一般社団法人

国際未来医療臨床医学会
発足記念シンポジウム

第1回　SIFCM シンポジウムプログラム

日　程：2023 年 6 月 25 日 (日)
会　場：京都市勧業館「みやこめっせ」
テーマ：未来医療 ～現代医療からのパラダイムシフト～
大会長：新垣実・福沢嘉孝
副大会長：岡本正人・川上智史

SIFCM 国際未来医療臨床医学会
一般社団法人 国際未来医療臨床医学会
Society of International Future Clinical Medicine

https://sifcm.org
事務局：〒113-0033　東京都文京区本郷 2-31-2-2F
TEL: 03-6240-0179　FAX: 050-3730-8505（お問い合わせ：平日 10:00～17:00）

●本誌記載のデータは、2023 年 5 月 31 日提出時点の物です。

代表理事挨拶

国際未来医療臨床医学会　代表理事

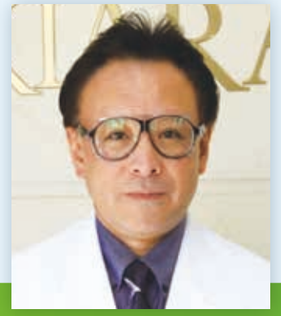
Representative Director of
the Society of International Future Clinical Medicine

新垣　実 Minoru Arakaki

（医）新美会新垣形成外科　理事長
日本臨床カンナビノイド学会　理事

Medical Corporation Shinbikai Arakaki Plastic Surgery Chairman,
Japanese Society of Clinical Cannabinoids Director

国際未来医療臨床医学会　代表理事



Representative Director of
the Society of International Future Clinical Medicine

福沢　嘉孝 Yoshitaka Fukuzawa

愛知医科大学大学院医学研究科（戦略的先制統合医療・健康強化促進学）
愛知医科大学病院 先制・統合医療包括センター（AMPIMEC）教授・部長
学校法人愛知医科大学　理事

Aichi Medical University and Hospital
Aichi Medical Preemptive and Integrative Medicine Center (AMPIMEC) Professor
Aichi Medical University Director

世の中は、目まぐるしく変わっています。私たち医療人を取り巻く環境も、再生医療、ゲノム医療、免疫療法、mRNA ワクチン、IoT、A I の導入など、新しい技術と知識の流入と共に大きく変わろうとしています。まさに「治療医学」から「予防医学」へと生まれ変わるパラダイムシフトが目の前までやってきています。２０世紀には現代医療から統合医療への扉が開かれ、多くの慢性疾患の治療成績が格段に上がりました。そして２１世紀現在、予防・先制医療を中心に、アンチエイジング、ピンピンコロリ社会を目指す未来医療への扉が開かれようとしています。

2021 年に始まった COVID-19 パンデミックは、人類社会に大きな影を落とす一方で、PCR 検査、mRNA ワクチンなど先進技術の飛躍的進歩をもたらしました。 さらには、ステイホームで普及したオンラインゲーム機の G P U（Graphics Processing Unit）は、図らずも A I の心臓としてその演算処理速度を飛躍的に高めました。
今や世界は、センシング技術と A I を合体させた Smart Home で、人体の big data を収集して、Digital Health を構築する段階に入っています。ベッドが、呼吸・心拍・睡眠・などのバイタルサインを計測し、トイレが排泄物の代謝物質を計測します。近い将来、健診のためにわざわざ病院に行く必要がなくなります。

これからの医療従事者は、従来の医療技術の習得はもちろんのこと、再生医療、ゲノム医療、mRNA ワクチン、IoT、A I、そして Big-Data の取り扱いにも精通しなければなりません。人類が百数十年かけて構築してきた診断学・治療学は、数年のうちに A I にとって変わられるかもしれません、そして人類はよりクリエイティブかつ未知な領域の医療技術の開拓に従事しなければなりません。

本学会は、従来の治療医学の枠にとらわれず、世界水準の未来医療を臨床に取り入れて、up to date に進化していく。
そのような人材の育成に力を入れ、人類のクオリティオブライフの向上に寄与することを目的とします。

代表理事：　新垣 実
福澤 嘉孝

Greetings from the Chairman of the Board of Directors

The world is changing at a dizzying pace. The environment surrounding us medical professionals is also undergoing significant changes with the influx of new technologies and knowledge, such as regenerative medicine, genome medicine, immunotherapy, mRNA vaccines, IoT, and the introduction of AI. In the 20th century, modern medicine opened the door to integrative medicine, dramatically improving the outcomes of many chronic diseases. Now, in the 21st century, the door is opening to the future of medicine, centered on preventive and preemptive medicine, aiming at anti-aging and a society of "Pinpinkorori" (meaning live well, die well).

While the COVID-19 pandemic that began in 2021 cast a heavy shadow over human society, it also brought about dramatic advances in advanced technologies such as PCR testing and mRNA vaccines. Furthermore, the G P U (Graphics Processing Unit) of online game consoles, which became popular in stay-homes, has dramatically increased computing speed as the heart of AI.
The world is now in building Digital Health by collecting extensive data about the human body in the Smart Home, which combines sensing technology and AI. The bed measures vital signs such as respiration, heart rate, and sleep, and the toilet measures metabolites in excretions. It will no longer be necessary to go to the hospital for medical checkups imminently.

Future medical professionals must master not only conventional medical technologies, but also become proficient in regenerative medicine, genome medicine, mRNA vaccines, IoT, AI, and handling Big-Data. Diagnostics and therapeutics, which humankind has been building for more than a hundred decades, may be replaced by A I in a few years, and humankind must engage in pioneering medical technologies in more creative and unknown areas.

This society will evolve to date by incorporating world-class future medicine into clinical practice, without being bound by the boundaries of conventional therapeutic medicine. We aim to contribute to the improvement of the quality of life of humankind by focusing on the development of such human resources.

MINORU ARAKAKI, MD, PhD.
Yoshitaka Fukuzawa, MD, PhD., FACP

国際未来医療臨床医学会（SIFCM） 発足記念シンポジウム
日 程 表

Time	プログラム	登壇・発表者	演題及び座長
9:00	開場・受付開始		
10:00	共同代表理事 トークセッション	新垣 実・福沢 嘉孝	座長 田中 善
10:30	**講演 1**	新垣 実	座長 田中 善 演題 エンドカンナビノイドと植物性カンナビノイドの作用機序 Mechanism of action of endocannabinoids and phytocannabinoids
11:05	質疑応答		
11:10	**講演 2**	川上 智史	座長 田中 善 演題 ブレインフォグのメカニズムと今後の戦略 ～COVID-19と環境化学物質の両面から～ Brain Fog Mechanism and Future Strategies -From the perspectives of both COVID-19 and environmental chemicals-
11:45	質疑応答		
11:50	休憩（10分間）		
12:00	ランチョンセミナー	東栄新薬株式会社	座長 福沢 嘉孝
13:00	休憩（60分間）		
14:00	**講演 3**	岡本 正人	座長 小林 正学 演題 癌に対する免疫・精密医療：免疫のアクセルとブレーキを操る Immuno-precision medicine for cancer: Regulation of the accelerator and brake of immunity
14:35	質疑応答		
14:40	**講演 4**	神保 太樹	座長 田中 善 演題 感覚器障害関連研究の活用と展望 Researches of olfactory Disorders for Utilization and Prospects
15:15	質疑応答		
15:20	休憩（25分間）		
15:45	**講演 5**	福沢 嘉孝	座長 小林 正学 演題 老化制御と健康長寿 戦略的未病予防と健康長寿～mRNAの応用解析システム～ Aging control and healthy longevity Strategic pre-disease prevention and healthy longevity ～applied analysis system by using mRNA～
16:20	質疑応答		
16:25	共同代表理事　所信表明	新垣 実・福沢 嘉孝	
16:30	終了		

※ 会場は17時完全撤退となります。何卒よろしくお願い申し上げます。

会場

京都市勧業館
みやこめっせ
（特別展示場　A・B）

〒606-8343
京都市左京区岡崎成勝寺町9番地の1
TEL： 075-762-2630

Access アクセス
https://www.miyakomesse.jp/access/

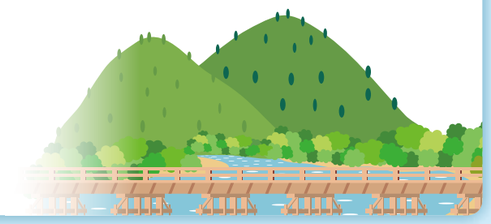
電車・バスでお越しの場合

最寄駅：京都市営地下鉄東西線「東山駅」より徒歩約 8 分

京都駅から
- 京都市営地下鉄
  地下鉄烏丸線～「烏丸御池駅」乗換え～地下鉄東西線～「東山駅（みやこめっせ前）」下車
  （乗車約 15 分、徒歩約 8 分）
- 市バス
  A-1 のりば　5 系統　「岡崎公園 美術館・平安神宮前」下車
  D-2 のりば　206 系統　「東山二条・岡崎公園口」下車
- タクシー（約 20 分）

四条河原町から
- 市バス
  H のりば　5 系統　「岡崎公園 美術館・平安神宮前」下車
  H のりば　32 系統　「岡崎公園 ロームシアター京都・みやこめっせ前」下車
  E のりば　46 系統　「岡崎公園 ロームシアター京都・みやこめっせ前」下車
  E のりば　31,201,203 系統　「東山二条・岡崎公園口」下車
- タクシー（約 10 分）

三条京阪から
- 市バス
  D のりば 5 系統　「岡崎公園 美術館・平安神宮前」下車
- タクシー（約 5 分）
- 徒歩（約 14 分）

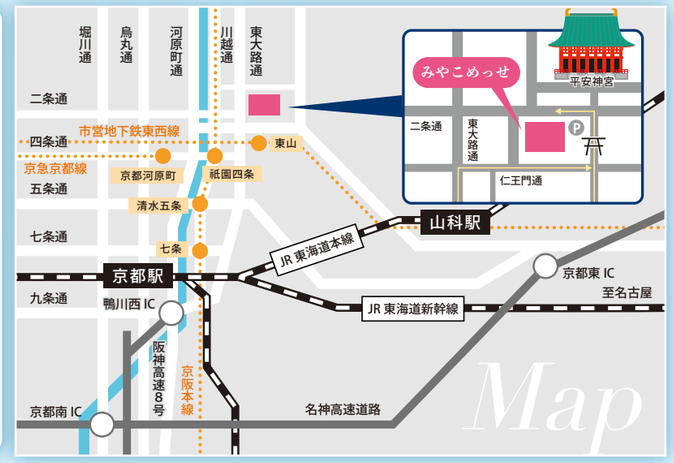


車でお越しの場合

高速道路 IC からのアクセス
- 名神高速道路
  京都東 IC ➡ 市内へ約 7km
- 第二京阪道路
  鴨川西 IC ➡ 市内へ約 6km

一般駐車場案内

【地下 2 階（163 台収容・高さ 2.1m、長さ 6m まで）】
- 平日＜月～土＞
  最初の 1 時間 520 円、以降 30 分毎に 200 円
  平日最大 1,500 円
  ※土曜日が祝日にあたる場合は日祝料金になります。
- 日祝
  最初の 1 時間 520 円、以降 30 分毎に 200 円
  ※最大料金は適用されません。



目次

各講演者プロフィール・演題・論文ページ

2023 6.25 Sun
Society of International Future Clinical Medicine Inauguration Symposium in KYOTO

新垣 実 *Minoru Arakaki*

×

福沢 嘉孝 *Yoshitaka Fukuzawa*

TALK SESSION

BY
co-Representative Director

共同代表理事トークセッション

「国際未来医療臨床医学会」学会名の由来

再生医療

最先端技術が担う医療分野について

IoT

ゲノム医療

mRNAワクチン

AI

エンドカンナビノイドシステム

ブレインフォグ

モデレーター：田中 善

【メモ欄】

（医）新美会新垣形成外科　理事長
日本臨床カンナビノイド学会　理事

新垣 実

国際未来臨床医学会(SIFCM) 代表理事

略 歴

1959年	沖縄県那覇市生まれ
1984年	長崎大学医学部卒業
1984～85年	沖縄県立中部病院外科研修
1986年	長崎大学医学部形成外科入局
1994年	中部徳洲会病院形成外科部長
1998年	スキンクリニック新垣開設
2004年	新垣形成外科開設、現在に至る

所属学会・役職等

日本形成外科学科正会員／専門医
国際形成外科学会正会員
日本美容外科学会正会員／専門医／理事
国際美容外科学会正会員
日本レーザー医学会正会員
日本抗加齢医学会正会員／専門医
日本統合医療学会正会員／専門医
日本臨床栄養学会正会員
NPO分子矯正医学協会／認定医
日本臨床カンナビノイド学会正会員／理事
国際医療カンナビノイド学会正会員／専門医アンバサダー

称号・資格

医学博士、イオンド大学名誉博士

Medical Corporation Shinbikai Arakaki Plastic Surgery Chairman,
Japanese Society of Clinical Cannabinoids Director

MINORU ARAKAKI

Representative Director of the Society of International Future Clinical Medicine (SIFCM)
MINORU ARAKAKI, MD, PhD.

Career

1984	Graduated at Nagasaki University School of Medicine
1985	Resident of Okinawa prefectural Chubu Hospital.
1986	Surgeon of Dept. of Plastic Surgery of Nagasaki University Hospital.
1994	Chief Surgeon of dept. of Plastic Surgery of Chubu Tokushukai Hospital.
1998	President of Skin Clinic Arakaki
2004	President of Arakaki Plastic Surgery

Affiliated academic societies

Certificate doctor of Japan Society of Plastic and Reconstructive Surgery (JSPRS)
Certificate doctor of Japanese Society of Aesthetic Plastic Surgery (JSAPS)
Certificate doctor of Japanese Society of Anti-aging Medicine (JAAM)
Certificate doctor of Integrative Medicine Japan (IMJ)
Certificate doctor of NPO orthomolecular Medical Nutrition & Associate
Board Member of JSAPS
Board Member of Japanese Clinical Association of Cannabinoids (JCAC)
Active Member of International Society of Aesthetic Plastic Surgery
Active member / Professional ambassador of International Association of Cannabinoids for Medicine (IACM)

Specialty

Plastic Surgery, Cosmetic Surgery, Anti-aging Medicine, Ortho-molecular medicine, Integrative Medicine,
Established Japanese first academic society for medical marijuana (JCAC)

座長：田中 善

講演者 新垣 実

演 題

エンドカンナビノイドと植物性カンナビノイドの作用機序

人体の恒常性を維持するシステムとして、免疫系、内分泌系、脳神経系の３大制御システムが知られている。さらに近年、第４の制御システムとして、機能性脂質であるエンドカンナビノイドをリガンドとするエンドカンナビノイドシステム（ECS）が注目を浴びている。
その発見は、大麻の主成分であるTHC(Tetrahydro　Cannabinol)がなぜ人体に作用し、脳の興奮作用を有するのかという研究が発端となった。さらには、興奮作用を持たない他の成分、CBD(cannabidiol)やCBG(cannabigerol)などの作用についても研究が進んでいる。

本講演では、これまでに解明されたECSと植物性カンナビノイドの作用について、最近の研究から得られた知見について紹介する。

Chairperson：Yoshimu Tanaka

Speaker Minoru Arakaki

Subject

Mechanism of action of endocannabinoids and phytocannabinoids

Three major regulatory systems are known to maintain homeostasis in the human body: the immune system, the endocrine system, and the cranial nervous system. More recently, a fourth regulatory system, the endocannabinoid system (ECS), which uses endocannabinoids, functional lipids, as ligands, has been attracting attention.
The discovery of this system was triggered by research into why THC (Tetrahydro Cannabinol), the main component of cannabis, acts on the human body and has an excitatory effect on the brain. Furthermore, research has also been conducted on the effects of other components that do not have excitatory effects, such as CBD (cannabidiol) and CBG (cannabigerol).

