六腑舒适才健康



<五行与脏腑的关系图>

由于现代疾病的复杂性，需要通过具有挑战性的研究来开发疾病调节药物



- ✓ 一种模型治疗一种疾病的研究
- ✓ 开发个别疾病药物的局限
- ✓ 慢性疑难杂症持续增加
- ✓ 未满足的医疗需求技术领域

- ✓ 不是一种模型，而是通过连接肠-肝-皮肤轴的方法治疗疾病
- ✓ 通过多种轴研究扩展到代谢性、大脑、皮肤疾病等研究
- ✓ 提出慢性病和疑难杂症的治疗范式
- ✓ 提出解决方案来解决未满足的医疗需求

2

Development of Skin Health LAB-based on Gut Function

- Sunguk CHAE I KIOM

Pharmabiotics

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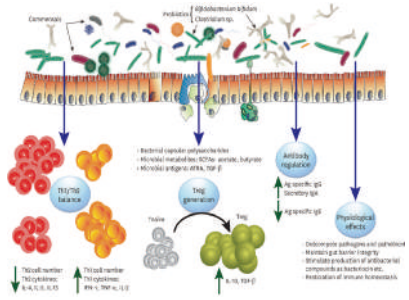
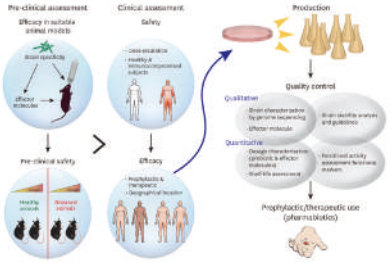
Pharmabiotics是意为医药的"Pharmaceuticals和意为有益活菌"益生菌(probiotics)"的合成词





SCIENTIFIC REPORTS

OPEN

Prevention of respiratory syncytial virus infection with probiotic lactic acid bacterium *Lactobacillus gasseri* SBT2055

SCIENTIFIC REPORTS

OPEN

Heat-killed *Lactobacillus casei* confers broad protection against influenza A virus primary infection and develops heterosubtypic immunity against future secondary infection

3

Gut-Brain-liver-Skin axis

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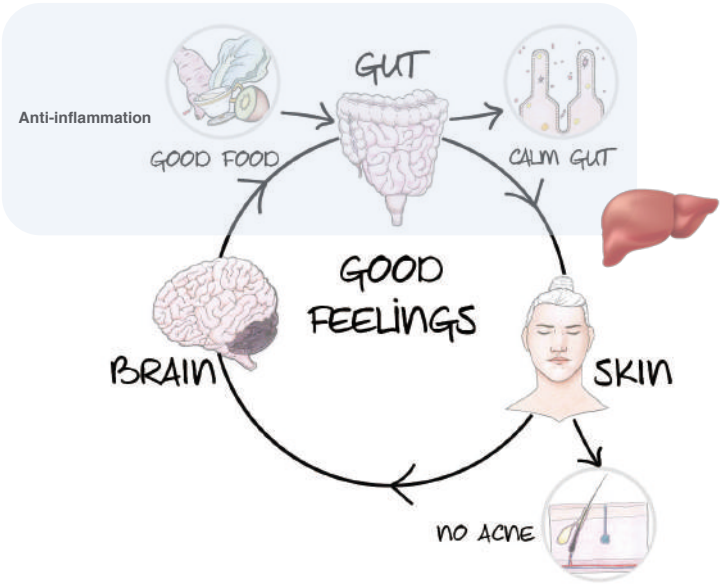

抗炎及免疫活性疗效评价

- 免疫细胞株的细胞增殖功能（in vitro）
- 脾组织分离免疫细胞的变化（in vivo）

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  - 测量表皮厚度和胶原蛋白的变化
  - 保湿（经皮水分蒸发量、保湿量）
- 诱发皱纹相关因子评价

https://www.janinetait.co.nz/29/the-new-science-on-acne/

4

Development of Skin Health LAB-based on Gut Function

- Sunguk CHAE I KIOM

Inflammation

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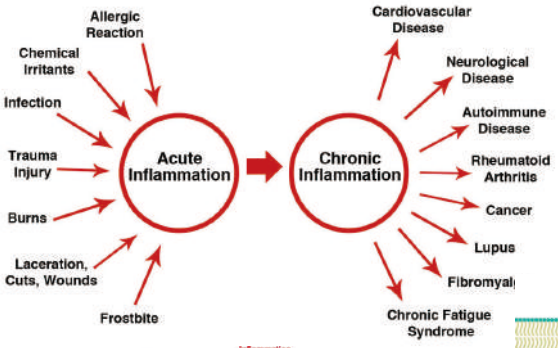
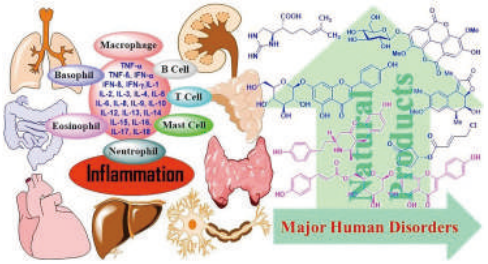
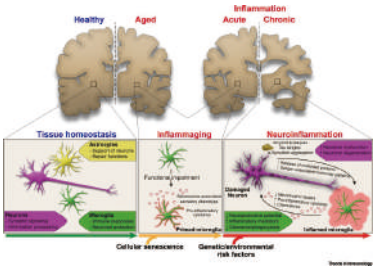
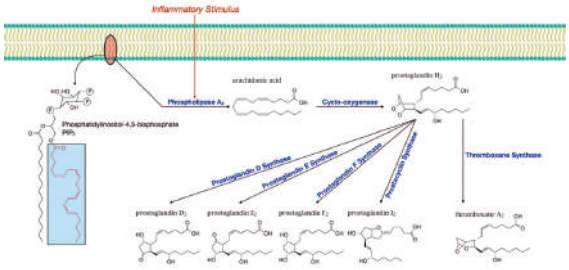
Acute Vs. Chronic Inflammation









5

Immune enhance

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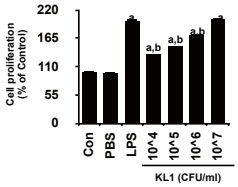
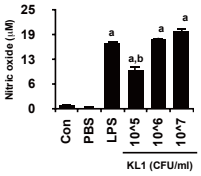
(A)



< Figure 1. Cell proliferation of RAW 264.7 cells (A) KL1 >

(A)



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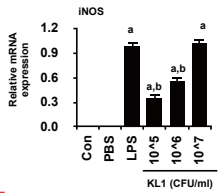
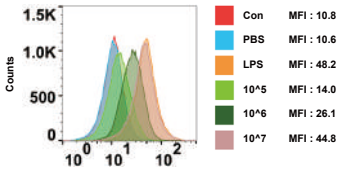
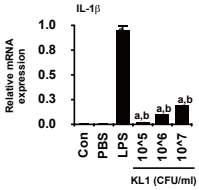


(C)

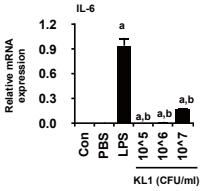


< Figure 2. The production of NO and ROS (A and B) KL1>

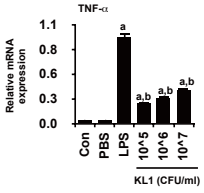
(A)



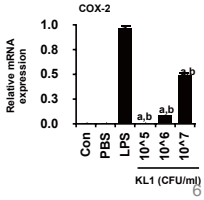
(B)



(C)



(D)



< Figure 3. The expression of inflammatory cytokines KL1>

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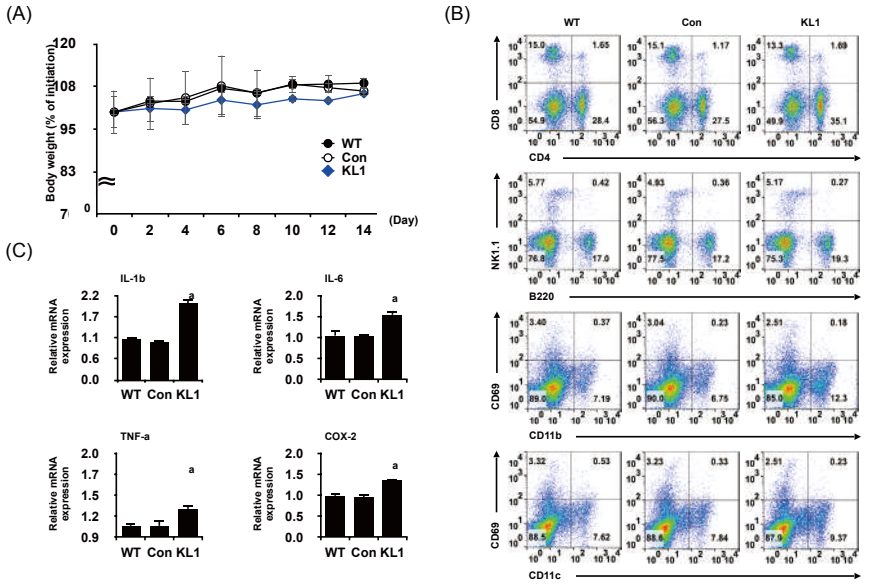
Development of Skin Health LAB-based on Gut Function

- Sunguk CHAE I KIOM

Immune enhance



< Figure 4. (A) Body weight (B) Immune cells population (C) Gene expression of inflammatory cytokines >

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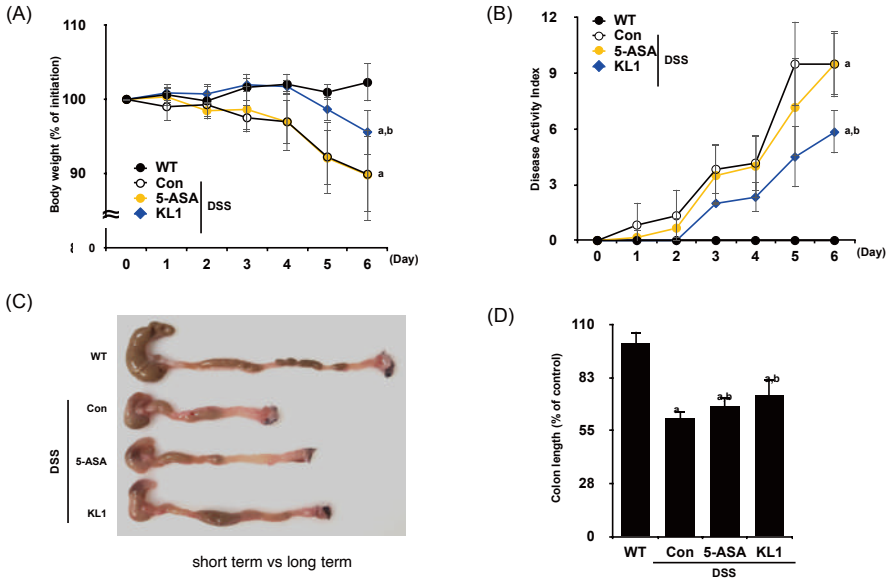
Inflammatory Bowel Disease



< Figure 5. Body weight DAI colon length>

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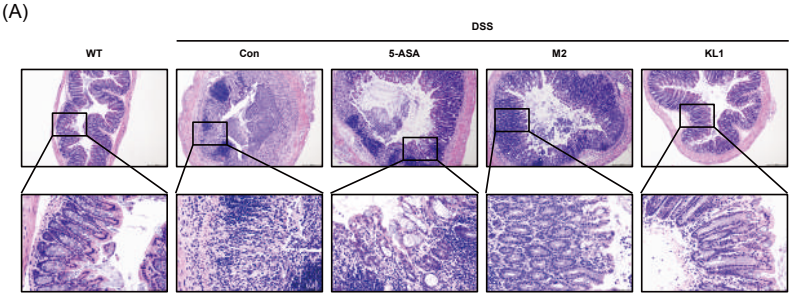
Inflammatory Bowel Disease

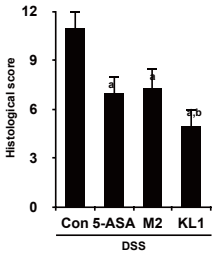
< Table 1. Disease activity index score >

Score	Weight loss	Stool consistency	Visible blood in rectal and feces
0	No weight loss	Well form pellets	No bleeding
1	1~5% weight loss		
2	5~10% weight loss	Loose stool	Slight bleeding
3	10~15% weight loss		
4	Over 15% weight loss	Diarrhoea	Gross bleeding

(A)



(B)



< Figure 6. Histology>

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Inflammatory Bowel Disease

< Table 2. Histological score >

Histological feature	Score	Description
Loss of epithelium	**0**	**None**
	1	**0~5% loss of epithelium**
	2	**5~10% loss of epithelium**
	3	**Over 10% loss of epithelium**
Crypt damage	**0**	**None**
	1	**0~10% loss of crypt**
	2	**10~20% loss of crypt**
	3	**Over 20% loss of crypt**
Depletion of goblet cells	**0**	**None**
	1	**Mild**
	2	**Moderate**
	3	**Severe**
Infiltration of inflammatory cells	**0**	**None**
	1	**Mild**
	2	**Moderate**
	3	**Severe**

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Inflammatory Bowel Disease

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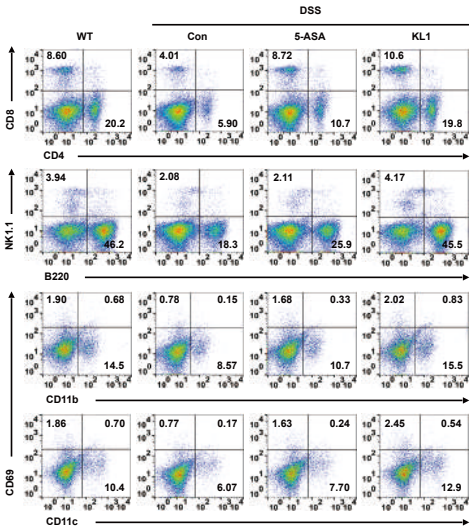
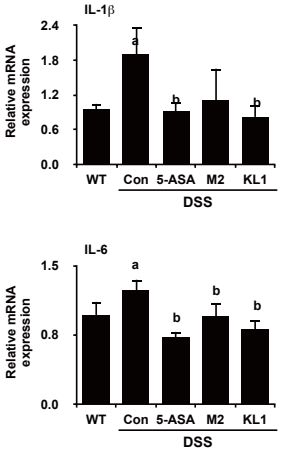
(A) Spleen



(B)



< Figure 7. Immune cell population and gene expression of inflammatory cytokines>

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Gut-Brain-liver-Skin axis

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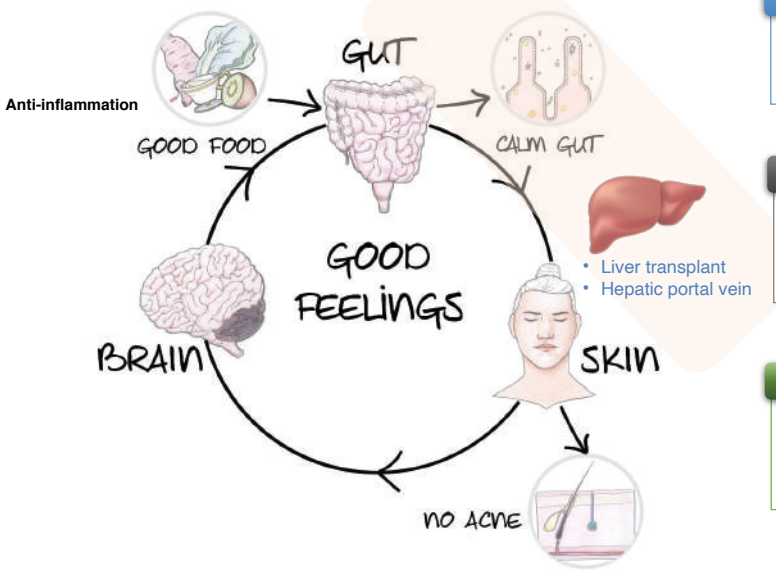

抗炎及免疫活性疗效评价

- ○ 免疫细胞株的细胞增殖功能 (in vitro)
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- ○ 诱发皱纹相关因子评价

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https://www.janinetait.co.nz/29/the-new-science-on-acne/

非酒精性脂肪肝(NAFLD)

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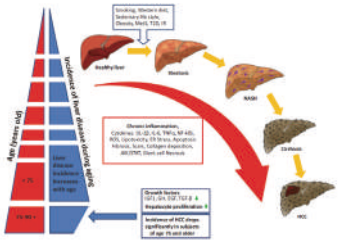
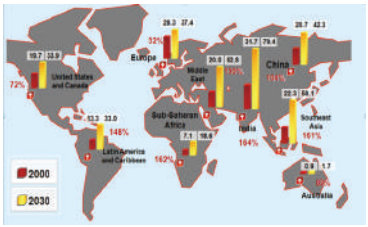
NAFLD患病率

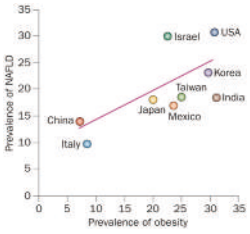
➢ Prevalence of NAFLD & Importance of NAFLD in Korean health care



< Liver disease proecess during aging>



<Worldwide prevalence of NAFLD>



<The prevalence of NAFLD and obesity>

References:
Aging Cell, 2013, 950-954
NEJM, 2007, 356, 213-215
Nat. Rev. Gastroenterol. Hepatol. doi:10.1038/nrgastro.2013.171
Curren Gerontology and Geriatrics Research, 2011, 831536

非酒精性脂肪肝(NAFLD)

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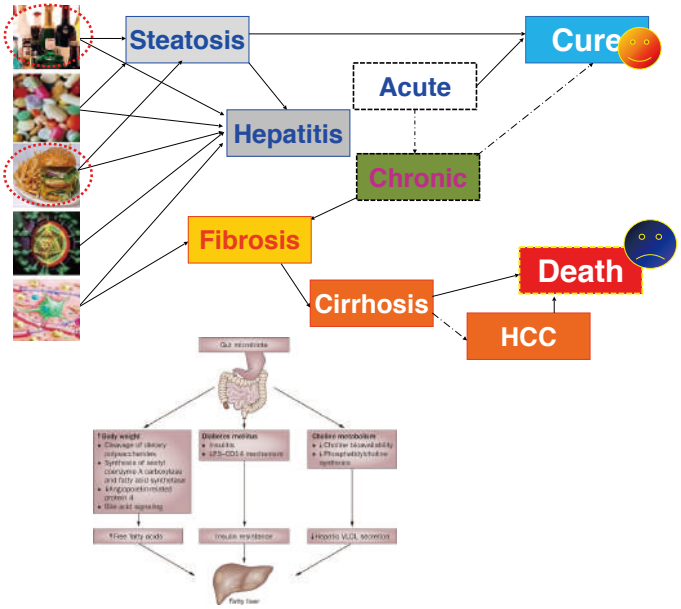
Complexity of Liver injury