In this talk, I will present the findings from recent studies on the effects of ECS and Phyto cannabinoids that have been elucidated so far.

nutrients

MDPI

Review

Personalized Nutritional Therapy Based on Blood Data Analysis for Malaise Patients

Minoru Arakaki [1,*], Li Li [2], Toshiyuki Kaneko [3], Hiromi Arakaki [1], Hiromi Fukumura [1], Chihiro Osaki [1], Maki Yonamine [1] and Yoshitaka Fukuzawa [4]

[1] Arakaki Plastic Surgery, 729 Uchidomari, Ginowan 901-2227, Okinawa, Japan; hiromi-a@cosmoe.ne.jp (H.A.); fukumura@arakakikeisei.com (H.F.); chihiro@arakakikeisei.com (C.O.); akcmac@gmail.com (M.Y.)
[2] QDU International Tele-Consultation Platform, Qingdao United Family Hospital, 319 Hong Kong East Road, Laoshan District, Qingdao 0532-266102, China; lilidoc@126.com
[3] Orthomolecular Nutrition Laboratory Inc., KYB Build. 3F, 1-6-13 Higashi, Sibuya-ku, Tokyo 150-0011, Japan; t.kaneko.19790402@gmail.com
[4] Aichi Medical Preemptive and Integrative Medicine Center, Aichi Medical University Hospital, 1-1 Yazakokarimata, Nagakute 480-1103, Aichi, Japan; yofuku@aichi-med-u.ac.jp
* Correspondence: info@arakakikeisei.com

Abstract: As medical doctors, we routinely check patient blood chemistry and CBC data to diagnose disease. However, these data and methods of analysis are very rarely used to find pre-disease conditions or treat undiagnosed malaise. Masatoshi Kaneko Ph.D. found that many pre-disease conditions and types of malaise could be detected using his unique method of blood data analysis, and could also be treated using personalized nutritional therapy as an alternative to using drugs. The authors of this article introduce personalized nutritional therapy based on blood data analysis (Kaneko's method), and present and discuss some clinical cases. In total, 253 pre-disease or undiagnosed patients were treated using this nutritional therapy approach, and most of them recovered from their chronic symptoms and pre-disease conditions. This novel nutritional therapy has the potential to help many presymptomatic and undiagnosed patients suffering from malaise.

Keywords: nutrition; preventive medicine; personalized medicine; ortho-molecular nutrition; blood examination; anti-aging

Citation: Arakaki, M.; Li, L.; Kaneko, T.; Arakaki, H.; Fukumura, H.; Osaki, C.; Yonamine, M.; Fukuzawa, Y. Personalized Nutritional Therapy Based on Blood Data Analysis for Malaise Patients. *Nutrients* **2021**, *13*, 3641. https://doi.org/10.3390/nu13103641

Academic Editor: Laura Di Renzo

Received: 14 September 2021
Accepted: 15 October 2021
Published: 18 October 2021

1. Introduction

Advances in molecular nutrition have generated the concept of ortho-molecular nutritional therapy. Dr. Masatoshi Kaneko pioneered the concept of ortho-molecular nutritional therapy in Japan. Kaneko determined the optimal range (ideal standard values) for blood examination by analyzing more than 350,000 blood data sets. He found that the minimum deviation from the optimal ranges for blood data can be used to diagnose deficiencies in various nutrients, and that certain combinations of blood data indicate suboptimal function of specific organs. For example, in the absence of liver or bone disease, a low alkaline phosphatase (ALP) level suggests zinc deficiency; a serum level of aspartate aminotransferase (AST) > alanine aminotransferase (ALT) indicates vitamin B6 deficiency; an increase in mean corpuscular volume (MCV) with low ferritin means weakness of cell membranes; and a reduction in blood urea nitrogen (BUN) without kidney disease means a low protein intake [1]. These physiological readings are never taught to the current generation of medical students or medical doctors.

Kaneko also found that many symptoms indicated by blood data can be treated with nutrients according to his defined optimal ranges. He applied personalized nutritional therapy based on the blood data analyses of patients experiencing malaise and prescribed

ScienceDirect

Personalized Medicine Universe
Volume 2, July 2013, Pages 28-33

Original article

Mineral fasting based on ortho-molecular medicine for healthy weight control

Minoru Arakaki [a], Li Li [b], Toyofumi Yamada [c]

Show more

Share Cite

https://doi.org/10.1016/j.pmu.2013.04.006
Get rights and content

Abstract

In slimming therapy in plastic and cosmetic surgery, treatment based on internal medicine rather than surgical treatments is a viable option. Such surgical treatments, which include liposuction and plastic surgery of the abdominal wall, are contour plasty or partial-slimming techniques, and are not intended for the purpose of weight loss. For reduction of body weight and visceral fat as well as relief from lifestyle-related diseases, this article describes the application of ortho-molecular medicine techniques that center on the use of mineral fasting. During this treatment, mineral fasting and nutrition therapy are conducted while monitoring of nutritional status and body tissue analysis based on blood biochemical testing is periodically performed. During the slimming therapy described here, metabolism becomes hypercatabolized, allowing partial slimming by mesotherapy to become very effective. By applying this slimming therapy in conjunction with surgical therapy, weight loss treatment can be

報　告

日本におけるカンナビジオール製品の使用実態に関する横断調査

How cannabidiol products are used and valued：A cross-sectional study in japan

正高佑志[1,2]・杉山岳史[1]・赤星栄志[3]・新垣　実[4]
Yuji MASATAKA　Takeshi SUGIYAMA　Yoshiyuki AKAHOSHI　Minoru ARAKAKI

要　旨：　背　景：大麻草に特異的に含有される化合物であるカンナビジオール（CBD）は抗てんかん薬として処方される以外にも諸外国では疼痛、不安、不眠などの症状緩和に利用されている。本邦でも近年、食品、化粧品、嗜好品として幅広く流通しているが、国内における CBD 製品の用途や有効性、安全性についての調査はこれまでに行われたことがない。
方　法：2021 年 8 月 16～31 日の期間に CBD 使用についてのオンライン調査フォームを作成し、SNS を用いて回答を呼びかけた。調査対象は CBD 使用経験者（過去 1 年以内に Δ9-tetrahydrocannabionol（THC）を含む大麻使用者を除く）とした。
結　果：回答した 1,351 名のうち、解析対象に該当した 799 名の 60.6％は男性で、平均年齢は 37.7 歳であった。用途として多かったのはリラクゼーション（77.8％）、睡眠改善（66.3％）、不安（56.2％）、健康増進（50.8％）、抑うつ（47.8％）であり、使用者は平均して 5.5 の目的に対して CBD を使用していた。使用前後の各症状についての重症度自己評価で 50％以上改善していた人の割合は以下のとおりであった：頭痛 70.9％、慢性痛 67.8％、睡眠障害 67.4％、物質使用障害 66.7％、神経痛 65.5％、抑うつ 62.4％、不安 59.6％、関節痛 54.5％、膠原病 50.0％、皮膚疾患 49.7％、てんかん 42.1％、ぜんそく 37.8％。副作用が疑われる症状の出現率は 7.4％で、重篤なものは認められなかった。
結　論：日本国内において、CBD 製品は主にメンタルヘルス領域のセルフケアの手段として活用され、ユーザーの多くが症状の改善を自覚していることが示唆された。

キーワード：カンナビジオール、大麻草、カンナビノイド、オンライン調査

ABSTRACT：Background：Cannabidiol(CBD), a compound specifically contained in the cannabis plant, is used in other countries to relieve symptoms of pain, anxiety, and insomnia, in addition to being prescribed as an antiepileptic drug. In Japan, it has been widely distributed in recent years in foods, cosmetics, and luxury goods. However, there have been no studies on the uses, efficacy, and safety of CBD products in Japan.
Methods：We created an online survey soliciting responses through social media from August 16 to 31, 2021. We limited the respondents to those who had previously used CBD and excluded respondents who had consumed cannabis that contained Δ9-tetrahydrocannabionol（THC）in the past year.
Results：Of the 1,351 respondents, 799 were included in the analysis, 60.6% of whom were male, with an average age of 37.7 years. The most common uses for CBD were relaxation (77.8%), sleep (66.3%), anxiety (56.2%), health improvement (50.8%), and depression (47.8%). Respondents used CBD for an average of 5.5 different purposes. Respondents assessed the severity of their illness/health problem before and after CBD use. The percentage of respondents for whom the severity was alleviated by more than 50% was as follows：headache (70.9%), chronic pain (67.8%), sleep disturbances (67.4%), substance use disorder (66.7%), nerve pain (65.5%), depression (62.4%), anxiety (59.6%), joint pain (54.5%), collagen disease (50.0%), and skin disease (49.7%). Epilepsy scored 42.1% and asthma 37.8%. The incidence of adverse events was 7.4%, and none of them were considered serious.
Conclusion：In Japan, it is suggested that CBD products are used as a means of self-care mainly in the area of mental health, and that many users have experienced improvements in their symptoms.

Key words：cannabidiol, cannabis, cannabinoids, online survey

1）一般社団法人 Green Zone Japan
2）医療法人山部会くまもと成城病院
3）日本大学生物資源科学部
4）医療法人新美会新垣形成外科

MEMO

【メモ欄】

桐生大学医療保健学部人体構造機能学 准教授
日野厚生クリニック 院長補佐

川上 智史

国際未来臨床医学会(SIFCM) 専務理事

略 歴

2006年	北里大学大学院医療系研究科にて博士号取得
2006年～2009年	北里大学医学部公衆衛生学研究室
2010年～2012年	東北大学加齢医学研究所
2013年～2017年	東北大学大学院歯学研究科講師
2017年～2021年	東海大学医学部予防医学系公衆衛生学 客員准教授
2020年	日野厚生クリニック副院長に就任
2022年	桐生大学医療保健学部人体構造機能学 准教授

所属学会・研究会

日本口腔機能水学会常任理事、日本統合医療学会理事、日本先制臨床医学会理事

称号・資格

微量有害化学物質が生体に与える影響について博士号取得。
主にエストロゲン感受性関連疾患について乳がん、自己免疫疾患、骨粗鬆症、腸管免疫中枢、
グリア細胞に対する影響など、疾患の関連性について研究、シックハウス症候群についての研究、
健康の維持増進に関わる研究。

Associate Professor of KIRYU UNIVERSITY Department of Nutrition
Assistant Director, Hinokosei clinic

SATOSHI KAWAKAMI

Vice Chairman of the Society of International Future Clinical Medicine (SIFCM)
Satoshi Kawakami, PhD.

Career

2006	Graduated at Kitasato University Graduate School of Medical Science .
2006	Researcher of Public Health, School of Medicine, Kitasato University.
2009	Researcher of Institute of Development, Aging and Cancer, Tohoku University.
2013	Associate professor / lecturer, Tohoku University Graduate School of Dentistry.
2017	Associate professor / lecturer, Tokai University School of Medicine.
2022	Associate Professor of KIRYU UNIVERSITY Department of Nutrition.

Affiliated academic societies

Associate Professor of KIRYU UNIVERSITY Department of Nutrition.
Assistant Director, Hinokosei clinic.
Permanent Director of The Japan Society for Oral Functional Water
Director of Japan Society of Preemptive and Clinical Medicine
Director of the Society for Integrative Medicine Japan
Director of the Japanese Society of Stem Cell Culture Supernatant for Clinical Medicine
Board Member of Brain Fog Study Group

Specialty

Public Health, Preventive Medicine, Environmental Medicine, Functional Food, Functional water, Integrative Medicine.
We place importance not only on Western medicine but also on Eastern medicine, and build a system that identifies possible diseases in the future through health examinations and monitoring in order to identify the possibility of pre-illness or near-healthy pre-symptomatic disease.

座長：田中 善

講演者 川上 智史

演 題

ブレインフォグのメカニズムと今後の戦略 ～COVID-19と環境化学物質の両面から～

COVID-19が最初に確認されてから世界的にパンデミックが起こり、日本においては世界的に見ても不織布マスクの着用率が高いにもかかわらず2022年8月には新規感染者数が世界で一位になってしまうなど、感染率が高い傾向にあった。COVID-19における近年の課題として「後遺症」が挙げられている。味覚障害等は以前から言われているが、最近では「ブレインフォグ」が注目されている。

このブレインフォグは「頭にもやがかかったような状態」を指し、倦怠感や集中力の低下、思考力の低下や傾眠などの症状が引き起こされてしまい、ADLに支障をきたしてしまうと言われている。
現段階では脳内における神経伝達不足がこれらの症状を引き起こす可能性が指摘されているが、これらもホメオスターシスの破綻の一種であると考えられる。この原因はタンパク質（抗体）等が神経伝達に必要な部位を攻撃してしまうことによってアセチルコリンをはじめとするセロトニンやドーパミンなどの物質が分泌低下してしまうことに起因していると考えられているが、実態は把握できていない。

一論によると活性酸素の関係性も指摘されている。抗酸化物質にはアスコルビン酸をはじめ、白金パラジウムや、NMN、イチョウ葉エキス含有プラズマローゲン、ポリフェノールなど多義にわたるが、これらの機能性成分を使用した予防・治療が今後先制臨床においては重要なポジションを担うと言うことが考えられる。
今後保険診療だけにとらわれない自由診療においてもこれら機能性食品を使用して疾患の予防・治療に役立てていく、そのような基準を学会として作っていきたい。

本講演においては自身の専門である環境医学、とりわけ化学物質についての講演を行いたい。
環境化学物質による化学物質過敏症からもブレインフォグのような症状も指摘されているために、化学物質と認知機能における相関性について検討を行う。

Chairperson：Yoshimu Tanaka

Speaker Satoshi Kawakami

Subject

Brain Fog Mechanism and Future Strategies

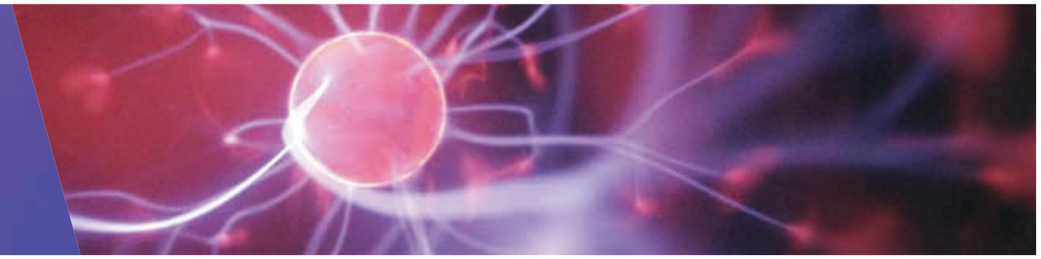
-From the perspectives of both COVID-19 and environmental chemicals-

Since COVID-19 was first confirmed, a global pandemic has occurred, and despite the high rate of non-woven masks being worn in Japan in August 2022, the number of new infections will be the highest in the world. The infection rate tended to be high, such as being ranked number one. In recent years, "aftereffects" have been cited as a challenge in COVID-19. Taste disorders have been mentioned for a long time, but recently, "brain fog" has been attracting attention.

This brain fog refers to ``a state in which the head is foggy'', and symptoms such as fatigue, reduced concentration, reduced thinking ability, and somnolence are caused, and it is said that it interferes with ADL. It is said. At the present stage, it is pointed out that insufficient neurotransmission in the brain may cause these symptoms, but these are also considered to be a kind of failure of homeostasis. It is believed that this is caused by proteins (antibodies) attacking the sites necessary for neurotransmission, resulting in decreased secretion of substances such as acetylcholine, serotonin, and dopamine. However, the actual situation has not been grasped.

According to one theory, the relationship of active oxygen is also pointed out. Antioxidants include ascorbic acid, platinum palladium, NMN, ginkgo biloba extract-containing plasmalogen, and polyphenols. It can be said that it carries In the future, we would like to create such a standard as an academic society that will use these functional foods for the prevention and treatment of diseases even in private medical practice that is not limited to insurance medical treatment.

In this lecture, I would like to give a lecture on environmental medicine, which is my specialty, especially chemical substances. Brain fog-like symptoms have also been pointed out from chemical hypersensitivity due to environmental chemicals, so we will examine the correlation between chemical substances and cognitive function.



Clinical Imaging and Case Reports (ISSN 2770-9205)

Anticancer action by natural ingredient NMN and its mechanism: Focusing on the molecular mechanism of NMN on breast cancer cells.

Satoshi Kawakami [1,2], Yoshitaka Fukuzawa [3], Hiroyuki Ichikawa [1], Takaharu Ide [4] Kensho Yorozu [5] and Kou Sakabe [2].

1. Tohoku University Graduate School of Dentistry, Oral and Craniofacial Anatomy.Sendai, Japan.
   Email : ksato21@dent.tohoku.ac.jp
2. Hinokosei Clinic, Tokyo, Japan
3. Aichi Medical Preemptive and Integrative Medicine Center (AMPIMEC), Nagakute, Japan.
   Email : yofu-ku@aichi-med-u.ac.jp
4. University of East Asia, Faculty of Human science.
   Email : ide@toua-u.ac.jp
5. YOROZU Clinic, Tottori, Japan.
   Email : incepk@gmail.com

Corresponding Author:
Satoshi Kawakami ,
Tohoku University Graduate School of Dentistry, Oral and Craniofacial Anatomy.Sendai, Japan
E-mail: ksato21@dent.tohoku.ac.jp

Article Type: Case Report

Received Date: December 15 2021
Accepted Date: December 16 2021
Published Date: January 18 2022

Abstract:
It was confirmed that NMN causes a decrease in breast cancer cells. Breast cancer is now a major problem for women because it is sensitive to estrogen. The standard treatments for breast cancer are generally surgery, anticancer drugs, and radiation therapy. In addition, as a complementary / alternative therapy, it is said that stress management, relaxation for stress re-duction, vitamins, and dietary fiber, which are said to have antioxidant effects as nutritional components, are used. However, although there is potential from an antioxidant perspective at this stage, no evidence is available at this time. Therefore, this time, this research group investi-gated the effect on breast cancer cells at the in vitro level using the component "NMN", which is currently attracting attention. When NMN was added to breast cancer cells, a significant reduc-tion in breast cancer cells was observed in a concentration-dependent manner. Therefore, this time, we investigated α-ketoglutaric acid, NAD +, and AMPK, which are thought to be related to the anticancer effect. It was found that NMN has the effect of activating these, suggesting that NMN may be used as a complementary / alternative therapy for breast cancer patients in the fu-ture

Keywords:
NMN, Functional Foods, nutritional therapy, complementary / alternative, nutrients, α-ketoglutaric acid, NAD +, AMPK

1. Introduction

In recent years, the number of deaths from breast cancer has been increasing world-wide, and countermeasures are urgently needed.[1] Therefore, we have conducted basic research using MCF-7 cells derived from human breast cancer. As a result, when NMN (nicotinamide mononucleotide) was allowed to act on MCF-7, a growth inhibitory effect was confirmed. Since MCF-7 cells have an estrogen receptor[2], they are sensitive to estro-gen and are known to be associated with the development of breast cancer in women. Current standard treatments for breast cancer are resection, antineoplastic treatment, hormone therapy, and radiation therapy. [3]In addition, since the existence of "active oxy-gen" is known as one of the factors promoting the growth of cancer cells[4], ingestion of nutritional components having antioxidant power has been attempted as a complemen-tary / alternative therapy.[5] At present, although the possibility of a cancer cell-reducing effect focusing on such an antioxidant effect is fully considered[6], detailed research re-sults such as the mechanism have not been obtained. Therefore, this time, we examined the mechanism at the in vitro level using the nutritional component "NMN (nicotinamide mononucleotide)", which is currently attracting attention. NMN is a substance contained in nicotinic acid (niacin), a coenzyme present in the cells of all living organisms, and is produced in the body.[7] NMN is also known as a precursor of NAD +.[7] In addition, NMN is a coenzyme present in all species and is found in various nutrient sources such as milk and broccoli. It has been reported that when NMN decreases due to aging, the amount of NAD + produced also decreases, and cell damage and mitochondrial activity also decrease.[8]It is believed that this causes cell damage and causes cancer.[9]There are no reports on the antioxidant activity of NMN, and there are reports that it improves mi-tochondrial function and increases metabolism. [10]NMN is an ingredient that is currently attracting attention in various fields as an "anti-aging substance" and is a substance made from vitamin B3.[11]In addition, NMN is said to

JOURNAL OF BIOMEDICAL RESEARCH & ENVIRONMENTAL SCIENCES
ISSN: 2766-2276
PHARMACOLOGY | PHARMACEUTICA ANALYTICA ACTA
DOI: 10.37871

RESEARCH ARTICLE

NMN "Nicotinamide Mononucleotide" Activates Intracellular Energy and Approaches the Prevention and Improvement of Aging

Satoshi Kawakami[1,2,7]*, Yoshitaka Fukuzawa[3], Hiroyuki Ichikawa[2], Tsutomu Sato[4], Takaharu Ide[5], Yusuke Maeda[6] and Takahiko Yamamoto[7]

[1]Kiryu University School of Health Care, Gunma, Japan
[2]Tohoku University Graduate School of Dentistry, Oral and Craniofacial Anatomy. Sendai, Japan
[3]Aichi Medical Preemptive and Integrative Medicine Center (AMPIMEC), Nagakute, Japan
[4]Tokai University School of Medicine, Faculty of Medicine and Nursing, Isehara, Japan
[5]University of East Asia, Faculty of Human science. Yamaguchi, Japan
[6]Gran Pro Clinic Ginza, Tokyo, Japan
[7]Wellness-One Co., Ltd. Iwate, Japan

ABSTRACT

Aging was defined as one of the diseases by ICD-11. Preventing aging may avoid the risk of various diseases. However, it is difficult to simply prevent aging in daily life. The presence of nutrients is essential there. This time, we reviewed NMN "nicotinamide nucleotide", which is attracting attention as an anti-aging component, and conducted additional experiments using AMPK "AMP-activated protein kinase" and NAD + as indicators to determine whether or not it actually prevents aging gone. As a result, a significant increase in AMPK and NAD + was confirmed, suggesting that NMN may help prevent aging in the future.

*Corresponding author

Satoshi Kawakami, Kiryu University School of Health Care, Gunma, Japan

Tel: +81-277-489-128
E-mail: kawakami-sa@kiryu-u.ac.jp

DOI: 10.37871/jbres1480

Submitted: 17 May 2022

Accepted: 20 May 2022

Published: 21 May 2022

Keywords

- Aging
- NMN
- AMPK
- NAD+
- Functional food
- Vitamins

MEDICINE GROUP
PHARMACOLOGY | PHARMACEUTICA ANALYTICA ACTA
VOLUME: 3 ISSUE: 5 - MAY, 2022

INTRODUCTION

From ICD-11, aging has been treated as a disease [1]. Aging is said to be a physical and mental decline associated with aging [2,3]. Since aging is considered to be the cause of all diseases [4], countermeasures are urgently needed. In order to prevent aging, it is said that active intake of nutrients that are good for the body [5], good sleep [6], and moderate exercise [7], but if it is not done by one's own will, it is said. Is said to cause stress and generate active oxygen that causes aging [8]. It is said that active oxygen and aging are closely related [8]. Reactive oxygen species are generated by various external and internal factors [9], weaken normal mitochondrial function [10], and may be a risk of aging-related diseases such as cancer. There are four types of active oxygen in a nutshell [11], which can be divided into superoxide, hydroxyl radical, hydrogen peroxide, and singlet oxygen [12]. Normally, these active oxygens are produced by enzymes for removing active oxygen, such as SOD (superoxide dismutase) and catalase that exist in the living body [12,13]. In addition, active oxygen is also removed by antioxidants taken from the diet, such as vitamin C and vitamin E [14,15]. However, these reactive oxygen species are usually produced in small amounts in the body and are involved in functions such as maintenance of homeostasis, signal transduction, gene expression, and receptor activation in cells [16], so it is not possible to remove them altogether. It is

Check for updates

SCAN ME

How to cite this article: Kawakami S, Fukuzawa Y, Ichikawa H, Sato T, Ide T, Maeda Y, Yamamoto T. NMN "Nicotinamide Mononucleotide" Activates Intracellular Energy and Approaches the Prevention and Improvement of Aging. J Biomed Res Environ Sci. 2022 May 21; 3(5): 560-565. doi: 10.37871/jbres1480, Article ID: JBRES1480, Available at: https://www.jelsciences.com/articles/jbres1480.pdf

JOURNAL OF BIOMEDICAL RESEARCH & ENVIRONMENTAL SCIENCES
ISSN: 2766-2276
SUBJECT AREAS: PULMONOLOGY | RESPIRATORY MEDICINE
DOI: 10.37871

CASE REPORT

Drinking Water Containing Platinum-Palladium (Functional Nutrient Water) Improved Interstitial Pneumonia and COPD: A Case Report

Satoshi Kawakami[1,2,4]*, Taro Shirakawa[2], Kou Sakabe[3], Tsutomu Sato[4], Takaharu Ide[5], Shoichi Wajima[6], Ryutaro Suma[7] and Yoshitaka Fukuzawa[8]

[1]Faculty of Health Care, Kiryu University, Gunma, Japan
[2]Hinokosei Clinic, Tokyo, Japan
[3]Department of Environmental Preventive Medicine, Center for Preventive Medical Sciences, Chiba University, Chiba, Japan
[4]Louis Pasteur Center for Medical Research, Kyoto, Japan
[5]Faculty of Human science, University of East Asia, Yamaguchi, Japan
[6]Toyokosei Seiyakusyo Co., Ltd. Tokyo, Japan
[7]Department of Frontier Health Sciences, Graduate School of Human Health Sciences Tokyo, Tokyo Metropolitan University, Japan
[8]Aichi Medical Preemptive and Integrative Medicine Center (AMPIMEC), Aichi, Japan

ABSTRACT

In this case, when a patient with interstitial pneumonia was given platinum palladium, improvement in respiratory function was observed. Generally, various treatment methods are used for interstitial pneumonia, but conservative therapy has been the main focus and no curative solution has been reached. In this case, there was a tendency for improvement in patients who took platinum palladium, so we reported it. Since it is only drunk, it is not invasive and has great benefits for patients. It has also been reported that COPD, which is also a respiratory disease, showed an improvement tendency by drinking platinum palladium. Although the mechanism is still unknown, it is considered that it is largely due to the antioxidant action by platinum palladium and the activation of AMPK. In the future, we would like to examine further cases and improve the mechanism.

*Corresponding author

Satoshi Kawakami, Faculty of Health Care, Kiryu University, Gunma, Japan

Tel: +81-277-48-9128
E-mail: kawakami-sa@kiryu-u.ac.jp

DOI: 10.37871/jbres1498

Submitted: 10 June 2022

Accepted: 13 June 2022

Published: 15 June 2022

Keywords

- Functional nutrient water
- Platinum-palladium
- Interstitial pneumonia
- COPD
- AMPK

Introduction

Interstitial pneumonia is a general term for diseases in which inflammation occurs mainly in the stroma of the lung [1]. The alveolar is roughly divided into parenchyma and stroma, the inside of the alveolar is called parenchyma, the wall of the alveolar and surrounding tissues are called stroma, and the disease that causes inflammation in this stroma is called interstitial pneumonia [2]. The causes of interstitial pneumonia include "autoimmune interstitial pneumonia", "occupational environmental interstitial pneumonia", and "medicinal interstitial pneumonia" causes [3-5]. Those that cannot be identified are referred to as "idiopathic interstitial pneumonia" [6]. In addition, interstitial pneumonia was classified by ATS / ERS in 2013.

1) Major IIPs

1. Idiopathic Pulmonary Fibrosis (IPF)
2. Idiopathic Nonspecific Interstitial Pneumonia (idiopathic NSIP)

MEDICINE GROUP
PULMONOLOGY | RESPIRATORY MEDICINE
VOLUME: 3 ISSUE: 6 - JUNE, 2022

How to cite this article: Kawakami S, Shirakawa T, Sakabe K, Sato T, Ide T, Wajima S, Suma R, Fukuzawa Y. Drinking Water Containing Platinum-Palladium (Functional Nutrient Water) Improved Interstitial Pneumonia and COPD: A Case Report. J Biomed Res Environ Sci. 2022 June 10; 3(6): 688-693. doi: 10.37871/jbres1498, Article ID: JBRES1498, Available at: https://www.jelsciences.com/articles/jbres1498.pdf

JOURNAL OF BIOMEDICAL RESEARCH & ENVIRONMENTAL SCIENCES
ISSN: 2766-2276
SUBJECT AREAS: PUBLIC HEALTH
DOI: 10.37871

CASE REPORT

Ginkgo biloba Extract Containing Plasmalogen May Improve Long COVID and Brain Fog: A Case Report

Satoshi Kawakami[1,5,6]*, Yoshimu Tanaka[2], Tsutomu Sato[3], Takaharu Ide[4], Masaaki Usui[5], Shigehisa Iida[5], Taro Shirakawa[6] and Yoshitaka Fukuzawa[7]

[1]Faculty of Health Care, Kiryu University, Gunma, Japan
[2]Tanaka Clinic, Osaka, Japan
[3]Faculty of medicine and Nursing, Tokai University School of Medicine, Isehara, Japan
[4]Faculty of Human science, University of East Asia, Yamaguchi, Japan
[5]Super Light Water Co., Ltd. Tokyo, Japan
[6]Hinokosei Clinic, Tokyo, Japan
[7]Aichi Medical Preemptive and Integrative Medicine Center (AMPIMEC), Nagakute, Japan

ABSTRACT

Other than pneumonia, Long COVID is currently cited as a problem with COVID-19. Among them, brain fog is a particular problem. Brain fog, as the name suggests, refers to a state in which the brain is foggy, and it is thought that there is a communication abnormality in the central nervous system, including fatigue. It has been pointed out that this may be caused by a cytokine storm, and since it lowers QOL (Quality of Life), countermeasures are urgently needed. In this study, we used plasmalogen containing *Ginkgo biloba* extract and found improvement in patients complaining of brain fog. As a result, we were able to confirm a case of excellent efficacy, which we report here.