非酒精性脂肪肝 - unmet needs

丙型肝炎 - 治愈率 90-100%

乙型肝炎 - 存在治疗药物

使用的治疗药物
- Vitamin E: fibrosis 没有改善
  No.1准则
- Pioglitazone：建议有糖尿病的患者服用

开发的治疗剂
- FXRagonist（胆汁酸衍生物）：有LDL增加的缺点
- PPAR-α/δ agonist
- Golden-505
- Aramchol

非酒精性脂肪肝(NAFLD)

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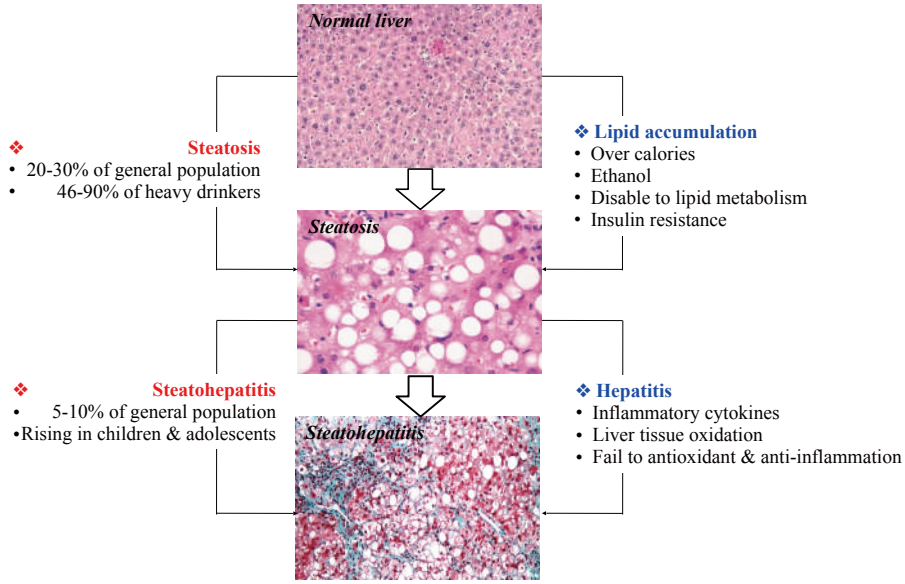
Distinguish between steatosis & steatohepatitis



Semin Liver Dis. 2007;27(2):173-193. [15]

非酒精性脂肪肝(NAFLD)模型

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Various animal models for adapting NASH

Table 1 Biochemical and pathological characteristics of animal models of nonalcoholic fatty liver disease/nonalcoholic steatohepatitis

	Model	Obesity	Insulin resistance	Steatosis	Steatohepatitis	Fibrosis
Genetic models	SREBP-1c transgenic mice	No (decreased adiposity)	Yes	Yes	Yes	Yes
	Ob/ob mice	Yes	Yes	Yes	No (does not develop spontaneously)	No (resistant to fibrosis)
	Db/db mice	Yes	Yes	Yes	No (does not develop spontaneously)	No (does not develop spontaneously)
	KK-A^y mice	Yes	Yes	Yes	No (does not develop spontaneously)	No (does not develop spontaneously)
	PTEN null mice	No	No	Yes	Yes	Yes
	PPAR-α knockout mice	No	No	No (steatosis occurs in the starved state)	No	No
	AOX null mice	No	No	Yes	Yes	No
	MAT1A null mice	No	No	Yes	Yes	Yes
Diet models	Methionine and choline deficiency	No (decreased weight and adiposity)	Hepatic insulin resistance	Yes	Yes (severe)	Yes
	High fat	Yes	Yes	Yes	Yes (mild)	Yes
	Cholesterol and cholate (atherogenic diet)	No (decreased weight)	Hepatic insulin resistance	Yes	Yes	Yes
	Fructose	No	Yes	Yes	No/Yes	No

SREBP: Sterol regulatory element binding protein; PTEN: Phosphatase and tensin homologue deleted on chromosome 10; AOX: Acyl-coenzyme A oxidase; MAT1A: Methionine adenosyltransferase-1A; PPAR: Peroxisome proliferator-activated receptor.

World J Gastroenterol 2012 21; 18(19): 2300-2308

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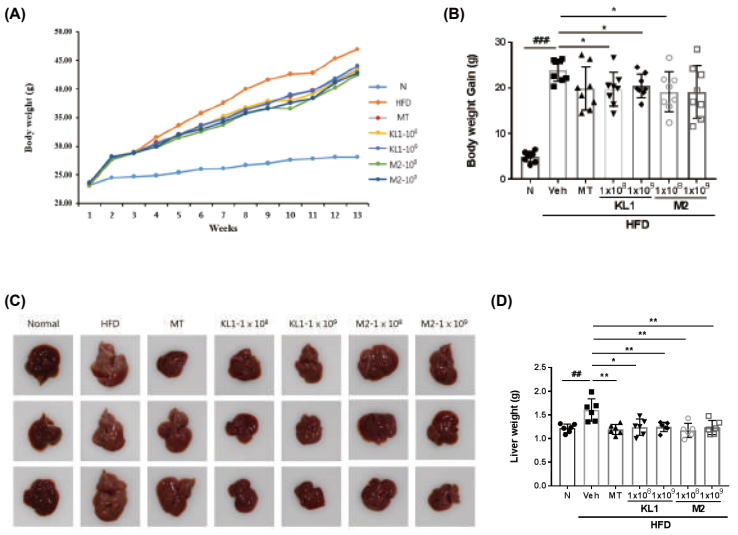
In vivo experiment



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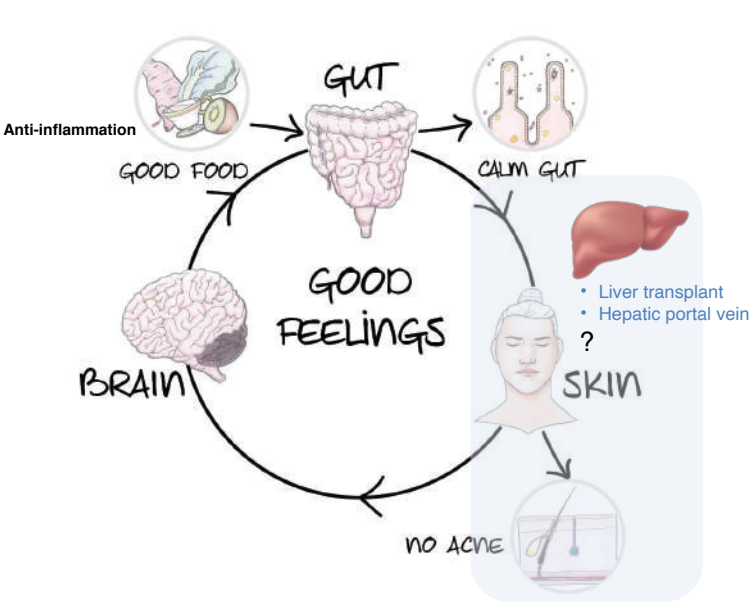
Gut-Brain-liver-Skin axis



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18

Development of Skin Health LAB-based on Gut Function

- Sunguk CHAE I KIOM

UVB induced photodamage or skin aging

This man was a trucker for 28 years... guess which side of his face was next to the window

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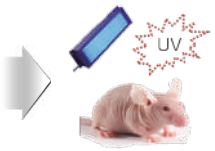
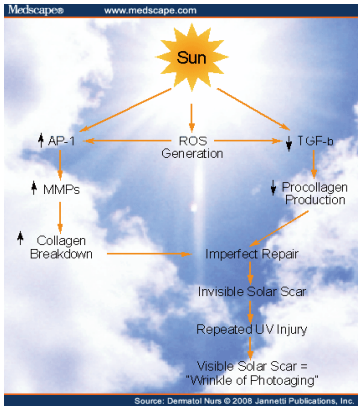
06/03/2012 12:08:00 Lena Sullivan / Dailymail





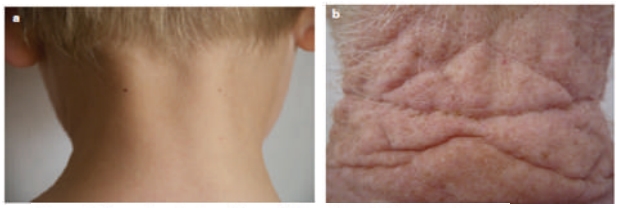
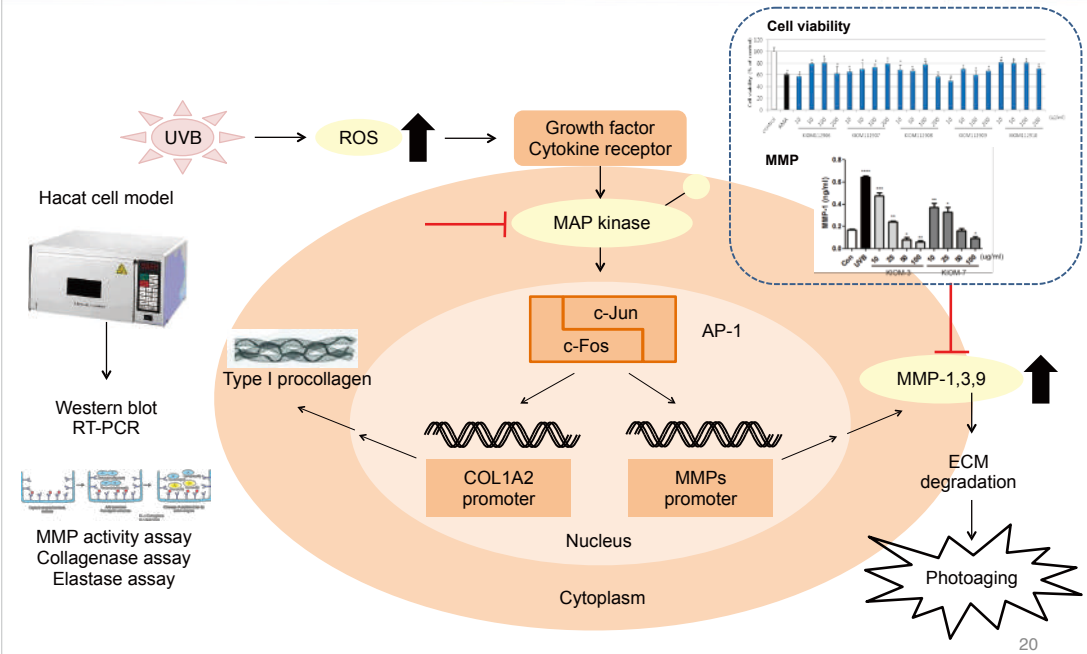


Figure 1 The neck region is readily, and often unknowingly, exposed to sunlight and is a primary site of photoaging. (a) Nonphotodamaged, youthful skin is smooth and elastic. (b) Elderly, photoaged skin is rough, mottled, rigid, and wrinkled.

19

In vitro experiment

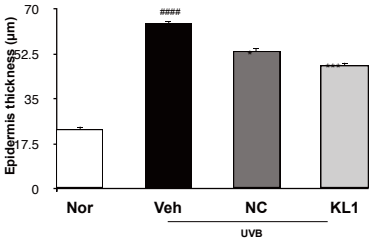


20

Development of Skin Health LAB-based on Gut Function

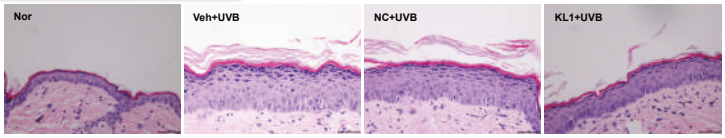
- Sunguk CHAE I KIOM

In vivo experiment

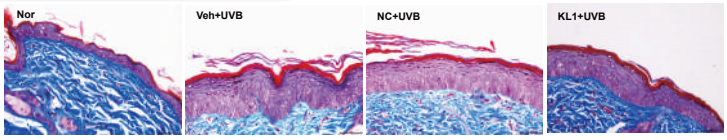


- UVB was applied three times a week for 12wks
- 60mJ/cm² at wk 1→ 90mJ/cm² at wk7

H & E staining

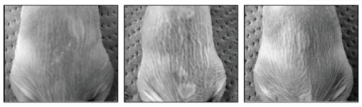


Masson's trichome staining



21

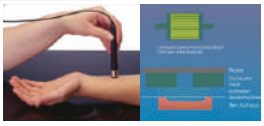
Skin barrier function

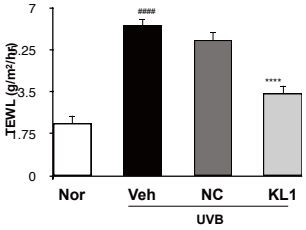


- UVB was applied three times a week
- Hairless mice
- Fillaggrin, involucrin, loricrin
- TM 300(C&K, Cologne, Germany)

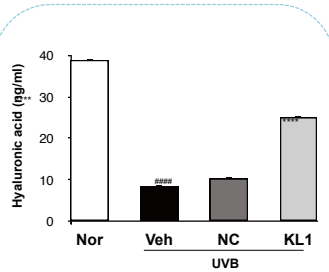
Tewameter

Corneometer

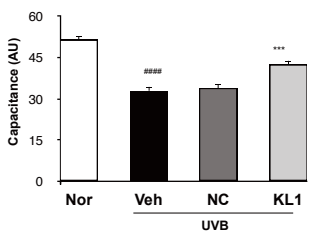




####: significantly different from normal (P<0.0001).
****: significantly different from UV (P<0.0001).



####: significantly different from normal (P<0.0001).
****: significantly different from UV (P<0.0001).



####: significantly different from control (P<0.0001).
***: significantly different from UV (P<0.001).

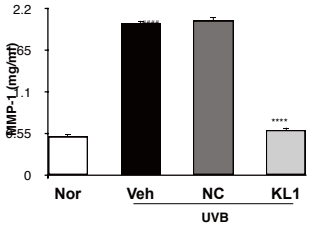
22

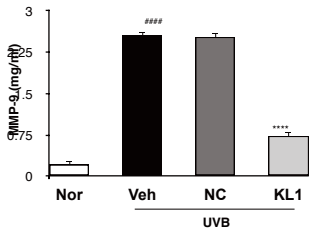
Development of Skin Health LAB-based on Gut Function

- Sunguk CHAE I KIOM

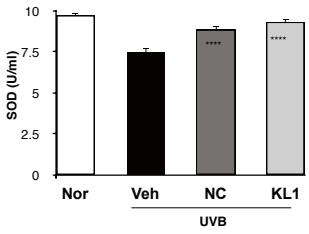
In vivo experiment

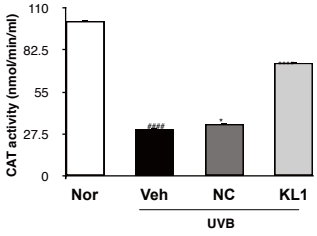
皱纹相关因子





抗氧化结果





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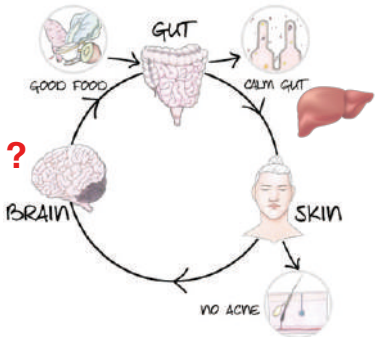
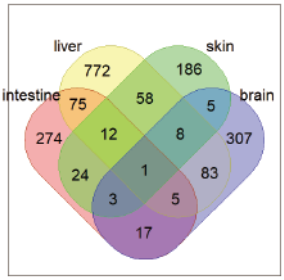
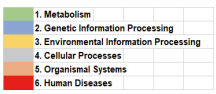
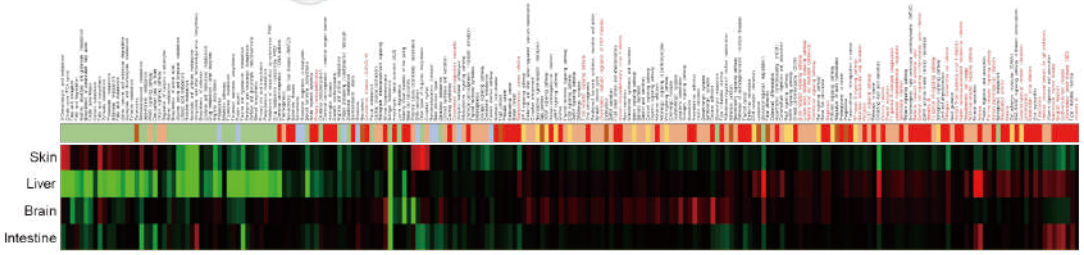
RNA-seq





	Intest	Liver	Skin	Br
Intest	2.921607	2.976151	3.006677	3.017026
Liver	2.976151	2.990348	3.048058	3.047496
Skin	3.006677	3.048058	3.071026	3.080604
Br	3.017026	3.047496	3.080604	3.045651





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Conclusion

한국한의학연구원 KOREA INSTITUTE OF ORIENTAL MEDICINE

改善非酒精性脂肪肝

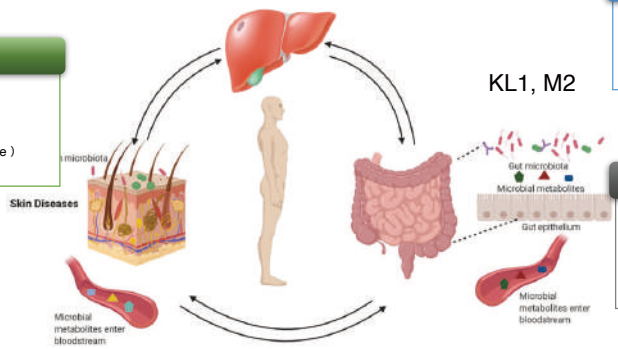
- ○ 肝组织和体重变化的测量
- - 脂肪组织、血液因子、体重及肝脏重量测量
- ○ 组织染色及相关因子评价

抗炎及免疫活性

- ○ 免疫细胞株的细胞增殖功能 (in vitro)
- ○ 脾组织分离免疫细胞的变化 (in vivo)

改善皮肤健康

- ○ 利用皮肤组织的疗效评价
- - 测量表皮厚度和胶原蛋白的变化
- - 保湿因子评价 (TEWL, capacitance)
- ○ 诱发皱纹相关因子评价



改善炎症性肠病

- ○ 炎症性肠病疗效评价
- - 测量体重变化和DAI变化
- ○ 评价免疫细胞的population变化
- - 脾组织分离免疫细胞变化

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한국한의학연구원 KOREA INSTITUTE OF ORIENTAL MEDICINE

Thank you for your attention

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PRESENTATION

Jiliang FANG
CACMS

THE BRAIN MECHANISM OF TAVNS ON MCI BY FMRI

Clinical Observation of taVNS Therapy for MCI and Study on its Brain Mechanism by fMRI

taVNS治疗MCI的临床观察及fMRI脑机制研究

Jiliang Fang MD. PhD, Professor
方继良 教授
Guang'anmen Hospital,China Academy of Chinese Medical Sciences
中国中医科学院广安门医院
Oct. 30, 2024, Daejeon

针灸是中华民族的瑰宝(非物质世界文化遗产)