*Corresponding author(s)

Satoshi Kawakami, Faculty of Health Care, Kiryu University, Gunma, Japan

Tel: +81-277-489-128
E-mail: kawakami-sa@kiryu-u.ac.jp

DOI: 10.37871/jbres1589

Submitted: 21 October 2022

Accepted: 27 October 2022

Published: 28 October 2022

Keywords

- COVID-19
- Brain fog
- *Ginkgo biloba* extract
- Plasmalogen
- Cerebral blood flow
- Cognitive function

Introduction

Although COVID-19, which has seen a global pandemic, seems to have calmed down somewhat, it has been repeatedly increasing and decreasing, so it cannot be said that it has converged yet [1]. Currently, although the number of people infected with COVID-19 itself has stabilized in Japan, there are many patients who are worried about the sequelae caused after infection, especially brain fog [2]. According to the WHO (World Health Organization), "in people with COVID-19, persisting for at least two months, and unexplained as a symptom of another disease (usually three months after the onset of COVID-19. It can also be seen after a month.)" and defines sequelae (post COVID-19 condition) [3]. Brain fog, as the name suggests, is a state in which the brain continues to be foggy [4], concentration is lost [5], a state of constant fatigue [6], and voice comes in even when spoken to a decline in cognitive function such as the inability to understand the content [7]. These are not medically defined diseases but are defined only as symptoms [1]. Since it is quite possible that Quality of Life (QOL) deteriorates in this symptom, countermeasures are urgently needed [8]. SARS-CoV-2, the cause of COVID-19, infects the epithelial cells of the upper respiratory tract, but if the infection ends there and inflammation occurs, the symptoms will be relatively mild [9]. However, when SARS-CoV-2 reaches the alveoli, it is known to cause fatal symptoms due to pneumonia and Acute Respiratory Distress Syndrome (ARDS) [10]. As mentioned above, the aftereffects of COVID-19 are a problem, and two factors are thought to be the causes. The first is thought to be caused by cytokine storm, which is the excessive release of cytokines after infection with COVID-19 [11]. Second, the virus itself destroys the Blood Brain Barrier (B.B.B),

MEDICINE GROUP
PUBLIC HEALTH
VOLUME: 3 ISSUE: 10 - OCTOBER, 2022

How to cite this article: Kawakami S, Tanaka Y, Sato T, Ide T, Usui M, Iida S, Shirakawa T, Fukuzawa Y. *Ginkgo biloba* Extract Containing Plasmalogen May Improve Long COVID and Brain Fog: A Case Report. 2022 Oct 28; 3(10): 1271-1275. doi: 10.37871/jbres1589, Article ID: JBRES1589, Available at: https://www.jelsciences.com/articles/jbres1589.pdf

口腔機水誌，J Jpn Soc Oral Funct Water, 22: 3 -10

原著論文

白金・パラジウムによる抗酸化能について
-白金・パラジウム含有清涼飲料水を用いた検討-

川上智史[1)2)]、市川博之[2)]、佐藤　勉[3)4)]、片岡洋樹[5)]、井手貴治[6)]、寺山隼人[3)]、坂部　貢[3)]

1）東海大学医学部看護学科
2）東北大学大学院歯学研究科口腔器官解剖学分野
3）東海大学医学部基礎医学系
4）公益財団法人　ルイ・パストゥール医学研究センター
　基礎研究部機能水研究室
5）東北大学大学院医学系研究科加齢医学研究所
6）東亜大学人間科学部

Antioxidant ability of platinum-palladium
-Study using soft drinks containing platinum-palladium-

Satoshi Kawakami[1)2)], Hiroyuki Ichikawa[2)], Tsutomu Sato[3)], Hiroki Kataoka[4)], Takaharu Ide[5)], Hayato Terayama[3)], Kou Sakabe[3)]

1) Tokai University School of Medicine, Faculty of Nursing
2) Tohoku University Graduate School of Dentistry, Oral and Craniofacial Anatomy
3) Tokai University School of Medicine, Division of Basic Medicine
4)Louis Pasteur Center for Medical Research, Division of　Basic Research, Functional Water Research Laboratory
5) Institute of Development, Aging and Cancer, Tohoku University
6) University of East Asia, Faculty of Human science

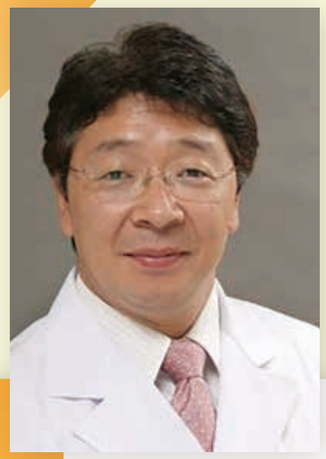
要旨：白金は白金族金属の一つで化学的に極めて安定した元素であり、様々な用途に利用されている。医科領域ではその錯体が抗がん剤として用いられており、また抗酸化作用に着目した活用法も報告されている。パラジウムは白金と同じく白金族金属元素で、工業用製品や歯科治療用の材料として、広く用いられている。パラジウムは還元反応に関与する白金に対して、再び還元力を付与する効果があることが知られており、白金とパラジウムを併用させた活用法も検討されている。その一つが、持続的な抗酸化能を期待する白金・パラジウム混合物の開発である。しかし、白金・パラジウムの抗酸化効果については、未だ明確にされていない点もある。

現在、白金・パラジウムを含む清涼飲料水が市販されている。しかしながら、同清涼飲料水の抗酸化作用について詳細は明らかにされていない。そこで、本研究は、4 種の存在が知られている活性酸素（Reactive Oxygen Species　：ROS）に着目し、これらに対する白金・パラジウム含有清涼飲料水の抗酸化作用について、基礎的な検討を行った、その結果、同清涼飲料水は 4 種の ROS を極めて短時間で除去する可能性があることが明らかになった、したがって、本研究の対象となった白金・パラジウム含有清涼飲料水は抗酸化という機能を有する飲料水となり得る可能性が示唆された。

キーワード：白金・パラジウム、白金・パラジウム含有清涼飲料水，活性酸素（ROS）

MEMO

【メモ欄】



（公財）仙台微生物研究所
研究所長・理事

岡本 正人

国際未来臨床医学会(SIFCM) 専務理事

略 歴

1988年	徳島大学歯学部　卒業
1992年	徳島大学大学院歯学研究科　修了
	徳島大学歯学部　口腔外科学第2講座　助手
1994年	米国ノースウェスターン大学医学部　病理学講座 Research Associate
2004年	徳島大学歯学部　口腔外科学第2講座　講師
2006年	武蔵野大学薬学部　薬物療法学研究室　客員教授
2011年	慶應義塾大学医学部　先端医科学研究所細胞情報研究部門　准教授
	鶴見大学歯学部　口腔内科学講座　臨床教授
2014年	北里大学薬学部　先端免疫治療学講座　特任教授
2017年	大阪大学大学院薬学研究科　先端免疫治療学講座　教授
2021年	United Family Healthcare　招聘教授
	（公財）仙台微生物研究所　研究所長・理事

関連する学術団体役職等

（旧）（一社）日本免疫・細胞治療学会 理事長（現SIFCM 専務理事）、（一社）日本統合医療学会 理事、（一社）日本バイオセラピィ学会 評議員、（一社）日本がん免疫学会 評議員、（一社）総合免疫学術機構 理事、米国癌学会　Active Member、米国臨床腫瘍学会 Full Member、エビデンスに基づく統合医療研究会 理事、（一社）日本口腔外科学会 専門医・指導医、（一社）日本輸血・細胞治療学会 細胞治療認定管理士（責任医師）その他数多くの学術団体において役職を歴任。

専門分野

複合免疫療法、免疫精密医療、癌免疫療法、免疫バイオマーカー、口腔外科医として口腔癌治療に従事するも標準治療の限界を感じて免疫療法の研究・開発を開始する。特に、Toll-like　receptorシグナルを利用した癌免疫療法および樹状細胞を用いた癌ワクチンの開発で功績を残した。現在は、免疫抑制解除技術（チェックポイント阻害剤等）と癌ワクチンの併用による「複合癌免疫療法」と、患者の状態を把握するための遺伝子・免疫検査を組み合わせた「免疫・精密医療」の確立に注力している。

発表論文

J Natl Cancer Inst, Cancer Res, Clin Cancer Res, Cancer Immunol Immunother, OncoImmunol, Pros One, Int J Cancer, Eur J Cancer, Neoplasia, Cancer Sci, 他多数

Chief and Director of Sendai Institute
of Microbiological Research

MASATO OKAMOTO

Vice Chairman of the Society of International Future Clinical Medicine (SIFCM)
Masato Okamoto, DDS, PhD.

Education and work histry

1988	Graduated at Tokushima Univ School of Dentistry
1992	Assistant Professor of 2nd Dept of Oral and Maxillofacial Surg, Tokushima Univ Sch of Dentistry
1994	Research Associate of Dept of Pathology, Northwestern Univ School of Medicine (Chicago, IL)
2004	Lecturer of 2nd Dept of Oral and Maxillofacial Surg, Tokushima Univ Sch of Dentistry
2011	Associate Professor of Division of Cellular Signaling, Institute for Advanced Medical Research, Keio University School of Medicine, Clinical Professor of Dept of Oral Medicine and Stomatol, Sch of Dental Medicine, Tsurumi Univ
2014	Professor of Dept of Advanced Immunotherapeutics, Kitasato Univ School of Pharmacy
2017	Professor of Dept of Advanced Immunotherapeutics, Osaka Univ School of Pharmaceutical Science
2021	Invited Professor of United Family Healthcare Chief and Director of Sendai Institute of Microbiological Research

Related Academic Organization Positions

President of Japan Society of Immunotherapy and Cell Therapy, Director of the Society for Integrative Medicine Japan
Councilor of the Japan Society for Biological Therapy, Councilor of Japanese Association of Cancer Immunology
Director of Evidence Based Integrative Medicine, Director of Academic Institute of Comprehensive Immunology
Active member of American Association for Cancer Research, Full member of American Society of Clinical Oncology
Certificate doctor of Japanese Society of Oral and Maxillofacial surgery,
Certificate doctor of cell therapy in the Japan Society of Transfusion Medicine and Cell Therapy
He has held positions in numerous other academic societies.

Research fields

Combined immunotherapy, immunoprecision medicine, cancer immunotherapy, immune biomarkers,
Although he was engaged in oral cancer treatment as an oral surgeon, he has started the research and development of cancer immunotherapy because cancer could not be controlled with standard treatment. He has made significant achievements in the development of cancer immunotherapy using Toll-like receptor signals and dendritic-cell cancer vaccine. Currently, he is focusing on the establishment of the “Immune-precision medicine” that is combination therapy with cancer vaccine, immunosuppression-canceling technologies (checkpoint inhibitors, etc.) and genetic and immunological examinations.

Papers

J Natl Cancer Inst, Cancer Res, Clin Cancer Res, Cancer Immunol Immunother, OncoImmunol, Pros One,
Int J Cancer, Eur J Cancer, Neoplasia, Cancer Sci, etc.

座長：小林 正学

講演者 岡本 正人

演 題

癌に対する免疫・精密医療：免疫のアクセルとブレーキを操る

我々はこの度、国際未来医療臨床医学会（SIFCM）を立ち上げました。未来医療とは、本当の意味での精密医療（Precision Medicine）であると考えます。癌や生活習慣病など様々な疾患に対するリスク検査を用いて患者の状態を把握し、それに合った予防法・治療法の組み合わせを提供する事が「真の精密医療」であり「未来医療」なのです。そのコンテンツの中で私が注目したのが、患者の免疫機能ならびにそれを整える為の免疫療法です。

様々な疾患の発症、予防ならびに治療効果や予後において、患者（未病、健常人含む）の免疫状態が重要な役割を果たしている事は疑う余地がありません。免疫関連バイオマーカーにより、①患者の免疫状態を明らかにして各々の治療法が効果的な患者（Responder）と効果がない患者（Non-responder）を判別する事、②各々の治療法が免疫状態にどのような影響を与えるかを明らかにする事、③　①②の結果から各々の患者に対して最も有効な複合治療（個別化複合治療）を提供する。これが未来医療の確立に直結すると考えています。

我々は、各治療を施行された癌患者において治療前の免疫パラメーターの解析を行い治療効果や予後との関連性を検討し、免疫療法、化学療法および放射線治療等の治療効果あるいは術後の再発等と関連する幾つかのバイオマーカー候補を同定しました。興味深い事に、これらのバイオマーカー候補の多くは免疫抑制に関連する因子、すなわち「免疫のブレーキ」でした。これらの免疫バイオマーカーは、個々の患者における治療法の選択基準となるのみならず、各患者の免疫抑制環境を把握し、それぞれの免疫抑制パターンを解除する事により、各治療の効果を高め良好な予後を獲得する事ができ、新規治療戦略の構築、さらに疾患予防戦略においても大きなベネフィットをもたらすと考えられました。

一方で、我々は、より有効な癌ワクチン「免疫のアクセル」の開発を行いました。従来の癌ワクチンの効果が、総じて満足できるものでない原因は、癌患者においては、癌ワクチンの効果発現に最も重要な働きをしている樹状細胞（Dendritic cell: DC）の数が少なく、機能低下が起こっている事です。我々は、患者由来のDCをex vivoで培養する事で数を増やし、機能を増強させる技術を開発し、この樹状細胞癌ワクチン（DCワクチン）の臨床応用を行い、膵癌、肺癌、頭頸部癌等、多くの癌種において良好な治療効果を獲得し報告してきました。

各患者の免疫抑制状態を把握し、免疫抑制を解除した後、DCワクチンを投与する事により更なる治療効果の向上が期待できると考えられます。

「免疫のブレーキを解除しアクセルをふかす」この考えに基づいて、我々は「エビデンスに基づいた新規免疫抑制阻害技術を併用した個別化複合免疫療法」を開発中であります。
本シンポジウムではその概要ならびに代表例を紹介させて頂きます。

Chairperson：Masanori Kobayashi

Speaker Masato Okamoto

Subject

Immuno-precision medicine for cancer: Regulation of the accelerator and brake of immunity

We have founded the Society of International Future Clinical Medicine (SIFCM). I believe that the future medicine should be the true precision medicine. Understanding the patient's condition using the risk examinations for various diseases such as cancer and lifestyle diseases, and treating preventive and therapeutic methods that match their condition is the true precision medicine that is "the future medicine". I focused on the immune function in patients and the immunotherapy to improve it among the contents of the future medicine.

The immune function of patients as well as healthy individuals plays a significant role in the prevention and therapeutic effects for various diseases. By using the immune-related biomarkers, (1) to clarify the patient's immune status and distinguish between patients for whom each treatment is effective (Responder) and patients who are not effective (Non-responder), (2) to clarify what effects of each treatment in the immune status, and (3) to provide the most effective combined therapy for each patient based on the results of (1) and (2), will lead directly to the establishment of the future medicine.

We have analyzed the relationship between the immune parameters in cancer patients before various treatments and therapeutic effects, and have identified several biomarkers associated with prognosis of the cancer patients. Interestingly, most of these biomarkers were factors associated with immunosuppression that is “Brakes of immunity”. These immune biomarkers not only serve as criteria for selecting treatment methods for individual patients, but also help us understand the immunosuppressive pattern of each patient, and cancel their immunosuppression, thereby enhancing the efficacy of each treatment. It would be thought that these approach would contribute in the establishment of novel therapeutic and disease prevention strategies and obtaining a favorable prognosis.

On the other hand, we have developed a more effective cancer vaccine, an Accelerators of immunity. The reason why the effects of conventional cancer vaccines are not effective enough, is that the number of dendritic cells (DCs), which plays the most significant role in the effect of cancer vaccine, is small and their function is low in cancer patients. We have developed a technique to increase the number of DCs, to enhance their function, and have clinically applied, then improved therapeutic effects have been obtained and reported in many types of cancer, including pancreatic cancer, lung cancer, head and neck cancer, and so on.

Further improvement of the therapeutic effect can be expected by understanding and canceling the immunosuppression and administering the DC vaccine.

Based on the concept of “Canceling the brakes and activating the accelerators of immunity, we are developing the "Precision combined immunotherapy".
In this symposium, we will introduce the overview and representative cases.