Acupuncture is the treasure of Intangible Cultural Heritage of Humanity from China (Nov.16.2010, UNESCO)

1. Chinese original non-drug green therapy
   中国原创的非药物绿色疗法
2. Protecting the Chinese nation for over 3000 years
   护佑中华民族繁衍生息3000余年
3. Effective, convenient, affordable, and easy to promote.
   有效、简便、价廉、易推广

Modern bronze statue of acupuncture in WHO office
Gift by China in 2017

Chairman Xi stated: "We must inherit, develop, and make good use of traditional medicine." when he visited WHO in 2017

2017年1月20日中国向世卫组织赠送了针灸铜人雕塑，习主席在致辞中说：要继承好、发展好、利用好传统医学

Current Status of Acupuncture

- 192 countries and regions. 192个国家和地区应用针灸
- The legal status in 59 countries. 59个国家明确了针灸的法律地位
- Health insurance coverage in 20 countries and regions. 20个国家和地区将中医针灸纳入医疗保险范畴
- Some universities have the faculty of acupuncture and offer courses
  部分大学设立针灸系、开设针灸课程
- Acupuncture centers as the primary model for providing traditional medical services in many countries.针灸中心已成为许多国家提供传统医药服务的主要模式和场所

More papers published in Top International Journals in the Past Decade

- **2015 Jiliang Fang and Peijing Rong's team**"Transcutaneous Vagus Nerve Stimulation Modulates Default Mode Network in Major Depressive Disorder. " **< Biological Psychiatry>** **（ IF 11.98）**
  2015年中国中医科学院方继良、荣培晶团队“耳电针刺激迷走神经调制抑郁症脑默认网络” 发表《生物医学精神医学》（ IF 11.98）
- **2016 Zhishun Liu and Baoyan Liu's team**"Acupuncture for Chronic Severe Functional Constipation: A Randomized Trial" **<Annals of Internal Medicine>（ IF 16）**
  2016年中国中医科学院刘志顺、刘保延团队的“电针治疗严重功能性便秘”发表于 **《内科学年鉴》（ IF 16）**
- **2017 Zhishun Liu and Baoyan Liu's team**"Effect of Electroacupuncture on Urinary Leakage Among Women With Stress Urinary Incontinence: A Randomized Clinical Trial."**< JAMA > (IF 44.41)**
  2017年 中国中医科学院刘志顺、刘保延团队“电针治疗女性压力性尿失禁的随机对照试验”。**发表于《美国医学会会刊》(IF 44.41)**
- **2017 Fanrong Liang's team** "The Long-term Effect of Acupuncture for Migraine Prophylaxis: A Randomized Clinical Trial. " **< JAMA Internal Medicine> IF 20.79）**
  2017年成都中医药大学 梁繁荣团队 “ 针刺预防偏头痛的长期效应：一项随机临床试验”发表于 美国医学会会刊：内科学》（IF 20.79）
- **2019 Fanrong Liang's team**"Acupuncture as Adjunctive Therapy for Chronic Stable Angina: A Randomized Clinical Trial. " **< JAMA Internal Medicine> IF 20.79）**
  2019年 成都中医药大学 梁繁荣团队“针灸辅助治疗慢性稳定性心绞痛临床随机试验” 发表于 《美国医学会会刊：内科学》（IF 20.79）

- **2020 Wei Wang's team“** Manual acupuncture versus sham acupuncture and usual care for prophylaxis of episodic migraine without aura: multicentre, randomised clinical trial. **” < BMJ >(IF 17)**
  2020年 同济大学王伟团队“ 针刺防治无先兆偏头痛的有效性研究 ” 发表于《英国医学会会刊》 上(IF 17)
- **2020 Cunzhi Liu's team“** Effect of Acupuncture for Postprandial Distress Syndrome: A Randomized Clinical Trial. **” <Annals of Internal Medicine>（ IF 19）**
  2020年5月13日，北京中医药大学刘存志教授团队 “ 针刺治疗餐后紧张综合症临床研究” 发表于《内科学年鉴》（ IF 19）
- **2021 Cunzhi Liu's team"** Efficacy of Intensive Acupuncture Versus Sham Acupuncture in Knee Osteoarthritis: A Randomized Controlled Trial.**” < Arthritis & Rheumatology>（ IF 7.87）**
  2021年北京中医药大学刘存志教授团队“针刺治疗膝骨关节炎的临床研究” 发表于风湿病学期刊< Arthritis & Rheumatology>《关节炎与风湿病》（ IF 7.87）
- **2023 Xiaoke Wu's team“**Acupuncture and Doxylamine-Pyridoxine for Nausea and Vomiting in Pregnancy : A Randomized, Controlled, 2 2 Factorial Trial.**” <Annals of Internal Medicine>（IF 51.6）**
  2023年黑龙江中医药大学吴效科团队“针刺联合多西拉敏治疗妊娠呕吐临床随机对照研究” 发表于《内科学年鉴》（IF 51.6）
- **2023 Ying Li's team“**Efficacy of Acupuncture for Chronic Spontaneous Urticaria : A Randomized Controlled Trial.**” <Annals of Internal Medicine>（IF 39.2）**
  2023年成都中医药大学 李瑛团队“针灸辅助治疗慢性荨麻疹临床随机试验” 发表于《内科学年鉴》（IF 39.2）

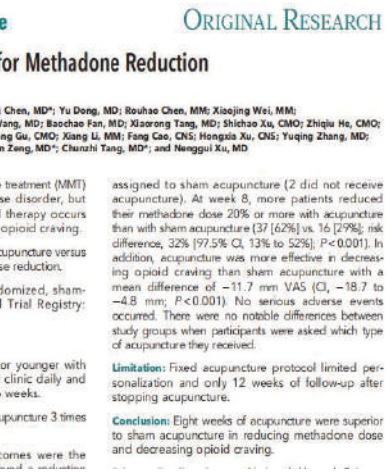
The Brain Mechanism of TaVNS on MCI by fMRI

- Jiliang FANG I CACMS

Annals of Internal Medicine 2023 IF 19.6

2024.7许能贵教授针灸戒毒

2024.7刘志顺教授针灸治疗椎管狭窄



Annals of Internal Medicine ORIGINAL RESEARCH

Effect of Acupuncture for Methadone Reduction

A Randomized Clinical Trial

Liming Lu, MD*; Chen Chen, MD*; Yiming Chen, MD*; Yu Dong, MD; Rouhao Chen, MM; Xiaojing Wei, MM; Chenyang Tao, MM; Cui Li, MM; Yuting Wang, MD; Baochao Fan, MD; Xiaorong Tang, MD; Shichao Xu, CMO; Zhiqiu He, CMO; Guodong Mo, CMO; Yiliang Liu, CMO; Hong Gu, CMO; Xiang Li, MM; Fang Cao, CNS; Hongxia Xu, CNS; Yuqing Zhang, MD; Guowei Li, MD; Xinxia Liu, CMO; Jingchun Zeng, MD*; Chunzhi Tang, MD*; and Nenggui Xu, MD

Background: Methadone maintenance treatment (MMT) is effective for managing opioid use disorder, but adverse effects mean that optimal therapy occurs with the lowest dose that controls opioid craving.

Objective: To assess the efficacy of acupuncture versus sham acupuncture on methadone dose reduction.

Design: Multicenter, 2-group, randomized, sham-controlled trial. (Chinese Clinical Trial Registry: ChiCTR2200058123)

Setting: 6 MMT clinics in China.

Participants: Adults aged 65 years or younger with opioid use disorder who attended clinic daily and had been using MMT for at least 6 weeks.

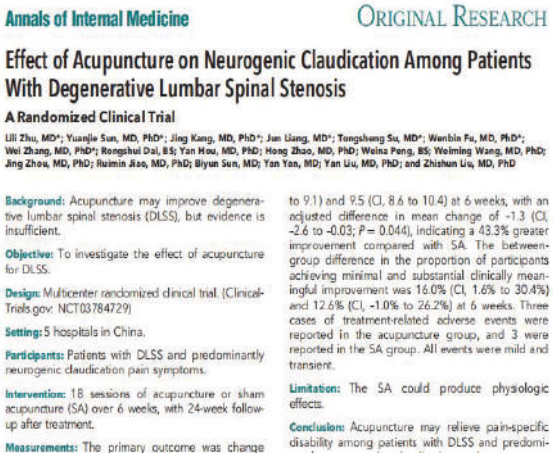
Intervention: Acupuncture or sham acupuncture 3 times a week for 8 weeks.

Measurements: The 2 primary outcomes were the

assigned to sham acupuncture (2 did not receive acupuncture). At week 8, more patients reduced their methadone dose 20% or more with acupuncture than with sham acupuncture (37 [62%] vs. 16 [29%]; risk difference, 32% [97.5% CI, 13% to 52%]; $P < 0.001$). In addition, acupuncture was more effective in decreasing opioid craving than sham acupuncture with a mean difference of −11.7 mm VAS (CI, −18.7 to −4.8 mm; $P < 0.001$). No serious adverse events occurred. There were no notable differences between study groups when participants were asked which type of acupuncture they received.

Limitation: Fixed acupuncture protocol limited personalization and only 12 weeks of follow-up after stopping acupuncture.

Conclusion: Eight weeks of acupuncture were superior to sham acupuncture in reducing methadone dose and decreasing opioid craving.



Annals of Internal Medicine ORIGINAL RESEARCH

Effect of Acupuncture on Neurogenic Claudication Among Patients With Degenerative Lumbar Spinal Stenosis

A Randomized Clinical Trial

Lili Zhu, MD*; Yuanjie Sun, MD, PhD*; Jing Kang, MD, PhD*; Jun Liang, MD*; Tongsheng Su, MD*; Wenbin Fu, MD, PhD*; Wei Zhang, MD, PhD*; Rongshui Dai, BS; Yan Hou, MD, PhD; Hong Zhao, MD, PhD; Weina Peng, BS; Weiming Wang, MD, PhD; Jing Zhou, MD, PhD; Ruimin Jiao, MD, PhD; Biyun Sun, MD; Yan Yan, MD; Yan Liu, MD, PhD; and Zhishun Liu, MD, PhD

Background: Acupuncture may improve degenerative lumbar spinal stenosis (DLSS), but evidence is insufficient.

Objective: To investigate the effect of acupuncture for DLSS.

Design: Multicenter randomized clinical trial. (ClinicalTrials.gov: NCT03784729)

Setting: 5 hospitals in China.

Participants: Patients with DLSS and predominantly neurogenic claudication pain symptoms.

Intervention: 18 sessions of acupuncture or sham acupuncture (SA) over 6 weeks, with 24-week follow-up after treatment.

Measurements: The primary outcome was change

to 9.1) and 9.5 (CI, 8.6 to 10.4) at 6 weeks, with an adjusted difference in mean change of −1.3 (CI, −2.6 to −0.03; $P = 0.044$), indicating a 43.3% greater improvement compared with SA. The between-group difference in the proportion of participants achieving minimal and substantial clinically meaningful improvement was 16.0% (CI, 1.6% to 30.4%) and 12.6% (CI, −1.0% to 26.2%) at 6 weeks. Three cases of treatment-related adverse events were reported in the acupuncture group, and 3 were reported in the SA group. All events were mild and transient.

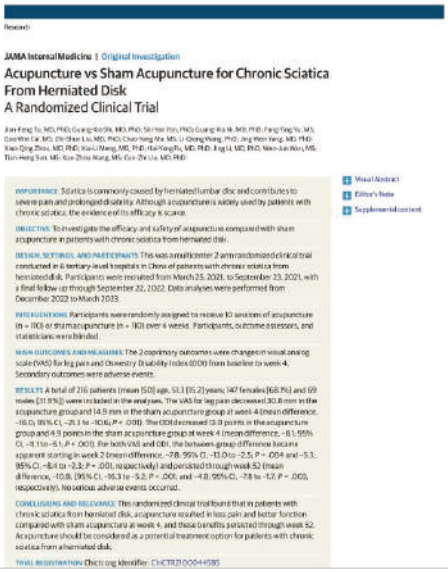
Limitation: The SA could produce physiologic effects.

Conclusion: Acupuncture may relieve pain-specific disability among patients with DLSS and predomi-

JAMA Internal Medicine IF 22.5 Q1

2024.10.刘存志教授针灸治疗坐骨神经痛

2024年10月14日，北京中医药大学刘存志教授团队在国际权威期刊《JAMA Internal Medicine》以原创性论著（Research，Original Investigation）形式全文发表《针刺治疗腰椎间盘源性慢性坐骨神经痛的随机对照临床研究》。针灸推拿常见腰椎间盘突出节段（L4-5、L5-S1）引起的坐骨神经痛症状表现与中医典籍中足少阳胆经和足太阳膀胱经的循行分布基本吻合。课题组基于此开展了90例小样本预试验发现循经取穴较非循经取穴和非经非穴疗效更佳。在长期临床经验和前期制定的专家共识（J Pain Res. 2021; PMID: 33447076）基础上，形成了大肠俞、关元俞及秩边、环跳深刺得气的循经配穴半标准化针刺治疗方案。此项临床研究共纳入216例腰椎间盘源性慢性坐骨神经痛患者，随机分为针刺组和假针组，前2周每周治疗3次，后2周每周治疗2次，4周共计10次。针刺操作均由获得中医执业医师资格证并具有3年以上临床工作经验的针灸师操作。在第4周时，针刺治疗可以使腿痛评分下降30.8分，假针下降14.9分，组间差异16.0分大于预设的最小临床重要性差值（15分）；针刺使腰椎功能改善13.0分，假针改善4.9分，组间差异8.1分大于预设的最小临床重要性差值（7分），疗效至少可维持1年。该试验为针灸循经取穴提供了现代临床试验数据支撑，也为针刺治疗慢性坐骨神经痛的临床疗效提供了高质量临床证据。



JAMA Internal Medicine | Original Investigation

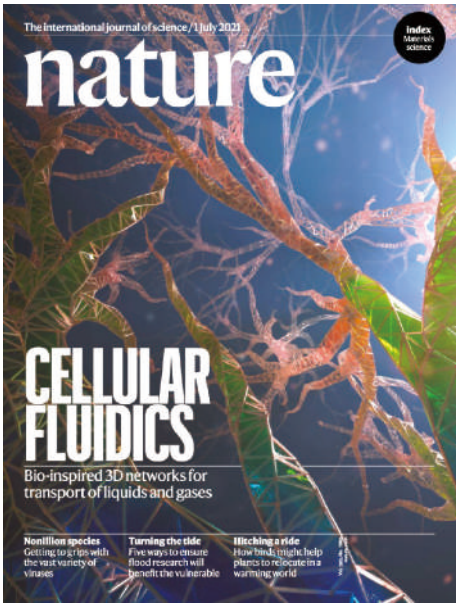
Acupuncture vs Sham Acupuncture for Chronic Sciatica From Herniated Disk

A Randomized Clinical Trial

World-class university hospital: Massachusetts General Hospital of Harvard University
世界一流大学医院:哈佛大学麻省总医院

Acupuncture Neuroimaging Center: NIH's Largest Project, PPG, with a Grant of US$5 Million for Research on the Brain Mechanism of Acupuncture (2004-2008)

针刺神经影像中心：NIH最大项目PPG 500万资助针灸脑功能机理研究（2004-2008）



EA anti imflamation by Prof. MA Qiufu in 2021

马秋富针灸抗炎论文--2021自然杂志


Nature Article

A neuroanatomical basis for electroacupuncture to drive the vagal–adrenal axis

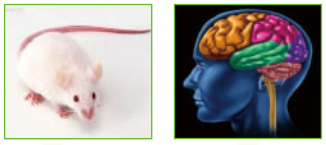
On October 13, 2021, Prof. Ma Qiufu's team from Harvard Medical School published a paper revealing the foundation of acupuncture's anti-inflammatory effects and achieving a historic breakthrough.

2021年10月13日，哈佛大学医学院马秋富教授团队在 Nature 发表论文揭示针灸抗炎基础，实现历史性突破。

9

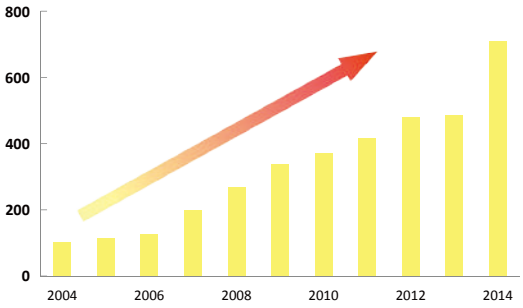
Global research on the mechanisms of acupuncture continues to heat up.
全球针刺机理研究持续升温

Research on acupuncture mechanisms
针刺机理研究



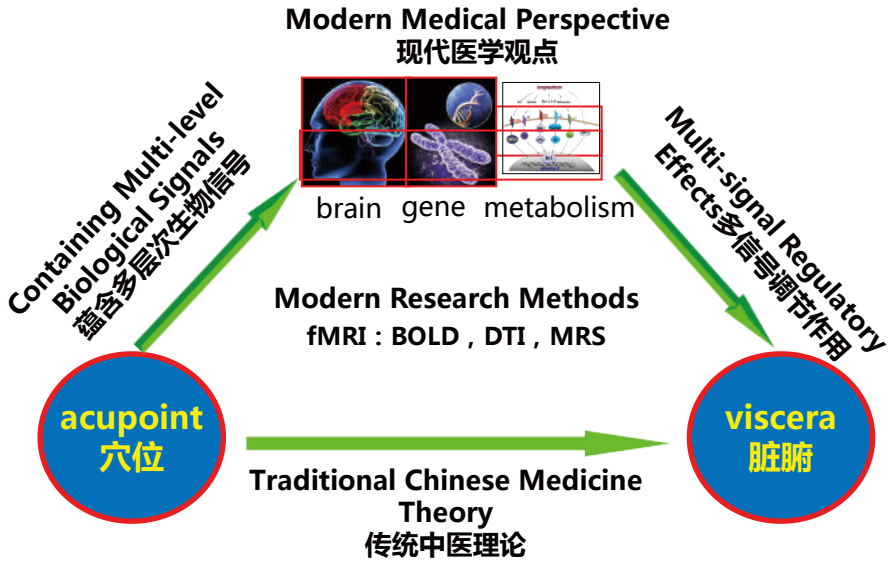
Animal experiments to search for molecular changes
动物实验寻找分子变化