Cutting Edge

複合免疫療法の開発
：免疫チェックポイント阻害剤とがんワクチン

Development of combined immunotherapy: immune checkpoint inhibitors and cancer vaccines

岡本 正人[1)]・吉田 徳之[1)]・小林 正学[1,2)]・小井戸 薫雄[3)]

1)大阪大学大学院薬学研究科 先端免疫治療学
2)セレンクリニック名古屋
3)東京慈恵会医科大学附属柏病院消化器・肝臓内科

Abstract

代表的な免疫チェックポイント阻害剤である抗 PD-1 抗体は、既にがん特異的免疫反応が誘導されている hot tumor では奏功するが、免疫反応が起こっていない cold tumor では反応しない事が明らかになってきた。さらなる研究により、がんワクチンにより cold tumor を hot tumor に変換できる、すなわち抗 PD-1 治療の Non-responder を Responder にする事ができる可能性が膵がんにおいて報告された。我々は従来より樹状細胞を用いたがんワクチン療法の開発を行っており、同ワクチンによりがん抗原特異的免疫反応を誘導し、特定の患者群には確実に反応し治療効果が得られる可能性等を報告している。ワクチン投与後にがん微小環境に T 細胞の動員も確認した。以上のデータより、より有効な複合免疫療法を開発するために、抗 PD-1 + 樹状細胞ワクチン併用免疫療法の臨床応用を試みている。

Key Words : Immune Checkpoint inhibitor
Cancer Vaccine, Cancer Immunotherapy

■はじめに

近年のがん免疫療法の進歩はめざましく、特に免疫チェックポイント阻害剤 (ICI) は、がん治療のコンセプトを転換させ「パラダイムシフト」をもたらした。ICI の臨床応用が進みその課題も見えてきた。①奏効率がおよそ 15 ～ 25% 程度に留まる事、②自己免疫反応に伴う有害事象、③高額な治療費である。これらを解決する為に、(1) バイオマーカーの同定と、(2) 複合免疫療法の開発が進められ、その中で、がん特異的免疫療法 (がんワクチン等) が重要な意味を持つ事も明らかになった。

本項では、ICI と我々が開発してきた樹状細胞 (DC) ワクチンの併用に関して検討する。

■ ICI の課題と解決法

「過剰な免疫反応」を制御するために免疫チェックポイント (IC) は存在する。CTLA-4, PD-1, TIM-3, LAG-3, BTLA, VISTA 等様々な IC 分子が報告されているが、最も開発が進んでいる抗 PD-1 抗体を中心に話を進める。ICI の詳細については他の総説を参照されたい。

1） 抗 PD-1 抗体の Responder はがん特異的免疫反応が誘導されている患者である

抗 PD-1 抗体 (nivolumab, pembrolizumab等) のバイオマーカーとして「PD-L1 発現」が有力であったが PD-L1 が治療効果と必ずしも相関しない事が報告された。PD-L1 は様々な刺激により反応性に発現が変化する分子であり普遍的な判定基準となり難い。その後、がん組織に CD8+T 細胞浸潤を認めたケースで抗 PD-1 抗体が有効である事が報告された[1,2)]。PD-L1 発現に加えて CD8+T 細胞浸潤が抗 PD-1 療法のバイオマーカーとなる可能

Masato Okamoto[1)], Noriyuki Yoshida[1)], Masanori Kobayashi[1,2)], Shigeo Koido[3)]

[1)]Department of Advanced Immunotherapeutics, Graduate School of Pharmaceutical Sciences, Osaka University
[2)]Seren Clinic Nagoya
[3)]Division of Gastroenterology and Hepatology, Department of Internal Medicine, The Jikei University School of Medicine, Kashiwa Hospital

[CANCER RESEARCH 64, 5461–5470, August 1, 2004]

Expression of Toll-Like Receptor 4 on Dendritic Cells Is Significant for Anticancer Effect of Dendritic Cell-Based Immunotherapy in Combination with an Active Component of OK-432, a Streptococcal Preparation

Masato Okamoto,[1] Sachiko Furuichi,[1] Yasuhiko Nishioka,[2] Tetsuya Oshikawa,[1] Tomoyuki Tano,[1] Sharif Uddin Ahmed,[1] Kiyoshi Takeda,[3] Shizuo Akira,[3] Yoshiki Ryoma,[4] Yoichiro Moriya,[4] Motoo Saito,[4] Saburo Sone,[2] Mitsunobu Sato[1]

[1]Second Department of Oral and Maxillofacial Surgery, Tokushima University School of Dentistry, Tokushima; [2]Third Department of Internal Medicine, Tokushima University School of Medicine, Tokushima; [3]Department of Host Defense, Research Institute for Microbial Diseases, Osaka University, Osaka; and [4]Product Research Laboratory, Chugai Pharmaceutical Co., Ltd, Tokyo, Japan

ABSTRACT

A lipoteichoic acid-related molecule OK-PSA is an active component of OK-432, a *Streptococcus*-derived anticancer immunotherapeutic agent. In the present study, we first examined the effect of OK-PSA on the maturation of dendritic cells (DCs) *in vitro* by using the DCs derived from 5 healthy donors and 10 patients with head and neck cancer with or without expression of *toll-like receptor 4* (*TLR4*) or *MD-2* mRNA. OK-PSA treatment effectively increased the surface expression of MHC class II, CD80, CD83, and CD86. OK-PSA-stimulated DCs secreted the cytokines that can induce helper T-cell 1 (Th1)-type T-cell response, and stimulated allogeneic T cells to produce IFN-γ and to elicit an allogeneic antigen-specific cytotoxicity. These activities almost depended on expression of *TLR4* and *MD-2* genes. We next investigated the *in vivo* anticancer effect of intratumoral administration of syngeneic DCs followed by OK-PSA against established tumors in mice. C57BL/6 mice, which express wild-type TLR4, and C57BL/6-derived TLR4-knockout ($TLR4^{-/-}$) mice were used. Although OK-PSA accelerated the antitumor effect of intratumoral DC administration in wild-type mice bearing syngeneic tumors, the antitumor effect of OK-PSA as well as of the combination therapy with DCs and OK-PSA was not significant in $TLR4^{-/-}$ mice. Interestingly, an administration of wild-type-mouse-derived DCs followed by OK-PSA exhibited a marked antitumor effect even in the $TLR4^{-/-}$ mice. These findings suggest that OK-PSA may be a potent adjuvant for local DC therapy, and that DC therapy followed by OK-PSA is able to elicit anticancer activity even in a TLR4-deficient host when TLR4 is expressed only in DCs injected intratumorally.

INTRODUCTION

OK-432, a penicillin-killed and lyophilized preparation of a low-virulence strain (Su) of *Streptococcus pyogenes* (group A) that was developed by Okamoto *et al*. (1), is successfully used as an immunotherapeutic agent in malignancies (2, 3). We have also reported that OK-432-based immunotherapy exhibits a marked antitumor effect in patients with oral squamous cell carcinomas (4, 5). It has been reported that OK-432 induces interleukin (IL)-12 and polarizes the T-cell response to a helper T-cell 1 (Th1)-dominant state in mice (6), that local injection of OK-432 augments the Th1-type T-cell response of tumor-draining lymph node cells (7), and that OK-432 induces lymphokine-activated killer cells that exhibit higher cytotoxic activities and have a different phenotype from the lymphokine-activated killer cells induced by IL-2 (8). Because OK-432 is a whole bacterial preparation containing many components, it remains uncertain which of those components makes the largest contribution to the Th1-inducing and antitumor activities of the preparation. We generated an IgM mouse monoclonal antibody, TS-2, that recognizes an IFN (IFN)-γ-inducing component of OK-432, and we succeeded in isolating the IFN-γ-inducing component [lipoteichoic acid (LTA)-related molecule: OK-PSA] by affinity chromatography of a butanol extract of OK-432 on cyanogen bromide-activated Sepharose 4B bound by the TS-2 (9, 10). We have reported that OK-PSA is a far more potent inducer of Th1-type cytokines as well as killer cell activities in human peripheral blood mononuclear cells (PBMCs) than the original OK-432, and that it engages in marked antitumor activity in tumor-bearing mice (9, 11–16). It was clearly demonstrated that OK-PSA is an active component of OK-432. Furthermore, we have reported that Toll-like receptor (TLR) 4 signaling is involved in regulating OK-PSA-induced anticancer immunity in tumor-bearing mice (17), and that oral cancer patients who do not express or faintly express *TLR4* or *MD-2* gene, did not secrete IFN-γ and did not obtain a satisfactory therapeutic effect in response to OK-432 (5). TLRs are transmembranal proteins and represent a newly recognized family of vertebrate pattern recognition receptors in the innate immune system (18). Among the identified family of TLRs, TLR4 recognizes bacterial cell wall components, namely lipopolysaccharide (LPS; Ref. 19). MD-2 acts as a significant coreceptor in the TLR4 signaling. It is physically associated with TLR4 on the cell surface, and the TLR4/MD-2 complex confers responsiveness on bacterial components (20).

Dendritic cells (DCs) are potent antigen-presenting cells that play a central role in initiating adaptive and innate immune responses. Since their original identification by Steinman, much attention has been focused on the role of DCs in eliciting the antitumor effect and in potential therapeutic applications, and the recent insights may provide the basis for generating more effective antitumor immune responses (21–23). In most tissues, including tumor tissues, DCs are present in an immature state. The immature DCs (iDCs) are unable to stimulate T cells and are extremely well equipped to capture antigens. The iDCs are matured by the stimulation associated with capturing antigens such as bacteria, viruses, and apoptotic cancer cells, and by other stimulating agents including LPS, tumor necrosis factor (TNF)-α, IL-1β and CD40 ligand. In the primary tumor sites, the antigen-bearing DCs that are followed by appropriate maturation and that strongly express CD80, CD83, CD86, MHC class I and MHC class II molecules, migrate to the paracortical T-cell-rich area of the draining lymph nodes, present antigens to T cells, and induce tumor-specific CTLs as well as Th cells (23). The immunomodulator that can induce the maturation of human DCs appropriately *in vivo* and *in vitro* may be a useful adjuvant for DC-based immunotherapy in patients with malignant diseases.

Recently, it has been demonstrated that OK-432 stimulates mature DCs, and that DCs stimulated with OK-432 can induce antigen-specific CTLs (24–26). In the present study, we first examined the effects of OK-PSA in the maturation of human DCs by *in vitro*

Received 12/22/03; revised 4/15/04; accepted 5/25/04.
Grant support: Grant-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science and Technology of Japan.
The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked *advertisement* in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.
Requests for reprints: Mitsunobu Sato, Second Department of Oral and Maxillofacial Surgery, Tokushima University School of Dentistry, 3-18-15 Kuramoto-cho, Tokushima, 7708504, Japan. Phone: 81-88-633-7353; Fax: 81-88-633-7462; E-mail: satomitu@dent.tokushima-u.ac.jp.

Cancer Immunol Immunother (2014) 63:797–806
DOI 10.1007/s00262-014-1554-7

ORIGINAL ARTICLE

Prognostic factors related to add-on dendritic cell vaccines on patients with inoperable pancreatic cancer receiving chemotherapy: a multicenter analysis

Masanori Kobayashi · Shigetaka Shimodaira · Kazuhiro Nagai · Masahiro Ogasawara · Hidenori Takahashi · Hirofumi Abe · Mitsugu Tanii · Masato Okamoto · Sun-ichi Tsujitani · Seiichi Yusa · Takefumi Ishidao · Junji Kishimoto · Yuta Shibamoto · Masaki Nagaya · Yoshikazu Yonemitsu · The DC Vaccine Study Group at the Japan Society of Innovative Cell Therapy (J-SICT)

Received: 3 January 2014 / Accepted: 13 April 2014 / Published online: 29 April 2014

Abstract
Objective Dendritic cell (DC)-based cancer vaccines may have a significant benefit to patients with advanced pancreatic cancer. However, variations among clinical studies make it difficult to compare clinical outcomes. Here, we identified factors that determined the clinical benefits by analyzing data obtained at seven Japanese institutions that employed the same DC preparation and treatment regimens.
Methods Of 354 patients who met the inclusion criteria, 255 patients who received standard chemotherapy combined with peptide-pulsed DC vaccines were analyzed.
Results The mean survival time from diagnosis was 16.5 months (95 % CI 14.4–18.5) and that from the first vaccination was 9.9 months (95 % CI 8.0–12.9). Known prognostic baseline factors related to advanced pancreatic cancer, namely ECOG-PS, peritoneal metastasis, liver metastasis, and the prognostic nutrition index, were also representative. Importantly, we found that erythema reaction after vaccination was an independent and treatment-related prognostic factor for better survival and that OK-432 might be a good adjuvant enhancing the antitumor immunity during DC vaccination.
Conclusions This is the first report of a multicenter clinical study suggesting the feasibility and possible clinical benefit of an add-on DC vaccine in patients with advanced

Electronic supplementary material The online version of this article (doi:10.1007/s00262-014-1554-7) contains supplementary material, which is available to authorized users.

M. Kobayashi
Seren Clinic Nagoya, Nagoya, Aichi 460-0008, Japan

S. Shimodaira
Cell Processing Center, Shinshu University Hospital, Matsumoto, Nagano 390-8621, Japan

K. Nagai
Transfusion and Cell Therapy Unit, Nagasaki University Hospital, Nagasaki 852-8501, Japan

M. Ogasawara
Department of Hematology, Sapporo Hokuyu Hospital, Sapporo, Hokkaido 003-0006, Japan

H. Takahashi · M. Tanii
Seren Clinic Fukuoka, Fukuoka 810-0001, Japan

H. Abe
Seren Clinic Kobe, Kobe, Hyogo 650-0001, Japan

M. Okamoto
Institute for Advanced Medical Research, Keio University School of Medicine, Tokyo 160-8582, Japan

S. Tsujitani
National Center for Global Health and Medicine, Tokyo 162-8655, Japan

S. Yusa · T. Ishidao
Research and Development Division, Tella Inc., Tokyo, Japan

J. Kishimoto
Data Management Center, Center for Clinical and Translational Research, Kyushu University Hospital, Fukuoka, Japan

Y. Shibamoto
Department of Radiology, Nagoya City University Graduate School of Medical Sciences, Nagoya 467-8601, Japan

M. Nagaya (✉)
Seren Clinic Tokyo, 2-10-2, Shirokanedai, Minato-ku, Tokyo 108-0071, Japan
e-mail: m2nagaya@marianna-u.ac.jp

M. Nagaya
Department of Immunology, St. Marianna University, Kawasaki 261-8511, Japan

PLOS | ONE

RESEARCH ARTICLE

Prognostic Significance of Interleukin-8 and CD163-Positive Cell-Infiltration in Tumor Tissues in Patients with Oral Squamous Cell Carcinoma

Yohei Fujita[1], Masato Okamoto[2,3]*, Hiroyuki Goda[1], Tomoyuki Tano[1], Koh-ichi Nakashiro[1], Atsuro Sugita[4], Tomonobu Fujita[3], Shigeo Koido[5], Sadamu Homma[6], Yutaka Kawakami[3], Hiroyuki Hamakawa[1]

1. Department of Oral and Maxillofacial Surgery, Ehime University Graduate School of Medicine, Ehime, Japan, **2.** Department of Advanced Immunotherapeutics, Kitasato University School of Pharmacy, Tokyo, Japan, **3.** Division of Cellular Signaling, Institute for Advanced Medical Research, Keio University School of Medicine, Tokyo, Japan, **4.** Department of Pathology, Ehime University Hospital, Ehime, Japan, **5.** Division of Gastroenterology and Hepatology, Department of Internal Medicine, The Jikei University School of Medicine, Tokyo, Japan, **6.** Department of Oncology, Institute of DNA Medicine, The Jikei University School of Medicine, Tokyo, Japan

*okamotom@pharm.kitasato-u.ac.jp

OPEN ACCESS

Citation: Fujita Y, Okamoto M, Goda H, Tano T, Nakashiro K-i, et al. (2014) Prognostic Significance of Interleukin-8 and CD163-Positive Cell-Infiltration in Tumor Tissues in Patients with Oral Squamous Cell Carcinoma. PLoS ONE 9(12): e110378. doi:10.1371/journal.pone.0110378

Editor: Renato Franco, Istituto dei tumori Fondazione Pascale, Italy

Received: June 17, 2014

Accepted: September 12, 2014

Published: December 2, 2014

Data Availability: The authors confirm that all data underlying the findings are fully available without restriction. All relevant data are within the paper.

Funding: This work was supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Cultures, Sports, Science and Technology of Japan (No. 25293412) (http://www.mext.go.jp/english/) (HH). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Competing Interests: The authors have declared that no competing interests exist.

Abstract

Purpose: We investigated whether serum interleukin (IL)-8 reflects the tumor microenvironment and has prognostic value in patients with oral squamous cell carcinoma (OSCC).

Experimental Design: Fifty OSCC patients who received radical resection of their tumor(s) were enrolled. Preoperative sera were measured for IL-8 by ELISA. Expression of IL-8 and the infiltration of immune cells in tumor tissues were analyzed by an immunohistochemical staining of surgical specimens.