Human trials to explore brain function
人体试验探索大脑功能



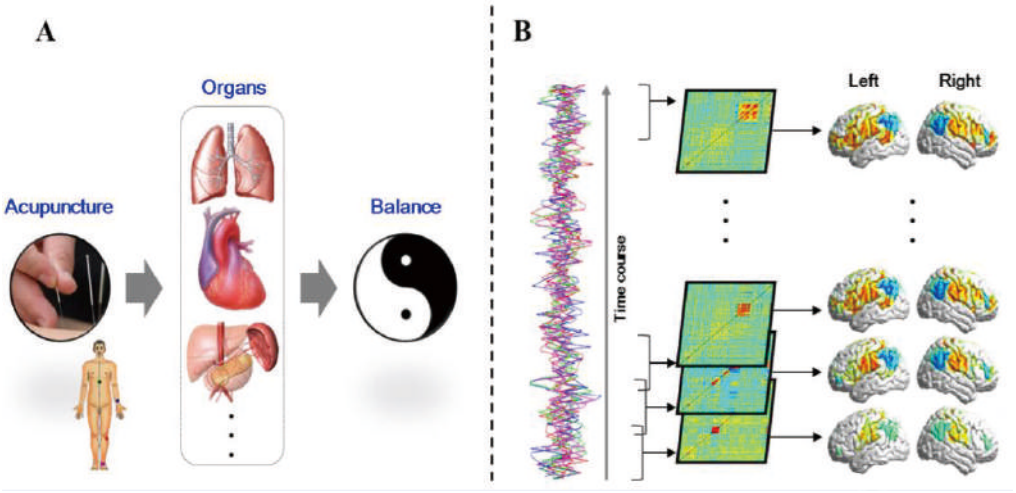
According to statistics from PubMed, the most authoritative professional database in the global medical field, there have been over 3,500 SCI-retrieved research articles on acupuncture mechanisms since 2000.
据全球医药领域最权威专业数据库PubMed统计，2000年至今，SCI检索的针刺机理研究文献已达3500多篇

Overview: Research on the Brain Mechanisms of Acupuncture (1)
概述: 针刺脑机理研究(1)



Overview: Research on the Brain Mechanisms of Acupuncture (2)

概述：针刺机理脑功能成像研究(2)



Examples：fMRI in Acupuncture Research

fMRI: 针灸研究的应用举例

--Research on the Brain Mechanisms of Tancutaneous Auricular Vagus Nerve Stimulation (taVNS) in Treating Diseases by fMRI

耳电针治疗疾病的脑影像机制研究

The Brain Mechanism of TaVNS on MCI by fMRI

- Jiliang FANG I CACMS

Research on Auricular Point--Vagus Nerve Connection
耳穴－迷走神经联系研究

- **Over the past decade, led by Professor Bing Zhu(the Institute of Acupuncture and Moxibustion) has established the "auricular point-vagus nerve connection."**

●20年来，针灸所在朱兵研究员率领下，在首次建立"耳穴－迷走神经联系"的基础上，注意到耳甲区存在唯一体表分布有迷走神经的区域，它的传入可直接投射到迷走神经中枢

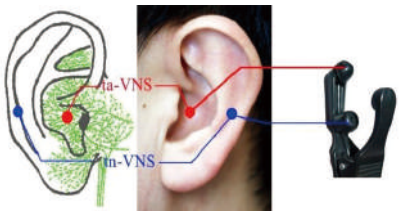
- **Invention of auricular vagus nerve electrical stimulation device, and was used for epilepsy and depression with significant therapeutic effect.**

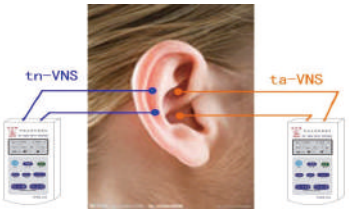
成功研制了耳迷走神经电刺激仪。已用于治疗癫痫病及抑郁症,初步发现有一定疗效

TABLE 1. Overview of the Innervation Pattern of the Lateral Surface of the Auricle

	ABVN	GAN	ATN
Crus of helix	20%		80%
Spine of helix		9%	91%
Tail of helix		100%	
Scapha		100%	
Crura of anthelix	9%	91%	
Antihelix	73%	9%	18%
Antitragus		100%	
Tragus	45%	46%	9%
Cymba conchae	100%		
Cavity of concha	45%	55%	
Lobule of auricle		100%	

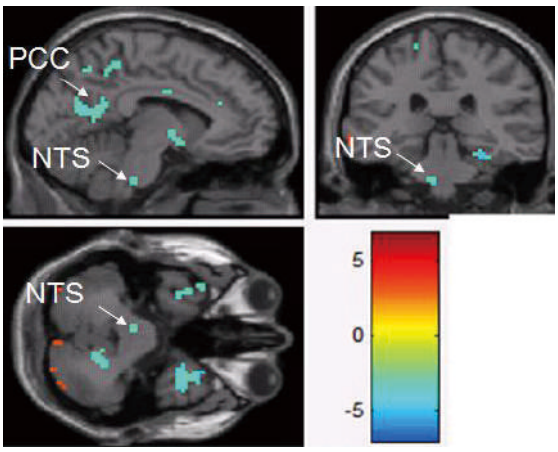
ABVN = auricle branch of the vagus nerve; GAN = great auricular nerve; ATN = auriculotemporal nerve.





1. Fang, et al.BP. 2016
2. Liu, et al. JAD. 2016

Brain Activation Pathways of taVNS

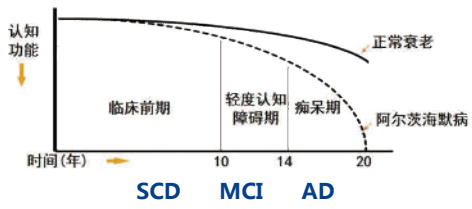


Jiliang Fang, Peijing Rong, Bing Zhu, et al. Journal of Magnetic Resonance Imaging, 2014
方继良, 荣培晶，朱兵，等. 磁共振成像杂志， 2014

Clinical Study on taVNS Treating MCI

taVNS治疗轻度认知障碍的临床研究

Epidemiological Overview



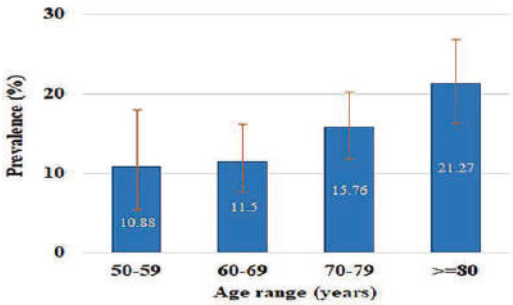
SCD MCI AD

In TCM), terms such as "forgetfulness" "prone to forgetting" and "easy to forget"

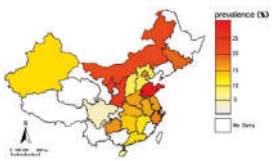
中医：“健忘”、“善忘”、“喜忘”等，多为气血、肾精不足，痰浊、瘀血蒙蔽清窍，脑脉不通所致

MCI patients have a higher risk of progressing to dementia (AD), which is approximately 14.9%.

Epidemiological Overview of MCI Among People Aged 50 and Above Worldwide



MCI Among People Aged 60 and Above in China



The prevalence of MCI is 14.71%.

中国老年人口中MCI的综合患病率为14.71%

MCI patients

1 Inclusion criteria

(1) Self-reported or family-confirmed cognitive decline, with basically normal daily living functions, and meeting the diagnostic criteria ;

(2) Aged 55-79 years old, right-handed ;

(3) The Montreal Cognitive Assessment Basic version (MoCA-B) scores meet the following criteria: a score of ≤19 for those with ≤6 years of education; a score of ≤22 for those with 7-12 years of education; and a score of ≤24 for those with >12 years of education ;

(4) No obvious parenchymal brain lesions, such as cerebral infarction or liquefactive necrosis, were observed on MRI ;

(5) Voluntarily signed the informed consent form.

2 Exclusion criteria

(1) Cognitive decline caused by clear etiologies, such as vascular cognitive impairment, Parkinson's disease-related cognitive impairment, and diabetic cognitive impairment ;

(2) Suffering from acute or severe life-threatening illnesses ;

(3) Unable to cooperate with cognitive scale assessments due to severe hearing, vision, or other impairments ;

(4) Taking medications for cognitive impairment, psychotropic drugs, or substance abuse ;

(5) Severe mental illnesses, such as major depressive disorder, anxiety disorders, and others ;

(6) Having contraindications for MRI scans (such as metal implants, claustrophobia, pacemakers, etc.)

MCI患者

1 纳入标准

（1）自觉或家人证实存在认知功能下降，但日常生活功能基本正常，且符合诊断标准；

（2）年龄55-79岁，右利手；

（3）蒙特利尔认知量表基础版（MoCA-B）评分符合以下标准：评分≤19分（受教育年限≤6年）；评分≤22分（受教育年限7-12年）；评分≤24分（受教育年限>12年）；

（4）核磁检查未见明显脑实质病变，如脑梗死、脑液化性坏死等；

（5）自愿签署知情同意书。

2 排除标准

（1）有明确病因导致的认知下降，如血管性认知障碍、帕金森认知障碍、糖尿病认知障碍等；

（2）患有急性或重大疾病威胁生命；

（3）严重的听力、视力等问题不能配合认知量表评估；

（4）服用治疗认知的药物、精神类药物或药物滥用；

（5）严重的精神疾病，如重度抑郁、焦虑症等；

（6）有核磁共振检查禁忌症（金属内置物、幽闭恐惧症、心脏起搏器等）。

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Healthy controls

1 Inclusion criteria

(1) Those without obvious complaints of memory decline or cognitive impairment, who do not meet the diagnostic criteria for cognitive decline based on cognitive assessments, and who have MoCA-B scores indicating no cognitive decline ;

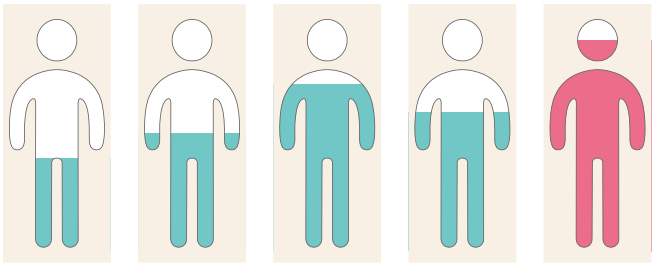
(2) Aged 55-79 years old, right-handed ;

(3) Voluntarily signed the informed consent form.

2 exclusion criteria

(1) Having contraindications for MRI scans (such as metal implants, claustrophobia, pacemakers, etc.) ;

(2) MRI scans reveal obvious cerebral organic lesions (such as old cerebral infarction).



健康对照

1 纳入标准

(1) 无明显记忆下降或认知障碍主诉，认知评估未达到诊断标准及MoCA-B评分未见认知下降者；

(2) 55-79岁，右利手；

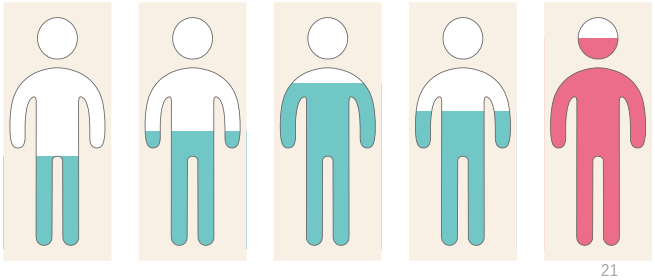
(3) 自愿签署书面知情同意书者。

2 排除标准

(1) 有核磁共振检查禁忌症 (金属内置物、幽闭恐惧症、心脏起搏器等) ；

(2) 神经精神疾病病史者；

(3) 核磁检查见明显脑器质性病变 (陈旧性脑梗死等) 。



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The Brain Mechanism of TaVNS on MCI by fMRI

- Jiliang FANG I CACMS

Treatment method

taVNS group：

（1）Stimulation site: Auricular points Heart and Kidney.

（2）Device: Huatuo Brand Electronic Acupuncture Therapy Device (Model SDZ-ⅡB, Suzhou Medical Supplies Factory Co., Ltd.).

（3）Treatment parameters：dense-disperse waves, 20/100Hz, 3-8mA.

Ear clips are worn on both ears simultaneously.

30 minutes each in the morning and evening, five days a week

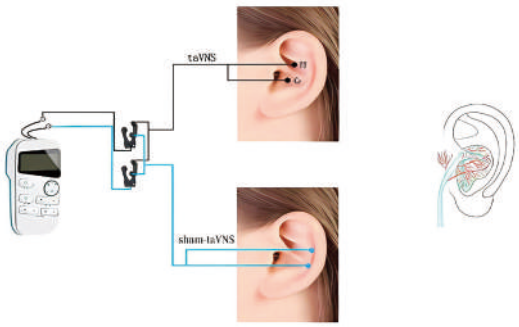
Total of 24 weeks of continuous self-served treatment at home.

sham taVNS group：

（1）Stimulation site: Auricular points Elbow and Shoulder located in the scaphoid fossa.

（2）Device: Same as taVNS group.

（3）Treatment parameters：Similar as taVNS group.



治疗方法

taVNS组：

（1）刺激部位：迷走神经耳支分布密集的耳甲腔内的耳穴心、肾。

（2）治疗仪：华佗牌电子针疗仪（SDZ-ⅡB型，苏州医疗用品厂有限公司）。

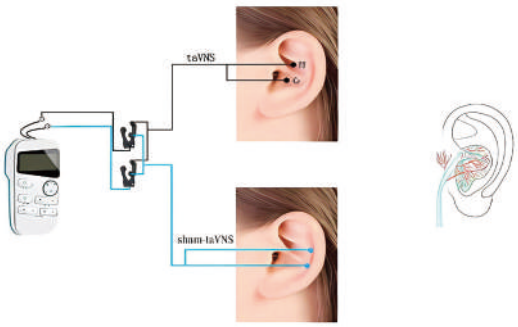
（3）治疗参数：疏密波，频率为20/100Hz，电流强度在3-8mA范围内调节，以患者能忍受无明显疼痛为度，双耳同时戴上耳夹，每天早晚各治疗30分钟，每周5天，居家自行治疗，连续治疗24周。

sham taVNS组：

（1）刺激部位：耳舟非迷走神经分布区的耳穴肘、肩。

（2）治疗仪：同taVNS组。

（3）治疗方法及治疗参数：同taVNS组。



Treatment assessment

Baseline Assessment (Patients + HCs):
1)Primary and Secondary Outcome Measures
2)Functional Activities Questionnaire (FAQ)
3)17-item Hamilton Depression Rating Scale (HAMD-17)
4)Hamilton Anxiety Rating Scale (HAMA)

Assessment after 24 Weeks of Treatment (Only Patients):
Primary and Secondary Outcome Measures
17-item Hamilton Depression Rating Scale (HAMD-17)
Hamilton Anxiety Rating Scale (HAMA)
Primary Outcome Measure:
Montreal Cognitive Assessment Basic Version (MoCA-B)
Secondary Outcome Measures:

- Auditory Verbal Learning Test - Huashan Version (AVLT-H)
- Shape Trail Making Test A and B (STT A&B)
- Animal Fluency Test (AFT)
- Boston Naming Test (BNT)

治疗评估

基线评估（患者+健康对照）：
主、次要疗效指标+社会活动功能量表(FAQ)
+17项汉密尔顿抑郁量表（HAMD-17）+汉密尔顿焦虑量表（HAMA）

治疗24周后评估（仅患者）：
主、次要疗效指标+17项汉密尔顿抑郁量表（HAMD-17）+汉密尔顿焦虑量表（HAMA）

•主要疗效指标：蒙特利尔认知评估量表基础版（MoCA-B）
•次要疗效指标:

① 华山版听觉词语学习测验（AVLT-H）
② 形状连线测验A和B (STT A&B)
③ 动物词语流畅性测试（AFT）
④ 波士顿命名测试（BNT）

The Brain Mechanism of TaVNS on MCI by fMRI

- Jiliang FANG I CACMS

Result : Study One

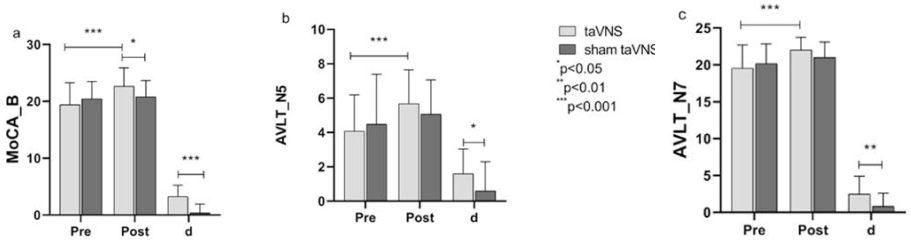
IF：9.18

The efficacy and safety of transcutaneous auricular vagus nerve stimulation in patients with mild cognitive impairment: A double blinded randomized clinical trial

This is the first Paper to confirm that taVNS can improve cognitive function in patients with MCI.

In 2022, the journal Brain Stimulation published a randomized controlled trial conducted by our team (led by Peijing Rong and Jiliang Fang).

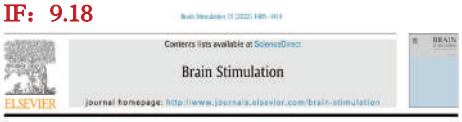
60 patients with MCI: 30 patients in the taVNS group and 30 in the sham taVNS group.
After 24 weeks' treatment :
patients in the taVNS group exhibited improvements in overall cognitive function episodic memory (including long-delay recall and recognition).



Wang L, Zhang J, Guo C, Fang J, Rong P, et al. Brain Stimul. 2022 Nov-Dec

Result : 研究一

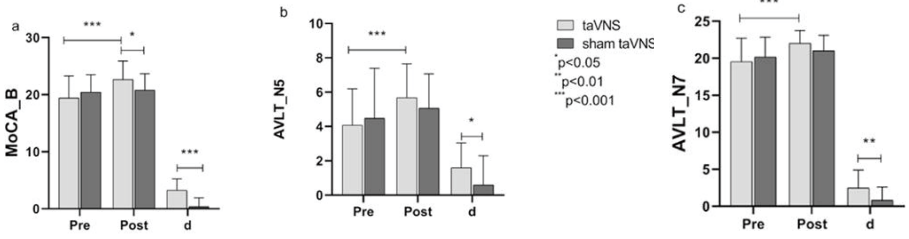
IF：9.18



The efficacy and safety of transcutaneous auricular vagus nerve stimulation in patients with mild cognitive impairment: A double blinded randomized clinical trial

首次证实taVNS可以改善MCI患者的认知功能

2022年 Brain stimulation 发表我们（荣培晶、方继良）团队开展的一项随机对照试验，共纳入60例MCI患者，taVNS组30例，假taVNS （sham taVNS）组30例，采用taVNS治疗MCI24周发现，与sham taVNS相比，taVNS组患者的整体认知功能和情景记忆(长延迟回忆及再认）改善，首次证实了taVNS对改善MCI有效。



1.Wang L, Zhang J, Guo C, Fang J, Rong P, et al. Brain Stimul. 2022 Nov-Dec

Result : Study Two

In 2023, the second study was completed for a total of 22 patients with MCI, with 10 patients in the taVNS group and 12 patients in the sham taVNS group, using the same treatment protocol as before.

Our team once again verified that 24 weeks of taVNS can improve the overall cognitive function and episodic memory of patients with MCI.

Additionally, it was newly found that taVNS has an improving effect on the executive function of patients.

[1]郭春蕾. 经皮耳穴迷走神经刺激治疗轻度认知障碍的疗效及脑机制fMRI研究[D].中国中医科学院,2023.

结果：研究二

2023年团队再次验证了24周 可以改善MCI患者的整体认知功能和情景记忆，此外，还发现taVNS对患者的执行功能也有改善作用。

该研究实际完成治疗共22例MCI患者，taVNS组10例，sham taVNS组12例，采用与前相同的治疗方案。

郭春蕾. 经皮耳穴迷走神经刺激治疗轻度认知障碍的疗效及脑机制fMRI研究[D].中国中医科学院,2023.

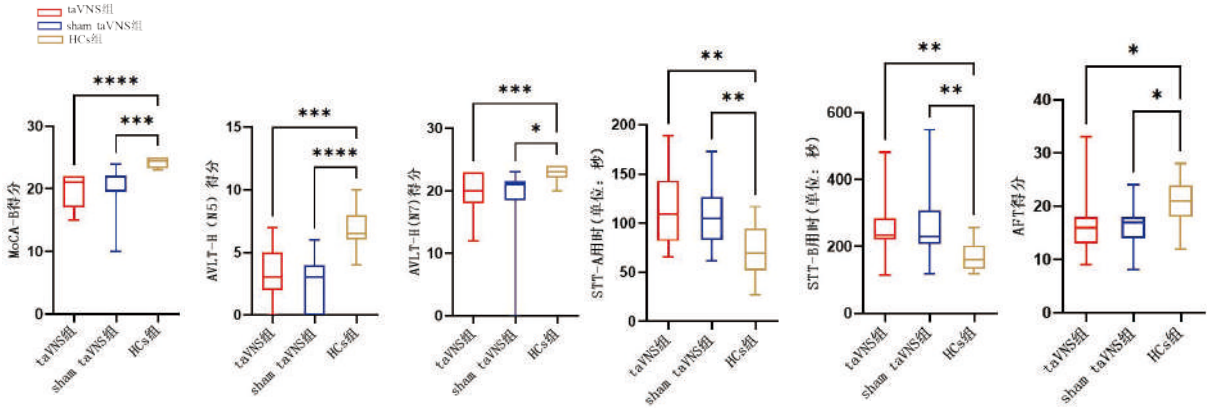
The Brain Mechanism of TaVNS on MCI by fMRI

- Jiliang FANG I CACMS

Baseline： MCI vs. HCs

Enrolled 36 MCI patients (19 in the taVNS group and 17 in the sham taVNS group), along with 20 HCs.

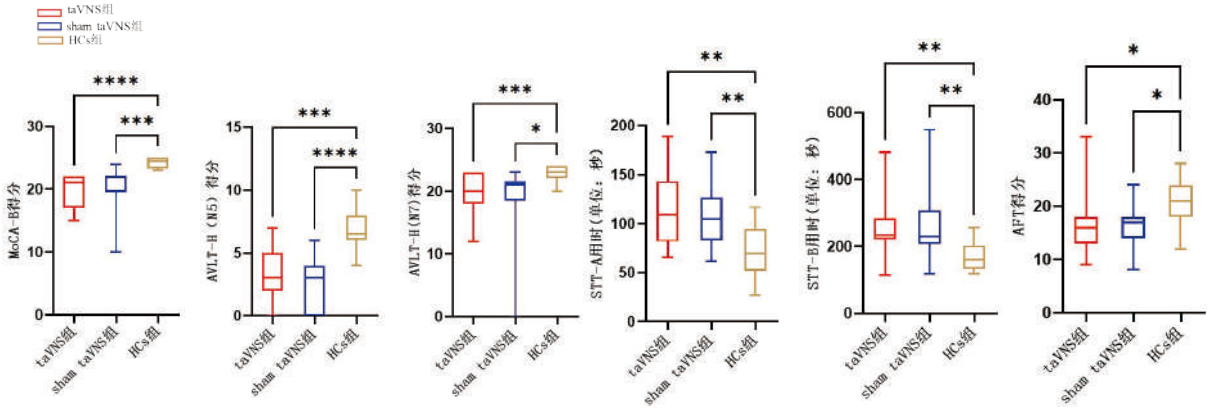
Assessments： AVLT-H, STT A&B, and AFT.



基线：MCI 与正常人比较

筛查合格入组的MCI患者共36例（taVNS组19例，sham taVNS组17例），健康对照（HCs）共20例。

华山版听觉词语学习测验（AVLT-H），形状连线测验A和B (STT A&B)，动物词语流畅性测试（AFT）



Baseline：taVNS group vs. Sham group

taVNS 10 patients VS.sham taVNS 12 patients.

Assessments：The FAQ, HAMD-17, and HAMA scores.

taVNSBaseline clinical data for the taVNS group and the sham taVNS group

	taVNS 组 (n=10)	sham taVNS 组 (n=12)	χ^2/t 值	P 值
性别（男/女）	4/6	6/6	/	0.691
年龄（岁）	65.10±7.25	67.25±6.08	-0.757	0.458
受教育年限（年）	10.90±2.33	10.83±2.209	0.069	0.946
FAQ	0-2	0-2	/	/
HAMD-17	0-5	0-1	/	/
HAMA	0-6	0-3	/	/

患者两组组基线比较

MCI组中taVNS组脱落3例，6例未到复查时间，实际完成10例，sham taVNS组脱落1例，4例未到复查时间，实际完成12例。

两组患者FAQ、HAMD-17和HAMA均在正常范围内。

taVNS组和sham taVNS组基线临床资料

	taVNS 组 (n=10)	sham taVNS 组 (n=12)	χ^2/t 值	P 值
性别（男/女）	4/6	6/6	/	0.691
年龄（岁）	65.10±7.25	67.25±6.08	-0.757	0.458
受教育年限（年）	10.90±2.33	10.83±2.209	0.069	0.946
FAQ	0-2	0-2	/	/
HAMD-17	0-5	0-1	/	/
HAMA	0-6	0-3	/	/

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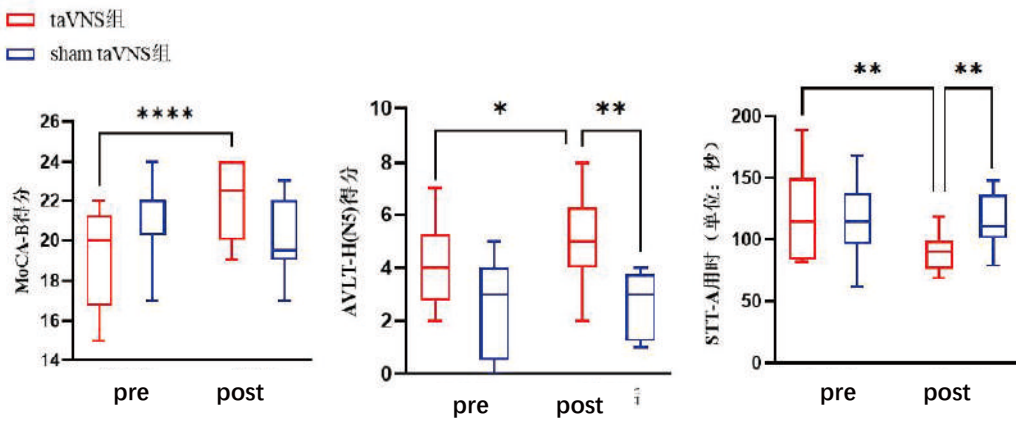
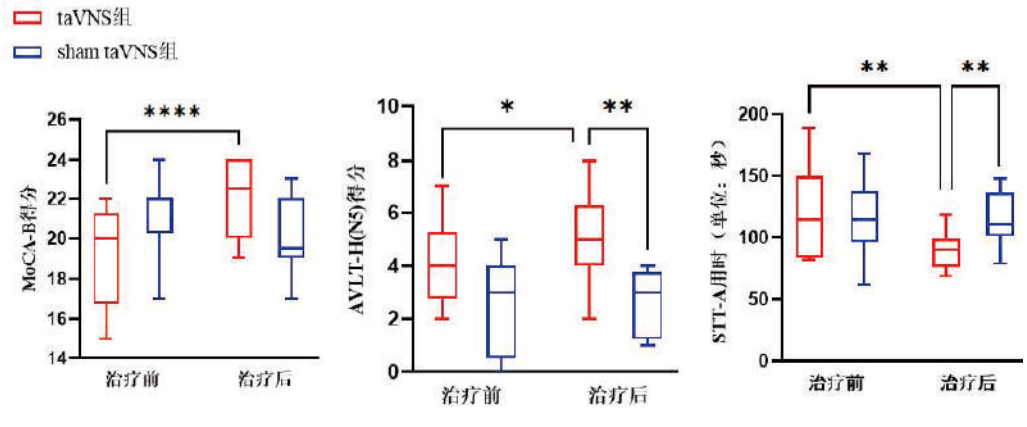
Therapeutic effect (24 weeks) (taVNS vs. Sham)



taVNS significantly improved the above functions in MCI patients
but sham taVNS has no significant improvement effect.

临床疗效评价（24周）：taVNS 与对照组



taVNS可以显著改善MCI患者以上功能，但sham taVNS无显著改善作用

fMRI Study on the Brain Mechanisms of taVNS in Treating MCI（Study Two）

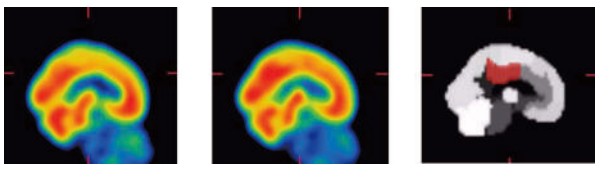
taVNS治疗轻度认知障碍的脑机制fMRI研究（研究二）

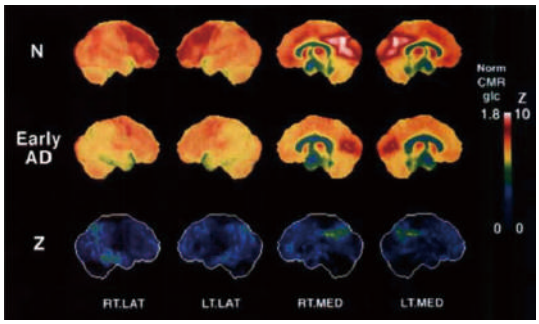
Reviewing：Brain Imaging Studies on MCI

Cingulate Gyrus and MCI and AD

MCI脑影像研究：扣带回结构和功能改变

- Early stages of AD：decreased functional activity in ACC).
- Atrophy of ACC volume can predict the conversion of MCI to AD.
  AD 早期，前扣带（ ACC ）就已经出现退行性改变和功能活动降低，且 ACC 体积萎缩可以 预测 MCI 向 AD 转化
- Early AD patients：Hypometabolism in the PCC.
  AD 患者的后扣带（ PCC ）早期即出现低代谢现象
- Hypoperfusion：a predictive factor for MCI to AD.
  MCI 患者的 PCC 低灌注也是 MCI 进展为 AD 预测因素





1.Jeong HJ, et al. J Alzheimers Dis. 2021
2. Minoshima S, et al. Ann Neurol. 1997
3. Huang C, et al. BMC Neurol. 2002

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Reviewing： Immediate Resting-State fMRI on MCI with taVNS

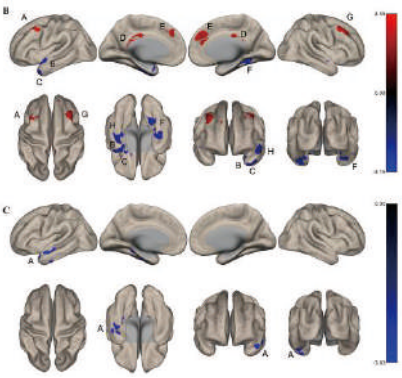
taVNS治疗MCI的即刻静息态fMRI研究

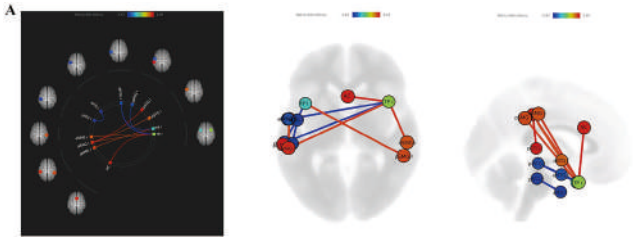
Functional connectivity： Temporal and Parietal regions associated with the semantic and salience networks, as well as in the hippocampal network.

These brain regions are all related to the progression of AD.

taVNS即刻刺激后，与语义和突显网络相关的颞叶和顶叶区域内的功能连接发生变化，海马网络发生功能连接变化）。

这些脑区都与AD的进展有关





Murphy AJ, et al. Neurotherapeutics. 2022

Objective 目标

1. **Using resting-state fMRI to explore the pathological mechanisms of MCI.**
   MCI VS. healthy.

2. **Elucidate the brain mechanisms of therapeutic efficacy (before and after 24 weeks of treatment).**
   taVNS group VS. the sham taVNS

Hypothesis: taVNS can improve cognitive function in MCI by modulating the function of brain regions including the cingulate gyrus.

采用静息态fMRI，比较基线水平MCI组、健康受试者脑功能差异，探索MCI病理机制。

分析taVNS组、sham taVNS组24周治疗前后脑功能差异，阐明相应的疗效脑机制。

假说：taVNS 可通过调节扣带回等脑区功能改善 MCI 的认知功能.

The Brain Mechanism of TaVNS on MCI by fMRI

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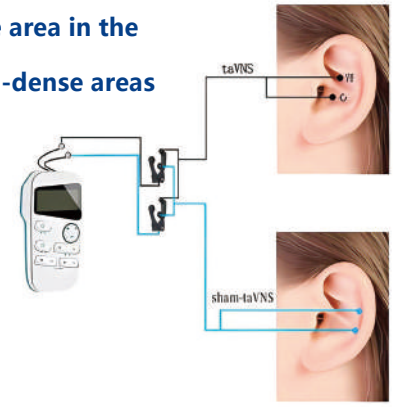
Method

Brain effects of taVNS

- **taVNS group : Stimulate the vagal nerve-dense area in the ear concha (heart and kidney)**
- **sham taVNS group : Stimulate non-vagal nerve-dense areas around the ear (elbow and shoulder)**
- **HCs group : no stimulation was adminitrated**



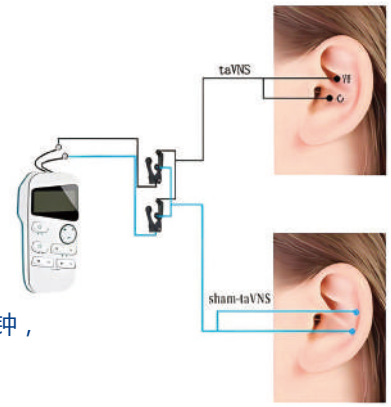
Stimulation parameters : 20/100Hz, dense-disperse waves, stimulation intensity of 3-8mA, for 30 minutes

方 法

taVNS脑效应及治疗机制

在长期（24周）治疗，观察taVNS对MCI的脑功能调节作用

- **taVNS组：刺激耳甲迷走神经密集区（心、肾）**
- **sham taVNS组：刺激耳周非迷走神经密集区**
- **HCs组：不予任何刺激**



刺激参数：20/100Hz，疏密波，刺激强度3-8mA，30分钟，每个患者只刺激一次

Results

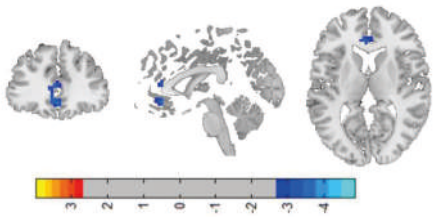
Baseline of fMRI MCI vs. HCs

Compared with the HCs group, the MCI group showed significantly decreased fALFF in the left ACC, corrected by GRF (two-tailed), with voxel *P*<0.01 and cluster *P*<0.05.

Brain regions with significant differences between the MCI group and the HCs group

脑区	R/L	BA	体素大小	MNI 坐标			t 值
				X	Y	Z	
前扣带	L	BA11	75	9	42	0	-4.1939

①左侧 ACC



结 果

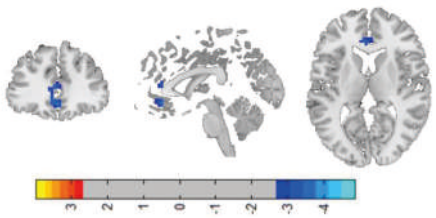
fMRI基线 MCI 与正常人比较

与HCs组相比，MCI组左侧前扣带（ACC）的fALFF显著降低，GRF校正（双尾），voxel *P*<0.01，cluster *P*<0.05

MCI组与HCs组两样本t检验显著的脑区

脑区	R/L	BA	体素大小	MNI 坐标			t 值
				X	Y	Z	
前扣带	L	BA11	75	9	42	0	-4.1939

①左侧 ACC

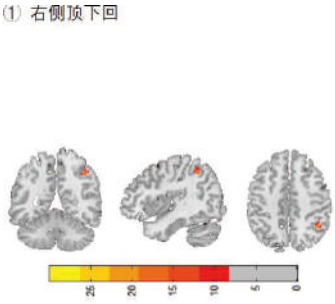


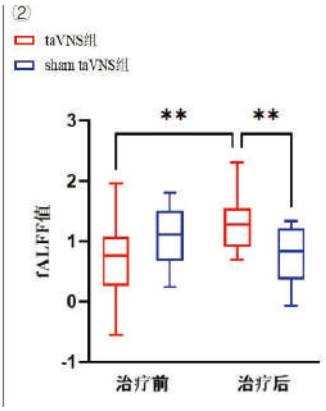
Results

fALFF change after post-treatment

The analysis results showed that the brain region with significant interaction effects was located in the right inferior parietal gyrus (corrected by GRF, two-tailed, voxel *P*<0.01, cluster *P*<0.05).

Brain regions with significant differences in fALFF between the taVNS group and the sham taVNS group





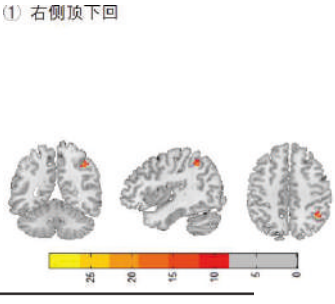
脑区	R/L	BA 分区	体素大小	MNI 坐标			*F* 值
				X	Y	Z	
顶下回	R	BA40	14	39	-51	48	19.3369

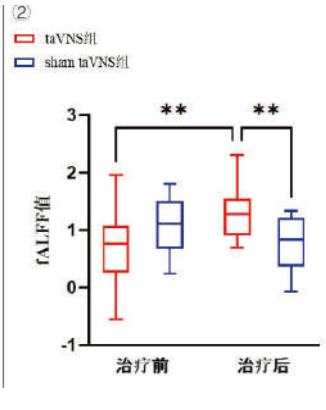
结 果

治疗后fALFF变化

分析结果显示，交互作用显著的脑区位于右侧顶下回.（GRF校正（双尾），voxel *P*<0.01，cluster *P*<0.05）

taVNS组与sham taVNS组fALFF重复测量方差分析显著的脑区





脑区	R/L	BA 分区	体素大小	MNI 坐标			*F* 值
				X	Y	Z	
顶下回	R	BA40	14	39	-51	48	19.3369

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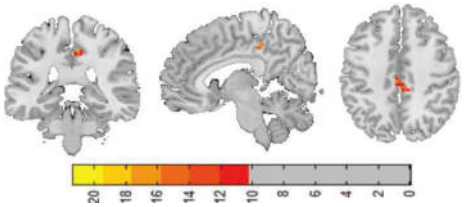
Results

FC between the left ACC and the right MCC related with clinical data

FC between the left ACC and the right middle cingulate cortex (MCC) increased in the taVNS group (corrected by GRF, two-tailed, voxel *P*<0.01, cluster *P*<0.05).