Results: We found that disease-free survival (DFS) was significantly longer in the Stage I/II OSCC patients with low serum IL-8 levels compared to those with high levels ($p=0.001$). The tumor expression of IL-8, i.e., IL-8(T) and the density of CD163-positive cells in the tumor invasive front, i.e., CD163(IF) were correlated with the serum IL-8 level ($p=0.033$ and $p=0.038$, respectively), and they were associated with poor clinical outcome ($p=0.007$ and $p=0.002$, respectively, in DFS) in all patients. A multivariate analysis revealed that N status, IL-8(T) and CD163(IF) significantly affected the DFS of the patients. Further analysis suggested that combination of N status with serum IL-8, IL-8(T) or CD163(IF) may be a new criterion for discriminating between OSCC patients at high and low risk for tumor relapse. Interestingly, the in vitro experiments demonstrated that IL-8 enhanced

Prognostic impact of preoperative serum interleukin-6 levels in patients with early-stage oral squamous cell carcinoma, defined by sentinel node biopsy

HIROYUKI GODA[1], MASATO OKAMOTO[2], KOH-ICHI NAKASHIRO[1], SATOSHI HINO[1], RYUICHI MURASE[1] and HIROYUKI HAMAKAWA[1]

[1]Department of Oral and Maxillofacial Surgery, Ehime University Graduate School of Medicine, Tōon, Ehime 791-0295; [2]Department of Advanced Immunotherapeutics, Kitasato University School of Pharmacy, Tokyo 108-8641, Japan

Received September 9, 2015; Accepted February 12, 2017

DOI: 10.3892/ol.2017.7183

Abstract. Failure to detect recurrence and lymph node metastasis early represents a fundamental barrier to the improvement of survival rate in early stage oral squamous cell carcinoma (OSCC). The present study evaluated the association between serum interleukin-6 (IL-6) level and clinical outcomes in patients with early stage OSCC patients defined by sentinel node biopsy (SNB). A total of 53 patients with clinical stage I/II OSCC who underwent SNB were enrolled. SNB was determined by a radioisotope method, and was evaluated by histopathological examination and genetic analysis. Preoperative sera were measured for IL-6 by ELISA. In the clinical stage I/II patients, disease-free survival (DFS) was demonstrated to be higher in patients with negative SNB compared with patients with positive SNB. In total, 13 patients were demonstrated to exhibit lymph node metastasis by SNB or were reclassified to pathological stage T4 subsequent to analysis of the surgically resected specimens. Thus, 40 patients were diagnosed with early stage OSCC. Of these 40 patients, DFS of the patients with low serum IL-6 was significantly higher compared with the patients with high serum IL-6 (P=0.012). In 19 patients with negative SNB and low serum IL-6, the disease-free rate was 100%. These findings suggested that SNB staging and serum IL-6 level have a high prognostic value in patients with early stage OSCC. Additional investigation and longer follow-up times are warranted to improve understanding of the group of patients that may benefit from this procedure.

Correspondence to: Dr Hiroyuki Goda, Department of Oral and Maxillofacial Surgery, Ehime University Graduate School of Medicine, 454 Shitsukawa, Tōon, Ehime 791-0295, Japan
E-mail: hiro9832@m.ehime-u.ac.jp

Key words: sentinel node biopsy, interleukin-6, oral squamous cell carcinoma, biomarker

Introduction

Oral squamous cell carcinoma (OSCC), the most common type of head and neck carcinoma, represents the fifth most frequently occurring cancer worldwide (1). An estimated 263,900 new cases and 128,000 mortalities occurred globally in 2008 (2). Despite advances in surgery, radiotherapy and chemotherapy, little improvement in the relative survival has been observed in OSCC during the past 30 years (3).

Early-stage OSCC (clinical stage I or II) (4) is primarily managed with surgery. The nodal status of the cervical lymph nodes remains an important prognostic factor in OSCC (5-6). The presence of cervical lymph node metastasis reduces the survival of patients with SCC of the upper aerodigestive tract by up to 50% (7). Therefore, early detection of cervical lymph node metastasis is hypothesized to improve survival. However, the diagnostic accuracy of lymph node metastasis using imaging tools including ultrasonography (US), computed tomography (CT), magnetic resonance imaging (MRI) and positron emission tomography (PET) is ~70% (8). Furthermore, patients with delayed neck node metastases generally exhibit a poor prognosis (9).

Sentinel node biopsy (SNB) has been demonstrated to be an oncologically safe staging modality in patients with early stage OSCC, allowing for an individualized and minimally invasive treatment of the neck, and significantly affecting tumor control and survival (10).

However, patients with tumor recurrence and metastases generally exhibit poor prognosis, and predictive biomarkers that identify the risk of tumor relapse may become a powerful tool for follow-up and development of effective treatment plans for these patients (11-13). Sera derived from patients with early stage OSCC were previously examined for multiple cytokines using a multiplexed measurement system (14) and serum interleukin-6 (IL-6) level was revealed to negatively correlate with a favourable outcome in these patients. IL-6 is a multifunctional cytokine that functions in the regulation of inflammatory and immune responses. IL-6 is produced by a variety of cells, primarily monocytes, macrophages and several types of tumor cell during infection and immunological challenge (15). Previous studies have revealed that IL-6 is involved in cancer progression,

MEMO

【メモ欄】

トリノ大学医学部 客員教授
株式会社令和メディカルリサーチ医学研究所 所長
愛知医科大学 先制・統合理療包括センター 研究員　他

神保 太樹

国際未来臨床医学会(SIFCM) 理事

略 歴

2013年	鳥取大学大学院医学系研究科（生体制御学）にて博士号取得
2013年～2016年	昭和大学医学部顕微解剖学教室兼任講師
2016年～2019年	株式会社T-LAB. 研究所長
2018年～2023年	トリノ大学医学部 客員教授
2019年～2023年	株式会社CHIKEN　取締役（臨床試験担当）
2020年～2023年	株式会社令和メディカルリサーチ 医学研究所 所長
2020年～2023年	愛知医科大学 先制・統合理療包括センター 研究員

所属学会

日本機能性香料医学会　理事長
日本ヘルスケアプロダクツ研究会　理事長
アジア国際健康促進・未病改善医学会　理事　他

受賞歴等

2013年度日本アロマセラピー学会若手奨励賞
2010年度日本認知症ケア学会「石崎賞」受賞
2009年度第８回キャンパスベンチャービジネスグランプリ中国大会日刊工業新聞社賞受賞
2009年度第８回キャンパスベンチャービジネスグランプリ中国大会新技術提案部門奨励賞
2008年度日本認知症ケア学会「石崎賞」受賞
2005年度日本認知症ケア学会「石崎賞」受賞
2002年度度鳥取大学課外活動学長賞受賞
2002年度鳥取大学発学生ベンチャービジネス賞
2002年度第１回キャンパスベンチャービジネスグランプリ中国大会
2002年度情報通信部門優秀賞受賞
2002年度ハイテク技術部門佳作受賞　他

Researcher, Aichi Medical Preemptive and Integrative Medicine Center, Aichi Medical University.

DAIKI JIMBO

Director of the Society of International Future Clinical Medicine (SIFCM)
Daiki Jimbo, PhD.

Brief summary

In April 2011, he joined the postdoctoral fellow of the Anatomy Department of the Showa University School of Medicine, then a part-time lecturer at Viadrina European University. At the Department of Bioregulation, Tottori University School of Medicine, he obtained a PhD in research on the treatment of dementia centered on Alzheimer's disease and on the incidence of olfactory dysfunction in patients with Alzheimer's disease. Currently, I am mainly elucidating the olfactory function. Recent research themes are elucidation and application of olfactory mechanism using brain function imaging such as fMRI and fNIRS, and examination of how to use olfaction in elderly care. He is also widely involved in the development of new diagnostic and therapeutic methods, and recently succeeded in developing a test kit using central sensory disorders.

Degree

Ph.D. (Health Science. Tottori University.)

Social contribution activity, Academic activities

Director of Japan Society for Longevity and Health Application, Director of Japan Society of Aromatherapy, Standing Director of Japan Society for Comprehensive Diagnostic and Medical Care, Secretary of Japan Society for Complementary and Alternative Therapy, Councilor of Japan Society for Health Promotion and Medicine, Regular Member of Japanese Society for Dementia, Regular Member of Japanese Society for Dementia Care, He has been a regular member of the Japanese Society of Geriatric Psychiatry. He has served as an editorial board member of Aroma Research, JSA, and the Journal of the Japanese Standards Association for Alternative Medicine.

Awards

2013 Japan Aromatherapy Society Young Encouragement Award
2012 Received the Urakami Award from the Japan Dementia Prevention Society
2011 8th Campus Venture Business Grand Prix China Tournament Nikkan Kogyo Shimbun Award
2011 Encouragement Award in the New Technology Proposal Category
2010 Received the Ishizaki Award from the Japan Dementia Care Society
2008 Received "Ishizaki Award" from the Japan Dementia Care Society
2005 Received the Ishizaki Award from the Japan Dementia Care Society
2002 Received the Tottori University Extracurricular Activities President's Award
2002 Student Venture Business Award from Tottori University
2002 1st Campus Venture Business Grand Prix China Tournament Information and Communication Division Excellence Award
2002 High-tech technology category honorable mention award, etc.

座長：田中 善

講演者 神保 太樹

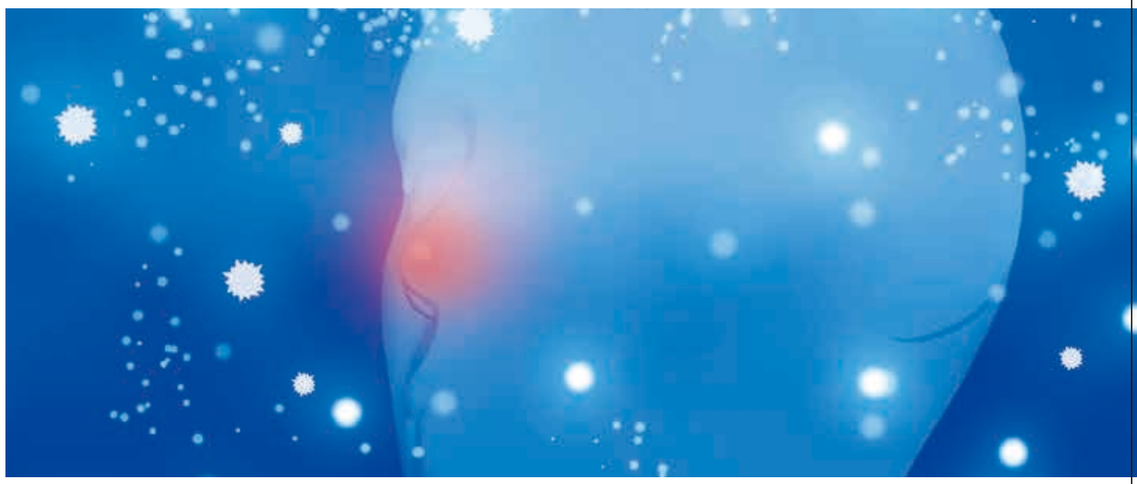
演 題

感覚器障害関連研究の活用と展望

本会の名称は、国際未来医療臨床医学会だが、この名前の示す通り、我々は未来の医療について考え、それを実現していくことが望まれていると言えるだろう。新型コロナウイルス感染症もそうだが、近年はこれまでになかったような医学的困難が人類を襲っていると言えるだろう。
ところで、現在はようやく新型コロナウイルス感染症については落ち着きつつある局面だが、完全にその脅威が去ったわけではない。なぜなら、これまでの類型患者数はかなり多く、今後、いわゆるウィズコロナの局面として、後遺症などへの対応が期待されるからだ。

ところでこれら後遺症の一つに嗅覚障害がある。もともと、私の研究として嗅覚障害の判定（特に中枢性）や、その治療についてを検討してきたこともあり、今後は新型コロナウイルスを原因とする嗅覚障害の治療も研究していくつもりである。

そこで、今回の講演では、私のこれまでの嗅覚障害に関する研究の成果を概説し、現在実施している最新の結果を踏まえて報告する。



Chairperson：Yoshimu Tanaka

Speaker Daiki Jimbo

Subject

Researches of olfactory Disorders for Utilization and Prospects

We are called upon to think about the medicine of the future and to make it happen. As is the case with new coronavirus infections, we are facing medical difficulties in recent years that have never been seen before.
Although the new coronavirus infection has finally settled down, the threat has not completely disappeared. This is because the number of patients has been quite large, and it is expected that we will have to deal with the aftereffects of the so-called with-coronavirus phase in the future.

One of these sequelae, by the way, is olfactory dysfunction. Since I have been studying the determination of olfactory dysfunction (especially central) and its treatment as part of my research, I intend to study the treatment of olfactory dysfunction caused by novel coronaviruses in the future.

Therefore, in this talk, I will outline the results of my research on olfactory disorders to date and report on the latest results of my current work.

PSYCHOGERIATRICS
The Official Journal of the Japanese Psychogeriatric Society

doi:10.1111/j.1479-8301.2011.00387.x PSYCHOGERIATRICS 2011; 11: 196–204

ORIGINAL ARTICLE

Specific feature of olfactory dysfunction with Alzheimer's disease inspected by the Odor Stick Identification Test

Daiki JIMBO,[1,3] Masashi INOUE,[2] Miyako TANIGUCHI[1] and Katsuya URAKAMI[1]

[1]Section of Environment and Health Science, Department of Biological Regulation, School of Health Science, Faculty of Medicine, [2]Information Media Center, Tottori University, Yonago, Tottori, and [3]Department of Anatomy, Showa University School of Medicine, Tokyo, Japan

Correspondence: Prof Katsuya Urakami MD, PhD, Section of Environment and Health Science, Department of Biological Regulation, School of Health Science, Faculty of Medicine, Tottori University 86 Nishimachi, Yonago 683-8503, Japan. Email: jinbo@society.jpn.org

Received 4 November 2010; revision received 11 May 2011; accepted 19 July 2011.

Abstract

Aim: Alzheimer's disease (AD) is one of the most significant diseases associated with ageing. As the disease progresses, symptoms including olfactory dysfunction often appear along with cognitive dysfunction. We examined olfactory and other indexes to investigate correlations between them and the validity of an olfactory test for screening for AD.

Methods: To assess whether odorant identification will be a useful diagnostic tool, we investigated the olfactory ability of Alzheimer's disease patients (ADs) using the Odor Stick Identification Test for the Japanese. As a control, we compared ADs to aged people without AD or dementia. To investigate the relationship between olfactory loss and severity of AD, we used the Mini-Mental State Examination, Alzheimer's Disease Assessment Scale, biomarkers in spinal fluid and single-photon emission computed tomography as brain imaging.

Results: In comparing the controls and ADs, we believe that there are significant differences, with ADs having particularly low activity with regard to olfactory function and some odorants. We showed that there was a definite correlation between cognitive and olfactory function. To confirm this, we sorted subjects by markers of severity scores for comparison. In all areas, the AD group had more serious olfactory dysfunction, including in the early stages of AD.

Conclusion: This study suggests that olfactory tests such as the Odor Stick Identification Test for the Japanese can be useful for assessing severity of AD, including cognitive dysfunction. Further investigations will enable us to establish an olfactory assessment method for the screening or diagnosis of AD.