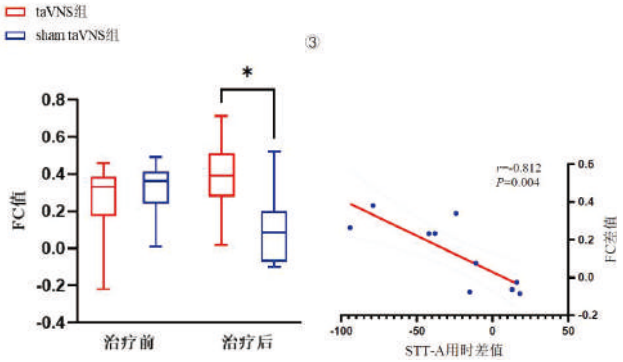
The results were significantly correlated with changes in executive function (STT A).

①右侧 MCC



脑区	R/L	BA 分区	体素大小	MNI 坐标 X	MNI 坐标 Y	MNI 坐标 Z	F 值
中扣带	R	BA23	21	6	-33	45	16.2519

②

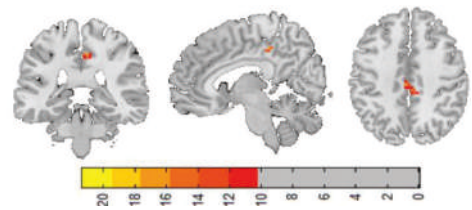


结 果

左侧ACC与右侧中扣带（MCC）脑功能连接与疗效相关

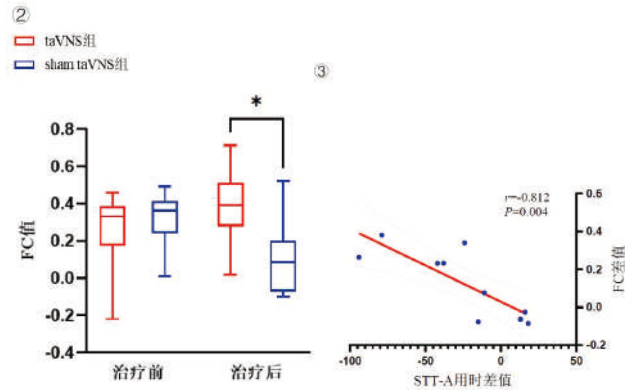
结果显示，taVNS组左侧ACC与右侧中扣带（MCC）的FC显著升高。（GRF校正（双尾），voxel *P*<0.01，cluster *P*<0.05），结果与执行功能变化显著相关 (STT A)

①右侧 MCC



脑区	R/L	BA 分区	体素大小	MNI 坐标 X	MNI 坐标 Y	MNI 坐标 Z	F 值
中扣带	R	BA23	21	6	-33	45	16.2519

②



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Conclusion

taVNS can regulate the SN function and the fronto-parietal control network in MCI.

结论

taVNS可以调节MCI突显网络功能和额顶控制网络.

Summary and Future Plan

1.This study further confirms the efficacy of taVNS in MCI and, for the first time, demonstrates its effectiveness in improving patients' executive function.

2. Explored firstly the brain functional mechanisms underlying the therapeutic effects of taVNS on MCI by resting-state fMRI.

3.The cingulate gyrus may be the key target brain region.

4.Limitation: small sample size and single fMRI model.

5. Future plan:

1) Multicenter,randomized double-blind clinical controlled trial to provide high-level evidence-based medical evidence.

2) Multimodal brain functional imaging and related metabolomics methods to elucidate the brain mechanisms.

小结与展望

1.本研究进一步证实taVNS对MCI的疗效，首次发现对患者执行功能有效。

2.首个采用静息态fMRI探索taVNS改善MCI的疗效脑功能机制。

3. 扣带回可能是重要治疗靶向脑区。

4. 局限性：小样本研究，单模态fMRI。

5. 未来计划：

1）未来将设计更大样本的多中心随机双盲临床对照实验，提供高等级循证医学证据。

2）进一步采用多模态脑功能成像及相关代谢组学方法，阐明脑机制。

Funding

Beijing Natural Science Foundation General Program (7212191): Mechanism Study of Transcutaneous Auricular Electrical Stimulation for Mild Cognitive Impairment Based on the Anterior Insular Cortex-Precuneus-Dorsolateral Prefrontal Cortex Circuit
(PI：Jiliang Fang, 2021-2023)

北京市自然基金面上项目（7212191）：基于前岛叶-楔前叶-背外侧前额叶环路经皮耳穴电刺激治疗轻度认知障碍的机制研究 （方继良 2021-2023）

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Acknowledgement

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5. Professor Ying Han's Team from Xuanwu Hospital , Capital Medical University

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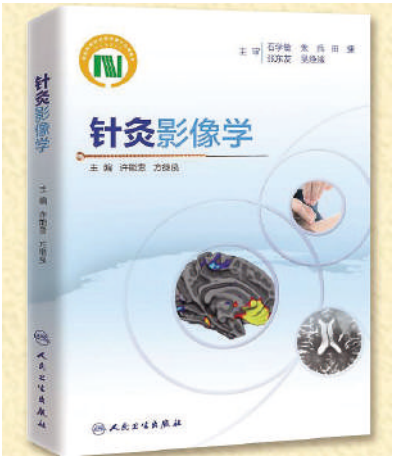
"Medical Imaging in Acupuncture and Moxibustion" (2018)



许能贵、方继良主编 《针灸影像学》2018

介绍了其理论、内容、技术和方法、目前成果

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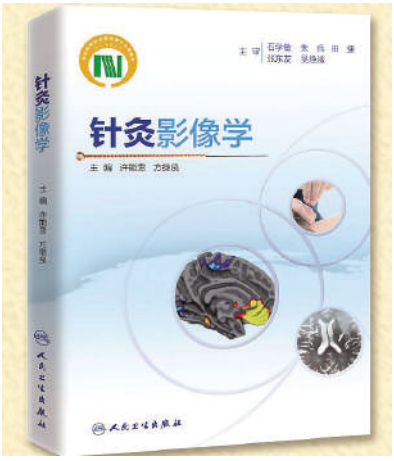

荣获国家科技出版基金

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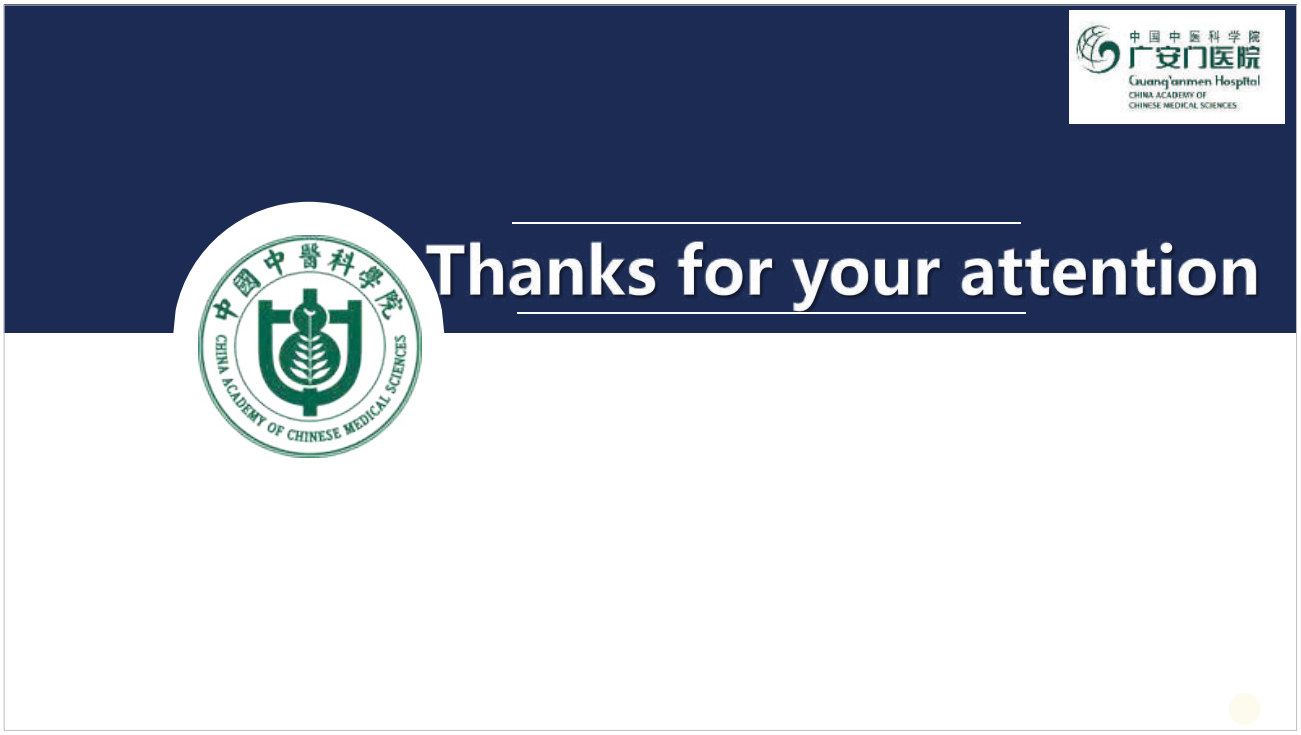


KOREA INSTITUTE OF ORIENTAL MEDICINE
INTERNATIONAL SYMPOSIUM

PRESENTATION

Jieun KIM
KIOM

ALTERATION OF ANTERIOR CINGULATE CORTEX NEUROMETABOLITES BY ELECTRO-ACUPUNCTURE IN PATIENTS WITH ANXIETY DISORDER

Alteration of Anterior Cingulate Cortex Neurometabolites by Electro-acupuncture in Patients with Anxiety Disorder

- Jieun KIM I KIOM

Korea – China International Symposium
KIOM-CACMS International Collaborative Researches

불안장애 환자에 전침치료에 의한 전대상회피질의 신경대사체 및 기능적 뇌 연결성 변화

Alteration of Neurometabolites and Functional connectcivity in ACC by Electroacupuncture in Patients with Anxiety Disorders

김지은

2024.10.30

한국한의학연구원

0. 발표 개요

KIOM

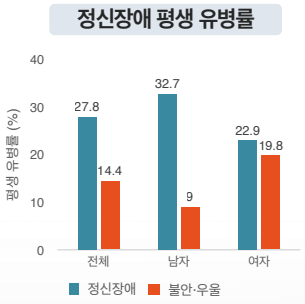
1. 연구배경
   - 불안 장애와 치료법
   - 전대상회피질 (Anterior Cingulate Cortex)
2. 연구목표
   - 전침치료의 뇌 기능 조절 평가
3. 연구방법
   - 연구대상자
   - 전침자극
   - 신경조절 평가를 위한 뇌 영상 분석
4. 연구결과
   - 전침자극의 신경대사체 조절
   - 전침자극에 의한 기능적 뇌 연결성 변화
5. 결론

Alteration of Anterior Cingulate Cortex Neurometabolites by Electro-acupuncture in Patients with Anxiety Disorder

- Jieun KIM I KIOM

1. 연구배경: 불안 장애 (Anxiety Disorders)

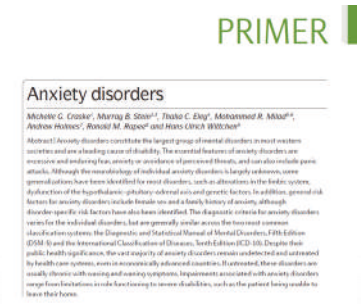
- 정신장애질환의 평생 유병율은 26.7%, 일반 성인 인구의 ¼, 불안 장애의 평생 유병률은 9.3%, 1년 유병률은 3.1%
- 불안 장애는 극도의 공포와 불안으로 일상생활에 장애를 유발함
  - 불안 장애는 범불안 장애, 공포증, 공황 장애, 사회불안 장애 등 다양한 질병으로, 하나의 요소를 원인으로 설명할 수 없음
  - 불안 장애 환자의 약 50%는 약물치료 또는 심리치료인 1차 치료에 반응하지 않음



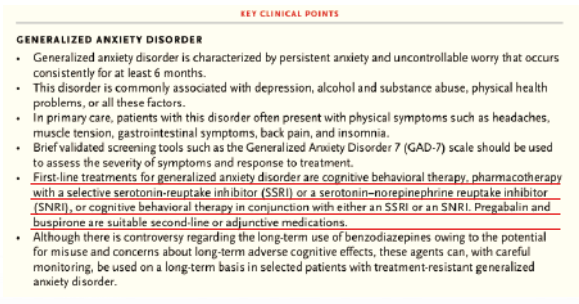
3

1. 연구배경: 불안 장애의 치료법(기존 치료)

- 불안 장애에 권고되는 1차 치료
  - 인지행동치료 Cognitive behavioral therapy (CBT)
  - 약물치료: 세로토닌 재흡수차단제 계열의 항우울제 selective serotonin-reuptake inhibitor (SSRI) or a serotonin-norepinephrine reuptake inhibitor (SNRI), 벤조다이아제핀계 항불안제
  - 제한적인 효과와 유해 부작용의 문제


PRIMER

Anxiety disorders


KEY CLINICAL POINTS

GENERALIZED ANXIETY DISORDER

- Generalized anxiety disorder is characterized by persistent anxiety and uncontrollable worry that occurs consistently for at least 6 months.
- This disorder is commonly associated with depression, alcohol and substance abuse, physical health problems, or all these factors.
- In primary care, patients with this disorder often present with physical symptoms such as headaches, muscle tension, gastrointestinal symptoms, back pain, and insomnia.
- Brief validated screening tools such as the Generalized Anxiety Disorder 7 (GAD-7) scale should be used to assess the severity of symptoms and response to treatment.
- First-line treatments for generalized anxiety disorder are cognitive behavioral therapy, pharmacotherapy with a selective serotonin-reuptake inhibitor (SSRI) or a serotonin–norepinephrine reuptake inhibitor (SNRI), or cognitive behavioral therapy in conjunction with either an SSRI or an SNRI. Pregabalin and buspirone are suitable second-line or adjunctive medications.
- Although there is controversy regarding the long-term use of benzodiazepines owing to the potential for misuse and concerns about long-term adverse cognitive effects, these agents can, with careful monitoring, be used on a long-term basis in selected patients with treatment-resistant generalized anxiety disorder.

Caren et al., *NEJM* (2015)

Craske et al., *Nat Rev Dis Primers* (2017)

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Alteration of Anterior Cingulate Cortex Neurometabolites by Electro-acupuncture in Patients with Anxiety Disorder

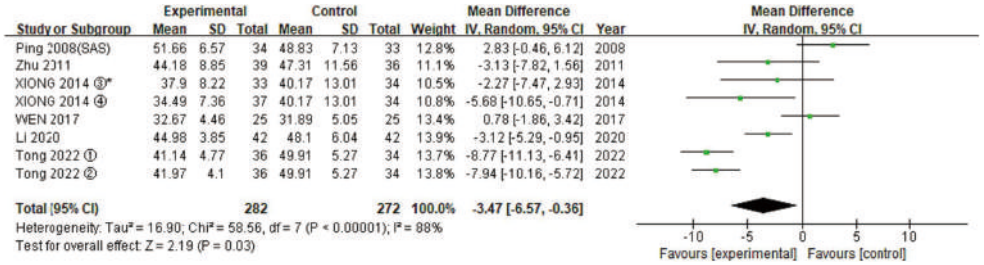
- Jieun KIM I KIOM

1. 연구배경: 불안 장애의 치료법(전침/침 치료)

KIOM

- 불안 장애에 전침/침 치료는 임상적 효능과 적은 부작용이 보고 1), 비약물 치료로 제안
- 약물치료에 저항성을 보이는 만성적 불안 장애에 장기간 치료를 위한 대안으로 제시 2,3)
- 체계적문헌고찰 연구 4) 에서 전침치료에 의한 유의한 불안관련 증상 완화를 보고

자가평가 불안척도

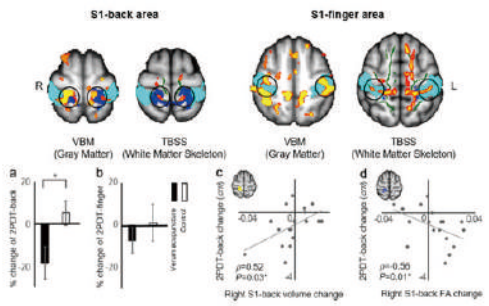


1) Acupunct Med. 2004; 22(3)
2) Rev Bras Enferm. 2016;69(3)
3) Complement Ther Clin Pract. 2018;31
4) Hong et al., Front. Psychol (2023)

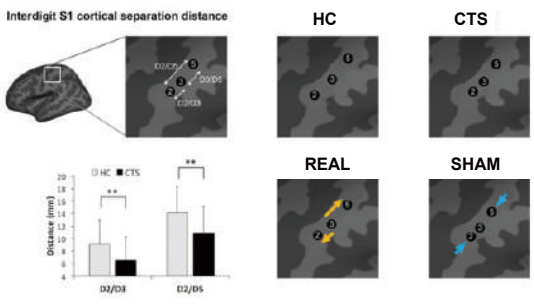
2. 연구목표

KIOM

- 임상연구에서 불안 장애치료에 침/전침치료의 유효성을 보고하고 있으나, 명확한 치료기전 탐색을 위한 연구가 필요
- 신경조절 치료기술로써 침치료의 가능성
  - 침치료에 의한 만성요통 환자의 뇌 구조변화
  - 침치료에 의한 손목터널 증후군 환자의 대뇌피질 기능 변화



Kim et al., *Neuroimage.* (2020)



Maeda et al., *Brain.* (2017)

2. 연구목표

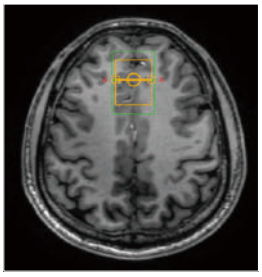
- 임상연구에서 불안 장애치료에 침/전침치료의 유효성을 보고하고 있으나, 명확한 치료기전 탐색을 위한 연구가 필요
- 전침/침 치료는 피부 또는 근육의 자극 이상의 신경조절 치료기술로의 가능성이 제시됨

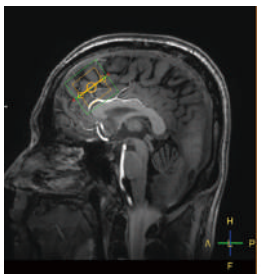
- 불안장애 환자를 대상으로 전침자극의 전대상회피질 기능을 조절하는 치료효과를 평가
  - 신경전달물질 (Metabolites)
  - 기능적 뇌 연결성 (Functional Connectivity)

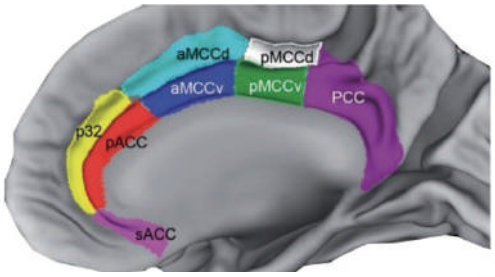
7

전대상회피질 Anterior Cingulate Cortex

- 대상회피질은 감정 및 자율신경, 감정이 연관된 사건의 기억처리 등에 관여
- 전대상회 피질 (p32, pACC, and sACC)
  - P32: 경험을 통한 긍정 또는 부정적인 기억처리 담당
  - pACC: 감정 인식 (emotional awareness), 감정을 느끼는 과정과 원인과 맥락을 인식







https://cingulumneurosciences.net/human-cingulate-cortex

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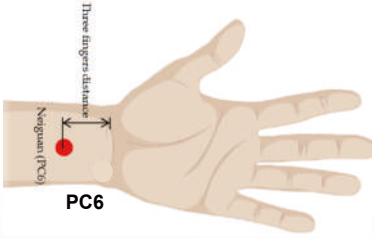
Alteration of Anterior Cingulate Cortex Neurometabolites by Electro-acupuncture in Patients with Anxiety Disorder

- Jieun KIM I KIOM

3. 연구방법

KIOM

- 연구대상자
  - SCID-5, DSM-5에 의해 진단된 불안장애 환자 (사회불안, 범불안, 공포증, 기타 불안 장애를 포함)
  - 21명의 불안장애 환자 모집 (남성 8명, 29.1±9.2 세)
  - 벡 불안척도(24.7±13.1) 와 우울척도(27.4±11.2) 평가
- 전침자극을 위한 경혈
  - 내관 (PC6)과 이신문 (TF4): 불안 장애 치료에 다빈도로 사용되는 혈위 선택
  - 내관과 이신문의 불안조절 효과 비교를 위해 두개의 치료그룹으로 무작위 배정함



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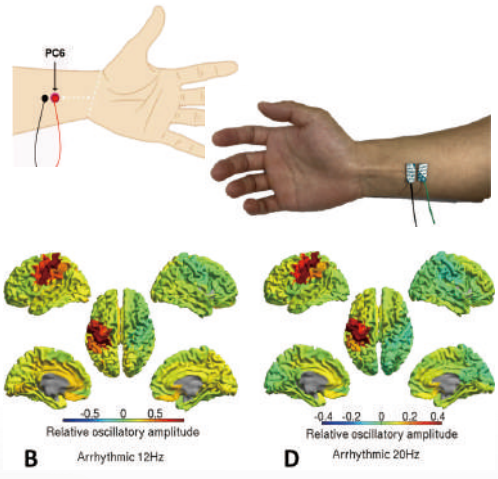
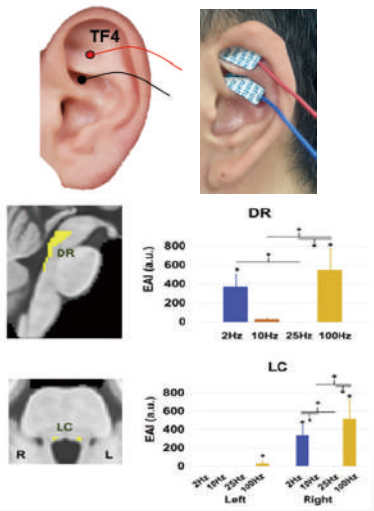
3. 연구방법

KIOM

- 전침자극 조건: 뇌의 기능조절 최대화를 목적으로 탐색
  - 내관 전침자극: 12Hz
  - 이신문 전침자극: 100Hz





Houlgreave et al., *Neuroimage.* (2022)

Sclocco et al., *Brain Stimulation.* (2020)

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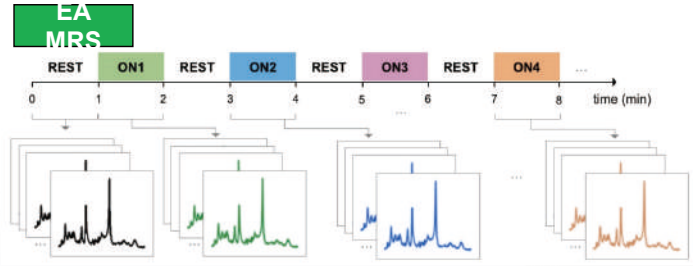
Alteration of Anterior Cingulate Cortex Neurometabolites by Electro-acupuncture in Patients with Anxiety Disorder

- Jieun KIM I KIOM

3. 연구방법

KIOM

- 뇌영상 데이터 수집 (MRI)
  - 초고자장 7.0T 필립스 MRI 스캐너와 32채널 헤드코일 사용
  - 전침자극 인가하지 않은 상태와 인가하는 상태에서 신경대사체와 기능적 뇌 연결성 데이터 수집



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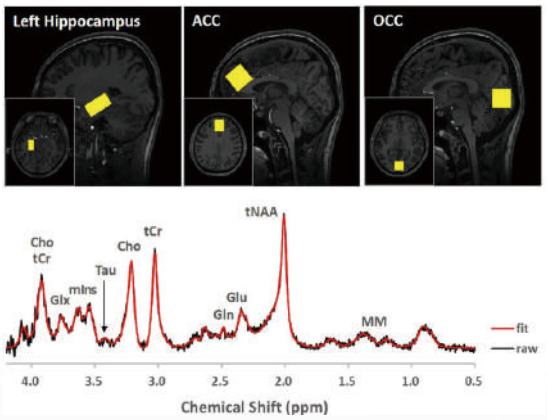
3. 연구방법

KIOM

- 뇌영상 데이터 수집 (MRI)
  - 초고자장 7.0T 필립스 MRI 스캐너와 32채널 헤드코일 사용
  - 자기공명분광법 (Proton MR Spectroscopy,1H-MRS)을 통한 뇌 영역의 신경대사체 정보를 수집
    - 전침자극 없는 상태와 전침자극을 인가하는 동시에 측정
    - 신경전달물질
      - ✓ GABA (γ-aminobutyricacid): 대표적 억제성 신경전달물질
      - ✓ Phosphocreatine (PCr): 세포 에너지 대사조절에 관여



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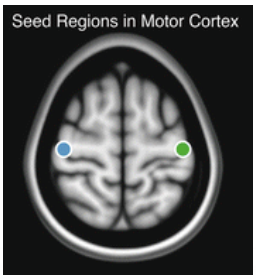
Alteration of Anterior Cingulate Cortex Neurometabolites by Electro-acupuncture in Patients with Anxiety Disorder

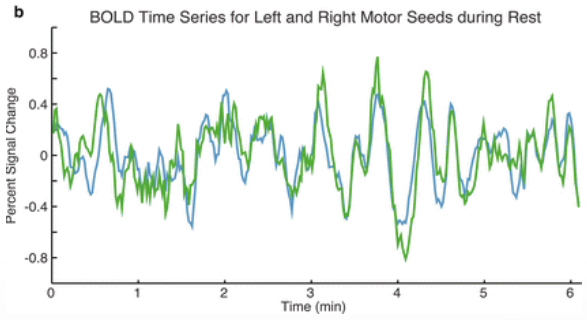
- Jieun KIM I KIOM

3. 연구방법

KIOM

- 뇌영상 데이터 수집 (MRI)
  - 초고자장 7.0T 필립스 MRI 스캐너와 32채널 헤드코일 사용
  - 기능적 뇌 연결성 (Functional connectivity): 뇌의 부위 간 연결상태를 평가하는 지표
  - 기능적으로 연결된 영역은 유사한 뇌의 리듬을 보임
  - 특정 과제수행이 없는 안정상태 (resting state)에서 동일한 기능을 수행하는 뇌의 영역들이 연결됨





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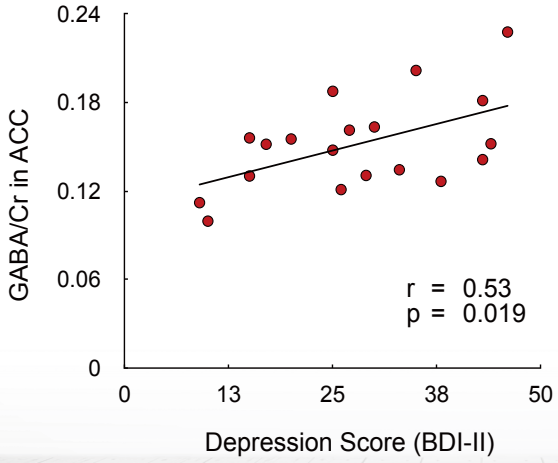
4. 연구결과

baseline MRS | rs-fMRI | EA fMRI | EA MRS | rs-fMRI

KIOM

- 전대상회피질의 GABA 농도와 임상변수 간의 상관관계
  - 전침자극이 인가되기 전에 측정된 GABA와 우울평가 변수 간의 상관관계
  - 높은 우울감을 보이는 대상자에서 강화된 억제성 신경활성 관찰



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Alteration of Anterior Cingulate Cortex Neurometabolites by Electro-acupuncture in Patients with Anxiety Disorder

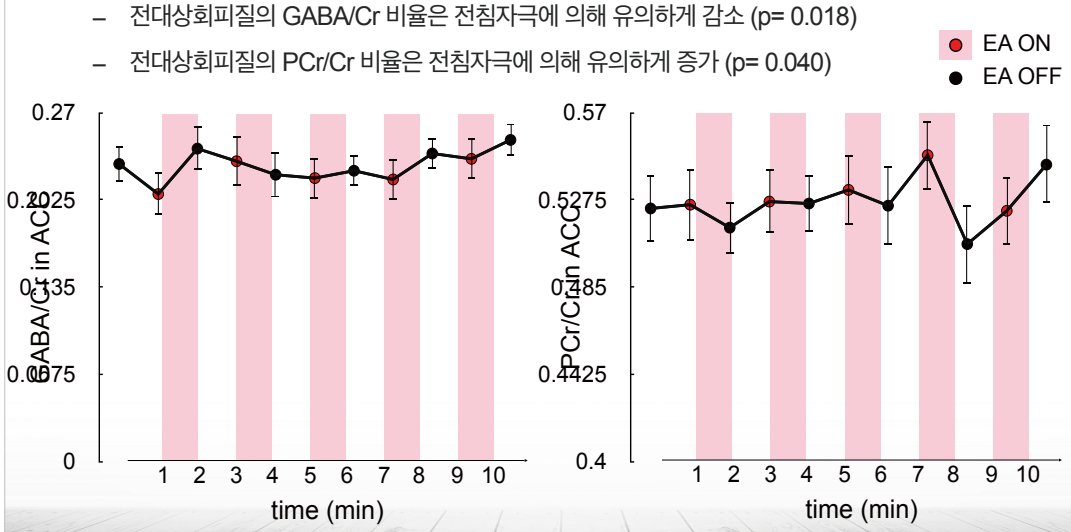
- Jieun KIM I KIOM

4. 연구결과

baseline MRS | rs-fMRI | EA fMRI | EA MRS | rs-fMRI

KIOM

- 전침자극에 의한 전대상회피질의 신경대사체 농도 조절
  - 일반선형모델 (General Linear Model, GLM) 분석을 통한 신경대사체 조절 분석
  - 전대상회피질의 GABA/Cr 비율은 전침자극에 의해 유의하게 감소 (p= 0.018)
  - 전대상회피질의 PCr/Cr 비율은 전침자극에 의해 유의하게 증가 (p= 0.040)



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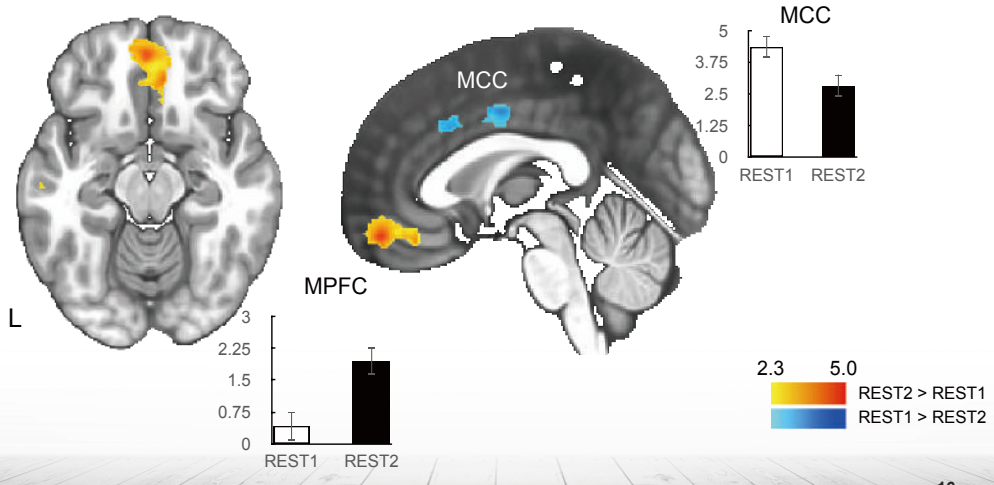
4. 연구결과

baseline MRS | rs-fMRI | EA fMRI | EA MRS | rs-fMRI

KIOM

- 전침자극에 의한 기능적 뇌 연결성의 변화 (전침자극 전후 비교)
  - 전대상회피질 (ACC)과 내측전두엽피질 (MPFC) 간의 기능적 뇌 연결성이 유의하게 증가
  - 전대상회피질 (ACC)과 중간대상회피질 (MCC)간의 기능적 뇌 연결성이 유의하게 증가



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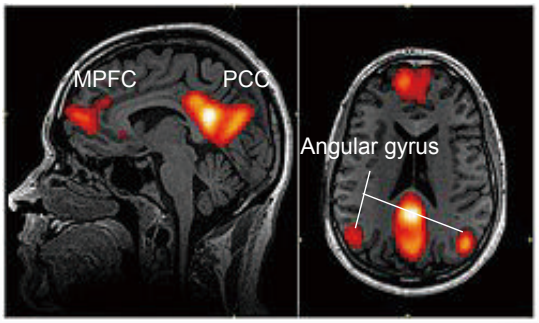
4. 연구결과

KIOM

- 기본 모드 네트워크 (Default Mode Network, DMN)
  - 특정 작업을 수행하지 않을 때 활성화되는 뇌 영역 네트워크
  - 내측전두엽피질(MPFC), 뒤대상회피질(Posterior Cingulate Cortex, PCC) 등의 뇌 영역이 연결
    - 내면의 세계에 집중할 때 활성화
    - 자서전적 사고, 반성 및 인식과 기억 회상, 미래 계획 등에 관여
    - MPFC는 과거의 경험을 기반으로 현재의 감정과 생각을 평가하고 조절하는 기능 담당



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5. 결론

KIOM

- 본 연구에서는 불안 장애 환자를 대상으로 감정을 처리하는 뇌 영역의 신경대사체와 뇌 기능적 연결성을 평가하고 전침자극으로 유도되는 변화를 관찰
  - 불안 장애환자에서 관찰된 전대상회피질의 GABA/Cr 비와 우울의 정도의 상관관계는 해당 뇌 영역의 증가된 억제성 신경활동이 환자군의 임상증상과 관계함
  - 신경전달물질의 농도는 전침자극에 의해 즉각적으로 조절됨
  - 전침자극에 의해 자서전적 감정조절(ACC-MPFC)에 관여하는 뇌 영역과 부정적 감정조절(ACC-MCC)에 관여하는 뇌 영역의 연결성이 변화함
- 연구결과는 적은 데이터 분석의 한계를 가지나, 전침치료의 신경조절 결과를 관찰함
- 추후, 임상증상 분석 결과와 함께 전침치료의 신경조절을 통한 치료기전 평가
- 또한, 내관과 이신문의 불안 장애 치료 효과를 비교하여 유효한 치료기술로 제안하고자 함

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마치며...

KIOM

한국한의학연구원 김형준, 정창진, 최선영, 은슬기 (KSN2213010)

노팅엄대학교 Stephen R. Jackson

Alteration of Anterior Cingulate Cortex Neurometabolites by Electro-acupuncture in Patients with Anxiety Disorder

- Jieun KIM I KIOM

Korea – China International Symposium
KIOM-CACMS International Collaborative Researches

焦虑症患者接受电针治疗后，前扣带皮层神经代谢物和功能连接的变化

Alteration of Neurometabolites and Functional connectcivity in ACC by Electroacupuncture in Patients with Anxiety Disorders

Kim Ji-eun
2024.10.30
韩国韩医学研究院

0. 发言概要

KIOM

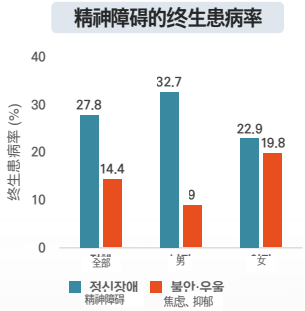
1. 研究背景
   - 焦虑症和治疗方法
   - 前扣带皮层(Anterior Cingulate Cortex)
2. 研究目标
   - 对电针治疗的脑功能调节评价
3. 研究方法
   - 研究对象
   - 电针刺激
   - 用于神经调节评价的脑成像分析
4. 研究结果
   - 电针刺激的神经代谢物调节
   - 电针刺激引起的功能连接变化
5. 结论

Alteration of Anterior Cingulate Cortex Neurometabolites by Electro-acupuncture in Patients with Anxiety Disorder

- Jieun KIM I KIOM

1. 研究背景：焦虑症（Anxiety Disorders）

- 精神障碍的终生患病率为26.7%，占一般成年人口的1/4，焦虑症的终生患病率为9.3%，一年患病率为3.1%
- 焦虑症由于极度恐惧和焦虑而导致日常生活困难
  - 焦虑症包括广泛性焦虑症、恐惧症、恐慌症、社会焦虑症等多种疾病，不能用一个单一因素来解释原因
  - 大约50%的焦虑症患者对药物治疗或心理治疗等一线治疗无反应



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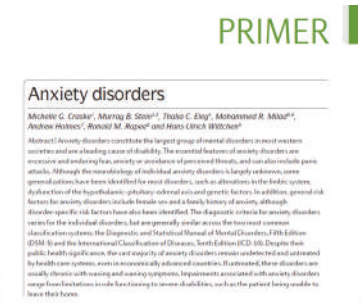
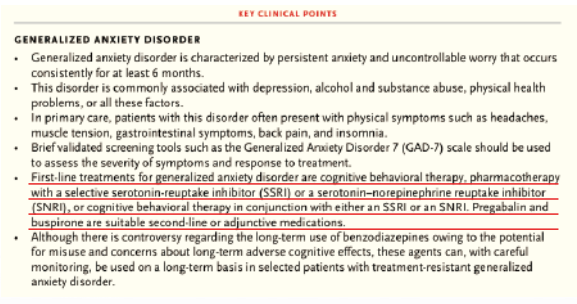
1. 研究背景：焦虑症的治疗方法（现有治疗）