Key words: *cognitive function, diagnosis, olfactory dysfunction, prevention, screening.*

INTRODUCTION

Because many diseases develop with ageing, the ageing of society has become a worldwide problem. Of these age-related diseases, dementia is one of the most serious, and its prevalence is increasing, especially for those over the age of 65 years. There are many primary diseases that present dementia as the main symptom, but Alzheimer's disease (AD) is the most common.[1] However, there are currently only a few treatment protocols for AD and dementia, including therapeutic drugs. Given this situation, early detection has become very important for timely treatment and care. Previous research has often been driven by the need to identify markers for AD,[2] and much of it has indicated that olfactory loss or dysfunction can be a symptom of AD prior to the development of neuropathology and cognitive dysfunction.[3–5] There are many common causes of olfactory dysfunction including head trauma, endocrine dysfunction, inflammatory sinusitis and other primary diseases, and with normal ageing, olfactory function often moderately worsens.[6] For example, over half of people aged 60 years and older have some problem with smell,[7] and previous studies have

JSHCP ヘルスケアプロダクツ

短報

論文種別 （短報）

新型コロナウイルス感染症における嗅覚障害への匂い付きマスクの可能性

The Potential of Scented Masks for Olfactory Disorders with COVID-19.

神保太樹[1,2]、福田克彦[3]、中河原毅[4]、福沢嘉孝[1]

1）愛知医科大学　2）株式会社令和メディカルリサーチ　3）福田内科クリニック　4）tantore 株式会社

キーワード：嗅覚障害、新型コロナウイルス後遺症、嗅覚トレーニング、マスク、はからめ
英文キーワード：Olfactory impairment, Symptoms Prognostic of Covid-19, Olfactory training, masks, Hakama

概要：　本研究は、新型コロナウイルス感染症罹患後に、嗅覚の異常を訴えている方を対象として、tantore 株式会社より無償で配布されたマスクの効果を検討したものです。新型コロナウイルス感染症の後遺症である嗅覚障害は、程度の差はあっても、陽性者の過半数に生じることが知られている。その一部は、症状が長期化し、日常生活に支障を来すことが若手いるが、この治療法としては、ステロイドの投与などが知られているが、この他に嗅覚に定期的に刺激を与える嗅覚トレーニングが有効であるという報告もある。過去の報告からは、精油と呼ばれる植物から抽出した匂いを、嗅覚障害の患者に暴露しただけで急速に症状が緩解したとする報告もある。一方、こうした療法の課題は、定期的に実施する方法が、特に嗅覚障害によって匂いが良く分からない対象にとっては、苦痛であるか、あるいは意味を見出しづらいという点にある。そこで、我々は意識をせずとも匂いに暴露することが可能であり、しかも定期的に実施するに際してハードルが低いということから、マスクに香りを添加する方法を選んだ。我々は、まず試作品として作成した香り付きマスク（tantore フレグランスマスク 使い捨てタイプ）を用いて、新型コロナウイルス感染症の罹患後に自覚症状として嗅覚障害を呈していた対象者5例に約2週間使用していただいた。その前後の嗅覚機能について評価し、その差を検討したところ、後検査では有意に嗅覚症状が改善していたので、ヘルスケアプロダクトとしての匂い付きマスクについて報告する。

Abstract: This study examined the efficacy of masks distributed free of charge by tantore, Inc. for those who complained of abnormal sense of smell after contracting novel coronavirus infection. Olfactory dysfunction, an aftereffect of new-type coronavirus infection, is known to occur in the majority of positive individuals, albeit to varying degrees. Some of these young people experience prolonged symptoms that interfere with their daily lives, and while steroid therapy is a known treatment for this, there are also reports that olfactory training, which regularly stimulates the sense of smell, can be effective. Past reports have shown that simply exposing patients with olfactory dysfunction to plant-derived odors called essential oils rapidly alleviated symptoms. On the other hand, the challenge with this therapy is that the method of regular implementation can be painful for the subject. Therefore, we chose the method of adding fragrance to masks because it is possible to expose patients to the smell without awareness, and because it is a low hurdle for regular use. We first created a prototype mask with a fragrance and used it for about two weeks on five subjects who had subjective olfactory impairment after contracting a new type of coronavirus infection. We evaluated the olfactory function before and after the use of the mask and examined the differences.

一般社団法人 日本先制臨床医学会　理事長
愛知医科大学大学院医学研究科(戦略的先制統合医療・健康強化促進学)
愛知医科大学病院 先制・統合医療包括センター（AMPIMEC）教授・部長
学校法人愛知医科大学　理事

福沢　嘉孝

国際未来臨床医学会(SIFCM) 代表理事

略 歴

1984年	愛知医科大学医学部医学科卒業
1999年	愛知医科大学内科学第１講座：助教授
2001年	愛知医科大学内科学講座臓器別診療科：消化器内科：助教授
2003年	愛知医科大学大学院担当助教授（消化器内科学：合教員）
2009年	愛知医科大学大学院医学研究科：医学教育センター長・教授
2014年	独逸：ミュンヘン大学医学部：客員教授
2014年	中国：河南中医薬大学医学部：客員教授（2021年UFH青島：特別招聘教授）
2015年	愛知医科大学大学院医学研究科 戦略的先制統合医療・健康強化推進学
現在至	愛知医科大学病院：先制・統合医療包括センター教授・部長

主な学会活動、役職等

日本先制臨床医学会（JSPCM）：理事長
臨床ゲノム医療学会（SOCGM）：理事長
日本珪素医科学学会（JMSIS）：理事長
国際未来医療臨床医学会（SIFCM）：理事長（2023年1月21日～設立）
アジア国際健康促進・未病改善医学会（AIHO/PIMS）：副理事長
日本臨床研究安全評価機構（SACRJ）：副理事長
臨床美容再生医療学会（SCARM）：常任理事
世界中医薬学会連合会（WFCMS）：理事
国際個別化医療学会（ISPM）：理事
日本健康医学会（JHMA）：理事
日本医学英語教育学会（JASMEE）：理事
日本統合医療学会（IMJ）：理事
学校法人愛知医科大学：理事
学校法人愛知医科大学：同窓会（愛橘会）理事長
学校法人愛知医科大学医師会：副会長
日本先進医療臨床研究会 (JSCFS)：理事長
米国内科学会：ACP：上級会員：FACP

受賞歴等

Best Doctors, Inc. Boston, MA, USA； Best Doctors in Japan (2006-2007) 選出
Best Doctors, Inc. Boston, MA, USA； Best Doctors in Japan (2010-2011) 選出
Best Doctors, Inc. Boston, MA, USA； Best Doctors in Japan (2014-2015) 選出
Best Doctors, Inc. Boston, MA, USA； Best Doctors in Japan (2018-2019) 選出
Best Doctors, Inc. Boston, MA, USA； Best Doctors in Japan (2020-2021) 選出
その他：多数（→福沢嘉孝：リサーチマップを参照）

Aichi Medical University and Hospital
Aichi Medical Preemptive and Integrative Medicine Center (AMPIMEC) Professor
Aichi Medical University　Director

YOSHITAKA FUKUZAWA

Representative Director　of the Society of International Future Clinical Medicine (SIFCM)
Yoshitaka Fukuzawa, MD, PhD., FACP

Career

1984	Graduated at AICHI MEDHIKAL UNV.
2006	Prof./Director of Aichi Medical UNV. Education Center.
2010	Study Abroad to South Illinois UNV. School of Medicine
2014	Visiting Prof. of Ludwig Maximilians UNV. Of Munich
2015	Director/Chairman of AMPIMEC
2016	Visiting Prof. of Henan University of Traditional Chinese Medicine

He researches most advanced mRNA examination for preemptive cancer therapy .
He published many papers for "Genomic Medicine " and is the textbook for many researchers.

Affiliated academic societies

President Japan Society of Preemptive and Clinical Medicine (JSPCM)
President of Society of Clinical Genomic Medicine (SOCGM)
Board Member of IMJ　　Board Member of JSHPM
Board Member of JMSIS　　Board Member of CICO
Board Member of ISPM　　Board Member of JASMEE
Representative Director of SIFCM
The Professor of Aichi Medical Univ. School of Medicine and Univ. Hospital

Specialty

Genomic Medicine, Preemptive Medicine (mRNA examination) and Integrative Medicine

座長：小林 正学

講演者 福沢 嘉孝

演 題

老化制御と健康長寿

戦略的未病予防と健康長寿 ～mRNAの応用解析システム～

国策の《健康日本21（第2次）》は、１）健康寿命の延伸、２）QOLの向上、３）生活習慣病予防、４）そのリスクの軽減を主な目標としている。平均寿命は女性が世界第1位、健康寿命は男女とも世界第1位であるが、平均寿命と健康寿命の格差は、未だ、男女共に約10年の開きがある。
今後、更に少子高齢化が進展し、2040年には3人に1人が65歳以上になり、現役層が半分以下になると推計されている。

最近の厚労省の統計では、老衰が死因の第3位に上昇して来ているとの驚愕のデータもあり、既述の高齢化を反映しているものと考えられる。その一方で、がんは、年々増加の一途を辿り、相変わらず死因の第1位となっている（2人に1人はがんに罹患し、3人に1人はがんで死亡する現況である）。この様な状況は、先進国の中では、類い希な状況である。
これらの背景を鑑み、超早期に現在の健康度とがんリスクを具現化（見える化）し、超早期に診断・治療を可能にし得るシステム（mRNAによる応用解析）を臨床ゲノム医療学会の故渥美和彦先生等のグループが約十数年前から開発して来た。
そこで、我々も本学会との連携の下、2015年4月から本院に国内外の医学部・医科大学で初めて導入し、5月からマーナ(mRNA)健康外来を設立・稼働して来た。本外来では、DNAではなく、mRNAを活用・解析して、１）長寿遺伝子（SIRT1）、２）がん関連遺伝子リスク（男性8臓器・女性11臓器）の現在の健康活性度とがん関連遺伝子リスクを5段階で評価・具現化して、受検者に意識付けし、行動変容（ブレスロー博士が提唱している7つの良い生活習慣への改善）させ、可及的生活習慣病の予防およびそのリスクの軽減に繋げている。

これにより、国策の主軸でもある健康寿命の延伸に繋がれば、大きな社会・医療貢献ができ得るものと考え、日々、自己研鑽しながら、診療を実践している。

今回のシンポジウムでは、実際の臨床例を供覧しながら、EBMも含めて、概説させて頂ければ幸いである。
皆様のご忌憚無きご意見・コメントを頂ければ、明日からの診療にも役立てられるものと考えている。
今後ともご指導・ご鞭撻の程、何卒、宜しくお願いします。

Chairperson：Masanori Kobayashi

Speaker Yoshitaka Fukuzawa

Subject

Aging control and healthy longevity

Strategic pre-disease prevention and healthy longevity ～applied analysis system by using mRNA～

The national policy <<Health Japan 21 (second stage)>> aims at 1) extension of healthy life expectancy, 2) improvement of QOL, 3) prevention of lifestyle-related diseases, and 4) reduction of their risk. The average life expectancy of women is the highest in the world, and the healthy life expectancy of both men and women is the highest in the world. However, the gap between average life expectancy and healthy life expectancy is still about 10 years for both men and women. In the future, the declining birthrate and aging population will progress further, and it is estimated that by 2040, one in three people will be over the age of 65, and the working class will be less than half.

According to recent statistics from the Ministry of Health, Labor and Welfare, there is shocking data that senility has risen to the third leading cause of death, which is thought to reflect the aforementioned aging of the population. On the other hand, cancer continues to increase year by year and remains the number one cause of death (1 in 2 people will be diagnosed with cancer, and 1 in 3 people will die from it). Such a situation is extremely rare among developed countries.
In view of these backgrounds, the General Incorporated Association Society of Clinical Genomic Medicine (SOCGM) has developed a system (applied analysis using mRNA) that can embody (visualize) the current level of health and cancer risk at an extremely early stage and enable diagnosis and treatment at an extremely early stage. It has been developed by a group led by Dr. Kazuhiko Atsumi and others for about ten years.
Therefore, in cooperation with this society, I introduced it to my university hospital for the first time in domestic and overseas medical schools and medical universities in April 2015, and since May we have established and operated the mRNA- health outpatient , namely “マーナ (mRNA) 健康外来”. In this outpatient, I utilize and analyze mRNA, not DNA, to study the current health activity and cancer-related effects of 1) longevity gene (SIRT1) and 2) cancer-related gene risk (8 organs for men and 11 organs for women), and so genetic risk is evaluated and embodied in five stages. In addition, the results are used to make the examinees aware of their behavior, to change their behavior (improvement to the seven good lifestyle habits advocated by Dr. Breslow), and to prevent lifestyle-related diseases and reduce their risk as much as possible.

I think that if this system leads to the extension of healthy life expectancy, which is the main axis of national policy, I can make a great contribution to society and medical care, and I practice medical care while improving myself every day.

At this symposium, I would appreciate it if I could give you an overview of EBM, including actual clinical cases. I believe that if I receive your frank opinions and comments, they will be useful for medical treatment from tomorrow. I appreciate your continued guidance and encouragement.

総　説

水溶性ケイ素と生活習慣病

福沢嘉孝*，神保太樹*

* 愛知医科大学病院；先制・統合医療包括センター（AMPIMEC）

Review ; Water-soluble silicon and lifestyle-related diseases

Yoshitaka Fukuzawa*, Daiki Jimbo*

* Aichi Medical University Hospital ; Aichi Medical Preemptive and Integrative Medicine Center

Key words: water-soluble silicon, functional ingredients, liver disease, lifestyle-related disease, fatty liver

ABSTRACT

Silicon "has excellent characteristics including excellent bacteriostasis and penetration, adsorptive purification effect, cellular inactivation, and anti-inflammatory effect" as defined by the Japan-Medical Science Institute of Silicon. Silicon is known to be effective in improving the intestinal environment and in suppressing vascular aging. In various animal studies, water-soluble silicon administered orally or by other routes has been reported to exert the following effects, improving and enhancing the functions of various internal organs and other organs: 1) alleviation of vascular disorders, 2) increase in bone mineral density, 3) promotion of osteoblast differentiation, 4) enhancement of immune functions, 5) immunoadjuvant effect, 6) active oxygen removal, 7) weight gain suppression, 8) suppression of hepatic steatosis, and 9) decrease in excretion odor. However, data on and evidence for the mechanism of physiological action of water-soluble silicon and its functionality and effectiveness in humans have not been sufficiently obtained.

Meanwhile, an association of nonalcoholic fatty liver disease (NAFLD) with obesity has been frequently noted, and the treatment of the disease still focuses on dietary and exercise therapies. There is no established treatment on which a global consensus has been obtained. However, for long-term adherence to dietary and exercise therapies, it is very difficult to heighten patients' awareness and to facilitate behavioral changes, and no drug therapy has been established for patients with no underlying disease. We conducted a randomized, controlled, clinical study, a world's first study of water-soluble silicon in humans, to investigate for an effect to alleviate hepatic steatosis associated with various lifestyle-related diseases. The study showed that water-soluble silicon was effective in reducing body weight and in improving liver function, exerting an "additional effect" to some extent. The study results are presented in the review article as part of a clinical experience of water-soluble silicon. This finding is an issue which merits further large-scale studies of oral administration of water-soluble silicon.

連絡先：　福沢　嘉孝　　愛知医科大学病院；先制・統合医療包括センター（AMPIMEC）
〒 480-1195 愛知県長久手市岩作雁又 1 番地 1
TEL：0561-76-2506　E-mal：ampimec@aichi-med-u.ac.jp

J Gastroenterol
https://doi.org/10.1007/s00535-022-01921-4

The Japanese Society of Gastroenterology

ORIGINAL ARTICLE—LIVER, PANCREAS, AND BILIARY TRACT

Trends of hepatitis B virus genotype distribution in chronic hepatitis B patients in Japan

Kazumasa Sakamoto[1] · Kiyoaki Ito[1] · Hiroshi Yotsuyanagi[2,3] · Hiroshi Yatsuhashi[4] · Yasuhito Tanaka[5] · Shuhei Hige[6] · Yasuhiro Takikawa[7] · Yoshiyuki Ueno[8] · Kazuhide Yamamoto[9] · Fumio Imazeki[10] · Jun Inoue[11] · Masayuki Kurosaki[12] · Takeji Umemura[13] · Hidenori Toyoda[14] · Eiji Mita[15] · Kojiro Michitaka[16] · Tatsuji Maeshiro[17] · Norie Yamada[18] · Atsushi Suetsugu[19] · Miwa Kawanaka[20] · Yuya Seko[21] · Kentaro Matsuura[22] · Akinori Okumura[1] · Yoshitaka Fukuzawa[1] · Masaya Sugiyama[23] · Masashi Mizokami[24] · Masashi Yoneda[1]

Received: 3 July 2022 / Accepted: 7 September 2022

Abstract

Background Hepatitis B virus (HBV) is one of the most prevalent chronic viral infections that causes chronic hepatitis B (CHB). In Japan, genotypes B and C account for most of acute and chronic cases of hepatitis. However, previous studies showed that the prevalence of genotype A in CHB gradually increased every 5 years. Therefore, we have conducted a nationwide survey to comprehensively investigate the trends of HBV genotype distribution in CHB patients in Japan.