- 推荐的焦虑症一线治疗方法
  - 认知行为疗法 Cognitive behavioral therapy (CBT)
  - 药物治疗：5-羟色胺重摄取抑制剂系列抗抑郁药selective serotonin-reuptake inhibitor (SSRI) or a serotonin-norepinephrine reuptake inhibitor(SNRI)、苯二氮卓类抗焦虑药
  - 效果有限和有害副作用的问题



Caren et al., NEJM (2015)



Craske et al., Nat Rev Dis Primers (2017)

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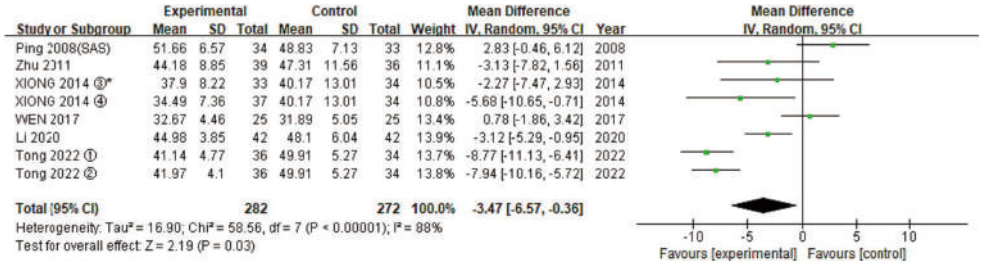
1. 研究背景：焦虑症的治疗方法(电针/针灸治疗)

- 据报告，对焦虑症的电针/针灸治疗有临床功效且副作用小[1)]，提议作为非药物治疗方案
- 提议作为对药物治疗显示耐药性的慢性焦虑症的长期治疗替代方案[2,3)]
- 在系统性文献考察研究[4)]中报告电针治疗可显著缓解焦虑相关症状

焦虑自评量表



1) Acupunct Med. 2004; 22(3)
2) Rev Bras Enferm. 2016;69(3)
3) Complement Ther Clin Pract. 2018;31
4) Hong et al., Front. Psychol (2023)

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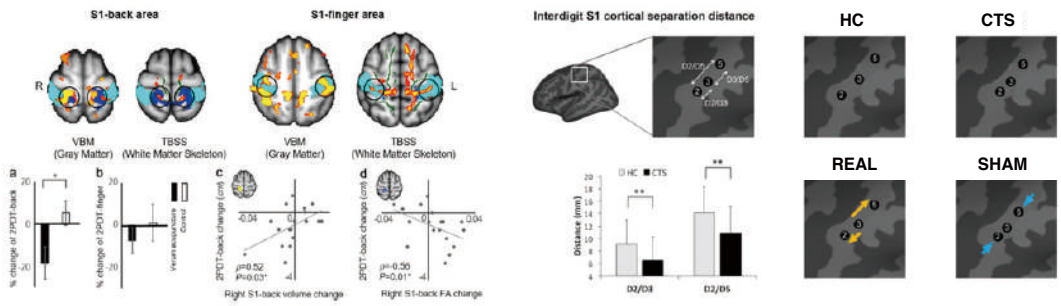
2. 研究目标

- 临床研究报告了针灸/电针治疗焦虑症的有效性，但仍需要研究来探索明确的治疗机制
- 针灸作为神经调节治疗技术的可能性
  - 针灸治疗带来的慢性腰痛患者脑结构变化
  - 针灸治疗带来的腕管综合征患者大脑皮层功能的变化



Kim et al., Neuroimage. (2020)

Maeda et al., Brain. (2017)

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2. 研究目标

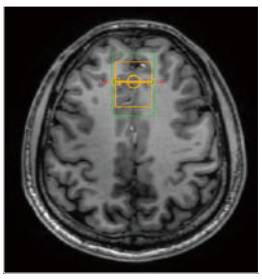
- 临床研究报告了针灸/电针治疗焦虑症的有效性，但仍需要研究来探索明确的治疗机制
- 电针/针灸疗法有望成为超越皮肤或肌肉刺激的神经调节治疗技术

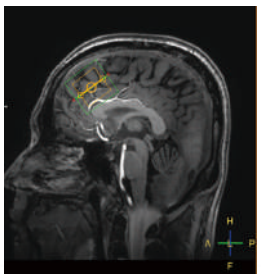
- 电针刺激对调节焦虑症患者前扣带皮层功能的治疗效果评价
  - 神经递质（Metabolites）
  - 功能连接（Functional Connectivity）

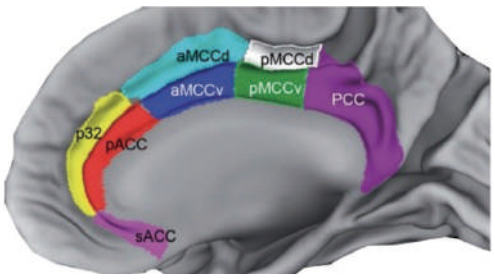
7

前扣带皮层Anterior Cingulate Cortex

- 扣带皮层参与情绪、自主神经系统以及情绪相关事件的记忆处理
- 前扣带皮层（p32、pACC 和 sACC）
  - P32：负责通过经历处理积极或消极的记忆
  - pACC：情绪意识 (emotional awareness), 识别感受情绪的过程、原因和脉络







https://cingulumneurosciences.net/human-cingulate-cortex

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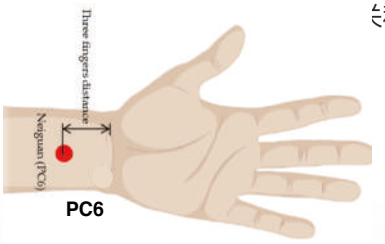
3. 研究方法

KIOM

- 研究对象
  - 通过SCID-5和DSM-5诊断的焦虑症患者（包括社交焦虑、广泛性焦虑、恐惧症和其他焦虑症）
  - 招募21名焦虑症患者（男性8名，29.1±9.2岁）
  - 贝克焦虑量表（24.7±13.1）和抑郁量表（27.4±11.2）评估
- 电针刺激的穴位
  - 内关（PC6）与里神门（TF4）：选择治疗焦虑症的高频率穴位
  - [illegible]和里神门的焦虑控制效果



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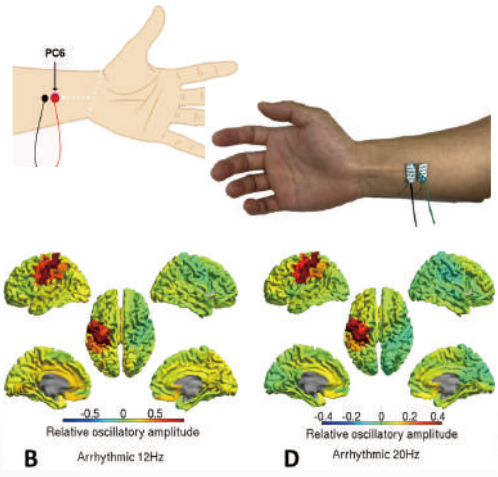
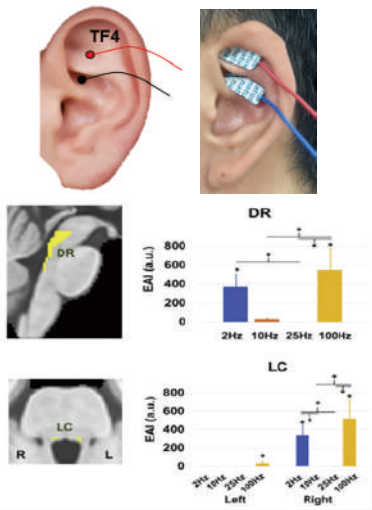
3. 研究方法

KIOM

- 电针刺激条件：以最大限度控制脑功能为目的的探索
  - 内关电针刺激：12Hz
  - 里神门电针刺激：100Hz





Houlgreave et al., Neuroimage. (2022)

Sclocco et al., Brain Stimulation. (2020)

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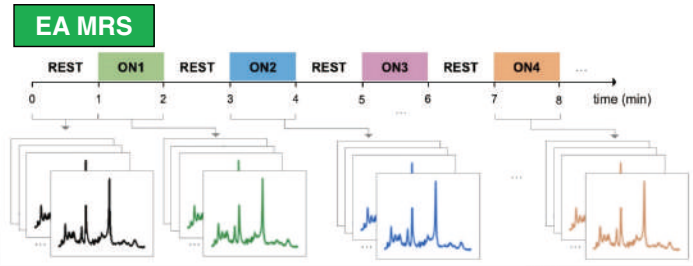
Alteration of Anterior Cingulate Cortex Neurometabolites by Electro-acupuncture in Patients with Anxiety Disorder

- Jieun KIM I KIOM

3. 研究方法

KIOM

- 采集脑成像数据(MRI)
  - 采用超高磁场7.0T飞利浦MRI扫描仪和32通道头部线圈
  - 在没有和有电针刺激的情况下收集神经代谢物和功能连接数据



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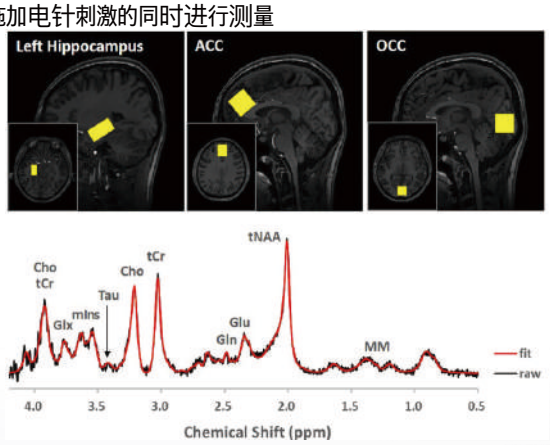
3. 研究方法

KIOM

- 采集脑成像数据(MRI)
  - 采用超高磁场7.0T飞利浦MRI扫描仪和32通道头部线圈
  - 通过氢质子磁共振波谱(Proton MR Spectroscopy,1H-MRS)收集脑区域的神经代谢物信息
    - 在没有电针刺激的情况下以及在施加电针刺激的同时进行测量
    - 神经递质
      - ✓ GABA (γ-aminobutyricacid)：代表性的抑制性神经递质
      - ✓ Phosphocreatine (PCr)：参与调节细胞能量代谢



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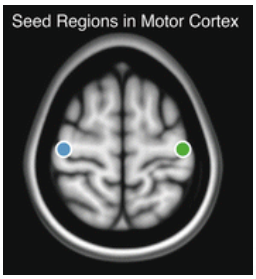
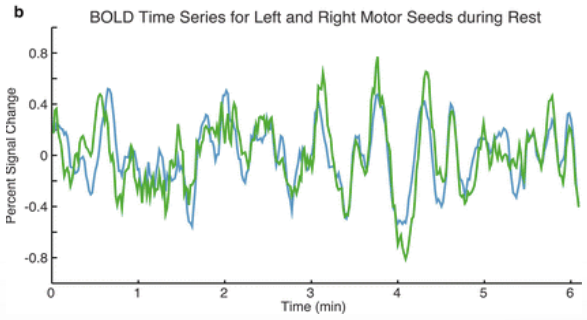
3. 研究方法

KIOM

- 采集脑成像数据(MRI)
  - 采用超高磁场7.0T飞利浦MRI扫描仪和32通道头部线圈
  - 功能连接（Functional connectivity）：评价大脑部位间连接状态的指标
  - 功能连接的区域呈现类似的大脑节律
  - 在不执行特定任务的静息状态（resting state）下，将执行相同功能的大脑区域连接起来





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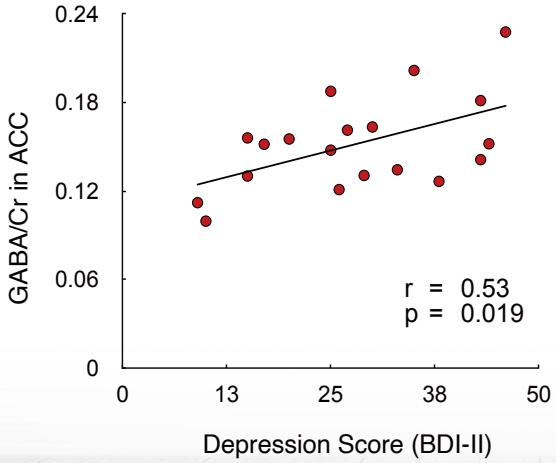
4. 研究结果

baseline MRS | rs-fMRI | EA fMRI | EA MRS | rs-fMRI

KIOM

- 前扣带皮层GABA浓度与临床变量之间的相关性
  - 应用电针刺激前测量的GABA与抑郁评估变量之间的相关性
  - 在抑郁程度较高的受试者中观察到抑制性神经活性增强



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Alteration of Anterior Cingulate Cortex Neurometabolites by Electro-acupuncture in Patients with Anxiety Disorder

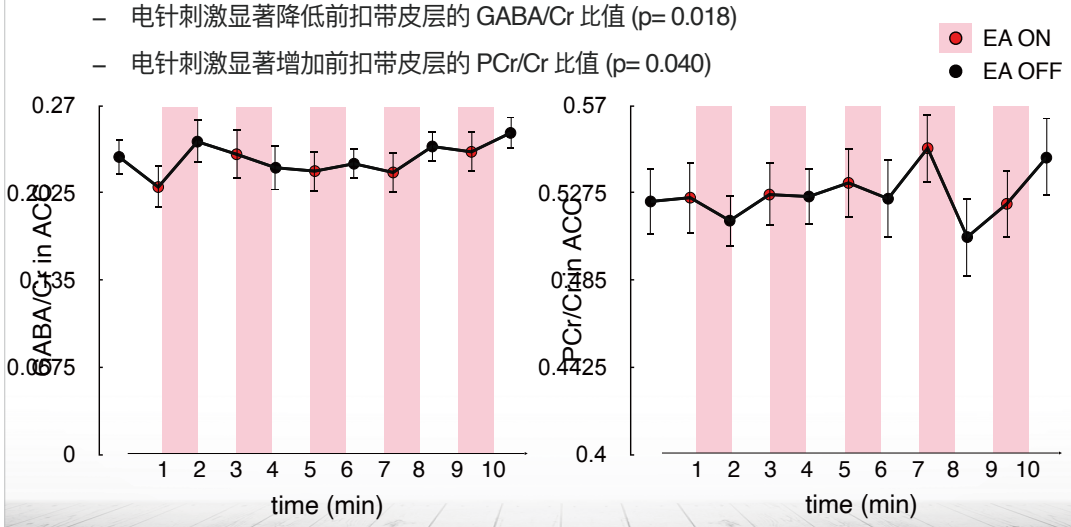
- Jieun KIM I KIOM

4. 研究结果

baseline MRS | rs-fMRI | EA fMRI | EA MRS | rs-fMRI

KIOM

- 通过电针刺激控制前扣带皮层神经代谢物浓度
  - 通过一般线性模型 (General Linear Model, GLM)分析，进行神经代谢物调节分析
  - 电针刺激显著降低前扣带皮层的 GABA/Cr 比值 (p= 0.018)
  - 电针刺激显著增加前扣带皮层的 PCr/Cr 比值 (p= 0.040)



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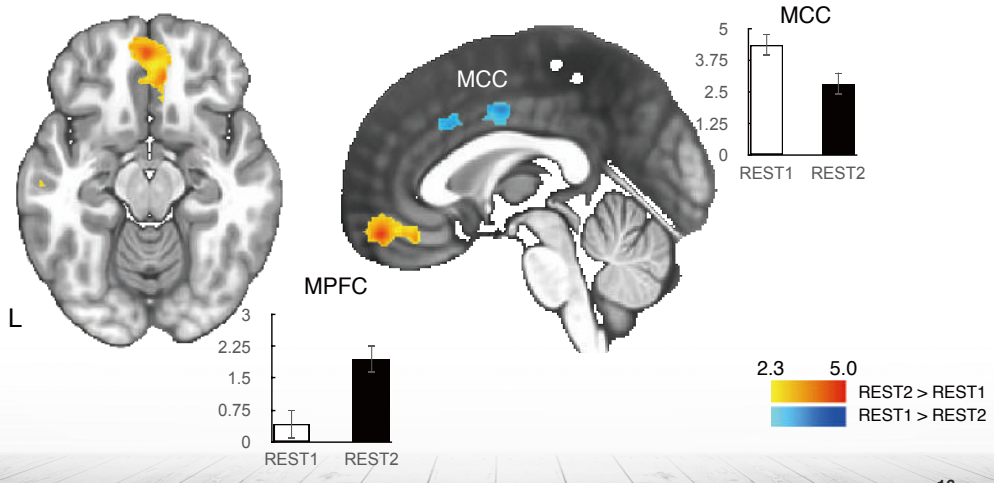
4. 研究结果

baseline MRS | rs-fMRI | EA fMRI | EA MRS | rs-fMRI

KIOM

- 电针刺激引起的功能连接变化（电针刺激前后比较）
  - 前扣带皮层 (ACC) 和内侧前额叶皮层 (MPFC) 之间的功能连接显著增强
  - 前扣带皮层 (ACC) 和中扣带皮层 (MCC) 之间的功能连接显著增强



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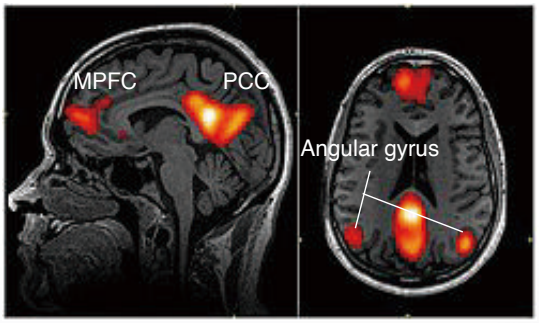
4. 研究结果

KIOM

- 默认模式网络(Default Mode Network, DMN)
  - 不执行特定任务时激活的大脑区域网络
  - 内侧前额叶皮层 (MPFC) 和后扣带皮层 (PCC) 等大脑区域是相连的
    - 专注于内心世界时激活
    - 参与自传性思考、反省、认识和记忆回忆、未来计划等
    - MPFC 负责根据过去的经验评估并调节当下的情绪和想法



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5. 结论

KIOM

- 本研究以焦虑症患者为对象，评价处理情绪的大脑区域的神经代谢物和功能连接，并观察了电针刺激引起的变化
  - 在焦虑症患者中观察到的前扣带皮层中的GABA/Cr比值与抑郁程度之间的相关性表明，相应大脑区域的抑制性神经活动增加与患者组的临床症状有关
  - 神经递质的浓度通过电针刺激得到即刻调节
  - 因电针刺激，参与自传性情绪调节（ACC-MPFC）的大脑区域和参与负面情绪调节（ACC-MCC）的大脑区域连接发生变化
- 尽管研究结果具有分析数据较少的局限性，但观察到了电针治疗的神经调节结果
- 以后，将结合临床症状分析结果，评价通过电针治疗调节神经的治疗机制
- 此外，比较内关和里神门的焦虑症治疗效果，提出有效的治疗技术

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结束...

KIOM

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