Methods 4421 CHB patients were recruited between 2015 and 2016. Clinical characteristics and distribution of CHB patients among different age groups and genotypes in 2015–2016 was compared with those in 2000–2001, 2005–2006, and 2010–2011.

✉ Kiyoaki Ito
kito@aichi-med-u.ac.jp

[1] Department of Gastroenterology, Aichi Medical University, 1-1, Yazakokarimata, Nagakute, Aichi 480-1195, Japan

[2] Division of Infectious Diseases, Advanced Clinical Research Center, The Institute of Medical Science, The University of Tokyo, Tokyo, Japan

[3] Department of Infectious Diseases and Applied Immunology, IMSUT Hospital of Institute of Medical Science, The University of Tokyo, Tokyo, Japan

[4] Clinical Research Center, Department of Hepatology, National Hospital Organization Nagasaki Medical Center, Nagasaki, Japan

[5] Department of Gastroenterology and Hepatology, Faculty of Life Sciences, Kumamoto University, Kumamoto, Japan

[6] Department of Gastroenterology, Sapporo Kosei General Hospital, Sapporo, Japan

[7] Department of Internal Medicine, Iwate Medical University, Iwate, Japan

[8] Department of Gastroenterology, Faculty of Medicine, Yamagata University, Yamagata, Japan

[9] Department of Internal Medicine, Okayama Saiseikai General Hospital, Okayama, Japan

[10] Safety and Health Organization, Chiba University, Chiba, Japan

[11] Division of Gastroenterology, Tohoku University Graduate School of Medicine, Sendai, Japan

[12] Department of Gastroenterology and Hepatology, Musashino Red Cross Hospital, Musashino, Japan

[13] Division of Gastroenterology and Hepatology, Department of Medicine, Shinshu University School of Medicine, Matsumoto, Japan

[14] Department of Gastroenterology, Ogaki Municipal Hospital, Ogaki, Japan

[15] Department of Gastroenterology and Hepatology, National Hospital Organization Osaka National Hospital, Osaka, Japan

[16] Gastroenterology Center, Ehime Prefectural Central Hospital, Matsuyama, Japan

[17] Department of Infectious, Respiratory, and Digestive Medicine, Graduate School of Medicine, University of the Ryukyus, Okinawa, Japan

[18] Department of Internal Medicine, Center for Liver Diseases, Seizankai Kiyokawa Hospital, Tokyo, Japan

[19] Department of Gastroenterology, Gifu University Graduate School of Medicine, Gifu, Japan

[20] Department of General Internal Medicine2, Kawasaki Medical School, Okayama, Japan

Published online: 29 September 2022

Springer

nutrients

MDPI

Review

Personalized Nutritional Therapy Based on Blood Data Analysis for Malaise Patients

Minoru Arakaki [1,*], Li Li [2], Toshiyuki Kaneko [3], Hiromi Arakaki [1], Hiromi Fukumura [1], Chihiro Osaki [1], Maki Yonamine [1] and Yoshitaka Fukuzawa [4]

1 Arakaki Plastic Surgery, 729 Uchidomari, Ginowan 901-2227, Japan; hiromi-a@cosmoe.ne.jp (H.A.); fukumura@arakakikeisei.com (H.F.); chihiro@arakakikeisei.com (C.O.); akcmac@gmail.com (M.Y.)
2 QDU International Tele-Consultation Platform, Qingdao United Family Hospital, 319 Hong Kong East Road, Laoshan District, Qingdao 266102, China; lilidoc@126.com
3 Orthomolecular Nutrition Laboratory Inc., KYB Build. 3F, 1-6-13 Higashi, Sibuya-ku, Tokyo 150-0011, Japan; t.kaneko.19790402@gmail.com
4 Aichi Medical Preemptive and Integrative Medicine Center, Aichi Medical University Hospital, 1-1 Yazakokarimata, Nagakute 480-1103, Japan; yofuku@aichi-med-u.ac.jp
* Correspondence: info@arakakikeisei.com

Abstract: As medical doctors, we routinely check patient blood chemistry and CBC data to diagnose disease. However, these data and methods of analysis are very rarely used to find pre-disease conditions or treat undiagnosed malaise. Masatoshi Kaneko Ph.D. found that many pre-disease conditions and types of malaise could be detected using his unique method of blood data analysis, and could also be treated using personalized nutritional therapy as an alternative to using drugs. The authors of this article introduce personalized nutritional therapy based on blood data analysis (Kaneko's method), and present and discuss some clinical cases. In total, 253 pre-disease or undiagnosed patients were treated using this nutritional therapy approach, and most of them recovered from their chronic symptoms and pre-disease conditions. This novel nutritional therapy has the potential to help many presymptomatic and undiagnosed patients suffering from malaise.

Keywords: nutrition; preventive medicine; personalized medicine; ortho-molecular nutrition; blood examination; anti-aging

Citation: Arakaki, M.; Li, L.; Kaneko, T.; Arakaki, H.; Fukumura, H.; Osaki, C.; Yonamine, M.; Fukuzawa, Y. Personalized Nutritional Therapy Based on Blood Data Analysis for Malaise Patients. *Nutrients* **2021**, *13*, 3641. https://doi.org/10.3390/nu13103641

Academic Editor: Laura Di Renzo

Received: 14 September 2021
Accepted: 15 October 2021
Published: 18 October 2021

1. Introduction

Advances in molecular nutrition have generated the concept of ortho-molecular nutritional therapy. Dr. Masatoshi Kaneko pioneered the concept of ortho-molecular nutritional therapy in Japan. Kaneko determined the optimal range (ideal standard values) for blood examination by analyzing more than 350,000 blood data sets. He found that the minimum deviation from the optimal ranges for blood data can be used to diagnose deficiencies in various nutrients, and that certain combinations of blood data indicate sub-optimal function of specific organs. For example, in the absence of liver or bone disease, a low alkaline phosphatase (ALP) level suggests zinc deficiency; a serum level of aspartate aminotransferase (AST) > alanine aminotransferase (ALT) indicates vitamin B6 deficiency; an increase in mean corpuscular volume (MCV) with low ferritin means weakness of cell membranes; and a reduction in blood urea nitrogen (BUN) without kidney disease means a low protein intake [1]. These physiological readings are never taught to the current generation of medical students or medical doctors.

Kaneko also found that many symptoms indicated by blood data can be treated with nutrients according to his defined optimal ranges. He applied personalized nutritional therapy based on the blood data analyses of patients experiencing malaise and prescribed typical courses of personalized nutritional therapy. Using this method, various organ malfunctions in presymptomatic, undiagnosed patients can be effectively corrected with

nutrients

MDPI

Review

Nutrition and Cancer Risk from the Viewpoint of the Intestinal Microbiome

Yoshimu Tanaka [1,2,*], Shin Shimizu [2,3], Masahiko Shirotani [2,4], Kensho Yorozu [2,5], Kunihiro Kitamura [2,6], Masayuki Oehorumu [2,7], Yuichi Kawai [2,8] and Yoshitaka Fukuzawa [2,9]

1 Jinzenkai Tanaka Clinic, 2-3-8, Ikunonishi, Ikuno-ku, Osaka 544-0024, Japan
2 The Association for Clinical Research of Fecal Microbiota Transplantation Japan, 2-1-40, Katamachi, Miyakojima-ku, Osaka 534-0025, Japan; shin@shinbiosis.com (S.S.); lukesashiya@gmail.com (M.S.); info@yorozu-cl.com (K.Y.); kunihiro@kitamura.or.jp (K.K.); info@lifeclinic-t.jp (M.O.); info@kawai-medical.com (Y.K.); yofuku@aichi-med-u.ac.jp (Y.F.)
3 Symbiosis Research Institute, 6-7-4-106, Minatojimaminami-machi, Chuo-ku, Kobe, Hyogo 650-0047, Japan
4 Luke's Ashiya Clinic, 8-2, Ohara-cho, Ashiya, Hyogo 659-0092, Japan
5 Ishinkai Yorozu Clinic, 1-118-4, Mihagino, Tottori 689-0202, Japan
6 Kitamura Clinic, 4-3-8, Nishiki-machi, Onojo, Fukuoka 816-0935, Japan
7 LIFE Clinic Tateshina, 3317-1, Toyohira, Chino, Nagano 391-0213, Japan
8 Yuakai Kawai Clinic for Internal Medicine, 3-7-14, Higashi-Nakahama, Joto-ku, Osaka 536-0023, Japan
9 Aichi Medical Preemptive and Integrative Medicine Center, Aichi Medical University Hospital, Yazakokarimata, Nagakute, Aichi 480-1103, Japan
* Correspondence: tnkzen@xa3.so-net.ne.jp

Abstract: There are various important factors in reducing the risk of cancer development and progression; these factors may correct an unbalanced intake of nutrients to maintain the living body's homeostasis, detoxify toxic materials, acting as an external factor, and maintain and strengthen the body's immune function. In a normal cell environment, nutrients, such as carbohydrates, lipids, proteins, vitamins, and minerals, are properly digested and absorbed into the body, and, as a result, an environment in which cancer can develop and progress is prevented. It is necessary to prevent toxic materials from entering the body and to detoxify poisons in the body. If these processes occur correctly, cells work normally, and genes cannot be damaged. The most important factor in the fight against cancer and prevention of the development and progression of cancer is the immune system. This requires a nutritional state in which the immune system works well, allowing the intestinal microbiome to carry out all of its roles. In order to grow intestinal microbiota, the consumption of prebiotics, such as organic vegetables, fruits, and dietary fiber, and probiotics of effective intestinal microbiota, such as fermented foods and supplements, is required. Symbiosis, in which these organisms work together, is an effective means of reducing the risk of cancer. In addition, fecal microbiota transplantation (FMT) using ultrafine bubble water, produced specially by the Association for Clinical Research of Fecal Microbiota Transplantation Japan, is also useful for improving the nutritional condition and reducing the risk of cancer.

Keywords: cancer; nutrition; intestinal microbiome; fecal microbiota transplantation; ultrafine bubble water; probiotics; prebiotics; symbiotics; immunity

Citation: Tanaka, Y.; Shimizu, S.; Shirotani, M.; Yorozu, K.; Kitamura, K.; Oehorumu, M.; Kawai, Y.; Fukuzawa, Y. Nutrition and Cancer Risk from the Viewpoint of the Intestinal Microbiome. *Nutrients* **2021**, *13*, 3326. https://doi.org/10.3390/nu13103326

Academic Editor: Lynnette Ferguson

Received: 10 August 2021
Accepted: 21 September 2021
Published: 23 September 2021

1. Introduction

The initiation and development of cancer are related to the deterioration of the cellular environment as a result of an imbalance in nutrient intake and contact with toxic substances. Dysbiosis (the alteration and simplification of the intestinal microbiota composition) can induce abnormal functioning of the immune system and chronic inflammation, and can also cause carcinogenesis and the promotion of cancer processes. Therefore, it is necessary to recognize the importance of intestinal microbiota and of the improvement of the intestinal environment in the prevention of carcinogenesis and ongoing cancer processes.

molecules

MDPI

Systematic Review

Green Tea Catechin Association with Ultraviolet Radiation-Induced Erythema: A Systematic Review and Meta-Analysis

Mahendra P. Kapoor [1,*], Masaaki Sugita [2], Yoshitaka Fukuzawa [3], Derek Timm [4], Makoto Ozeki [1] and Tsutomu Okubo [1]

[1] Nutrition Division, Taiyo Kagaku Co. Ltd., 1-3 Takaramachi, Yokkaichi 510-0844, Japan; mozeki@taiyokagaku.co.jp (M.O.); tohkubo@taiyokagaku.co.jp (T.O.)
[2] Faculty of Sport Science, Nippon Sport Science University, 7-1-1 Fukusawa, Setagaya-Ku, Tokyo 158-8508, Japan; m-sugita@nittai.ac.jp
[3] Preemptive and Integrative Medicine Center, Aichi Medical University Hospital, 1-1 Karimata, Yazako, Nagakute 480-1195, Japan; yofuku@aichi-med-u.ac.jp
[4] Taiyo International Inc., 5960 Golden Hills Dr, Minneapolis, MN 55416, USA; derek@taiyoint.com
* Correspondence: mkapoor@taiyokagaku.co.jp; Tel.: +81-70-6479-6004

Abstract: Catechins are a part of the chemical family of flavonoids, a naturally occurring antioxidant, and a secondary metabolite in certain plants. Green tea catechins are well recognized for their essential anti-inflammatory, photo-protective, antioxidant, and chemo-preventive functions. Ultraviolet radiation is a principal cause of damage to the skin. Studies observed that regular intake of green tea catechins increased the minimal dose of radiation required to induce erythema. The objectives of this systematic review and meta-analysis are to determine the effectiveness of green tea catechins in cutaneous erythema and elucidate whether green tea catechin consumption protects against erythema (sunburn) inflammation. A comprehensive literature search was conducted to identify the relevant studies. Two researchers carried out independent screening, data extraction, and quality assessment according to the guidelines of Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA). The pooled effect of green tea catechins on protection against erythema was assessed using approaches fixed-effects or random-effects model to quantify the effectiveness of green tea catechins in the erythema dose–response. Studies not be included in meta-analyses were summarized narratively. Six randomized controlled studies of enrolled studies regularly administrated green tea catechins orally for 6 to 12 weeks involving healthy volunteers comprising a total of 100 participants were included in the analysis. The results revealed green tea catechins have favorable protection against erythema inflammation even at increased minimal erythema dose (MED) of ultraviolet radiation. Meta-analysis results confirm oral supplementation of green tea catechins is highly effective at low-intensity ultraviolet radiation-induced erythema response (MED range; 1.25–1.30) compared to placebo, showing a significant pooling difference ($p = 0.002$) in erythema index (SMD: −0.35; 95% CI, −0.57 to −0.13; $I^2 = 4\%$, $p = 0.40$) in the random-effects model. The pro-inflammatory signaling pathways through oral supplementation with green tea catechins are an attractive strategy for photo-protection in healthy human subjects and could represent a complementary approach to topical sunscreens. Therefore, studies that involved green tea catechin in topical applications to human subjects were also evaluated separately, and their meta-analysis is presented as a reference. The evidence indicates that regular green tea catechin supplementation is associated with protection against UV-induced damage due to erythema inflammation.

Keywords: green tea catechins; meta-analysis; ultraviolet radiation; skin; erythema (sunburn)

Citation: Kapoor, M.P.; Sugita, M.; Fukuzawa, Y.; Timm, D.; Ozeki, M.; Okubo, T. Green Tea Catechin Association with Ultraviolet Radiation-Induced Erythema: A Systematic Review and Meta-Analysis. *Molecules* **2021**, *26*, 3702. https://doi.org/10.3390/molecules26123702

Academic Editor: Yukio Yoneda

Received: 10 May 2021
Accepted: 15 June 2021
Published: 17 June 2021

1. Introduction

Ultraviolet radiation in sunlight is the primary etiological element in major skin-related diseases. Vasodilatation of the dermal vasculature is one of the complex features of skin

MEMO

【メモ欄】

医療機関専用サプリメント

露地栽培アガリクスKA21製品

製造元／東栄新薬株式会社
販売元／株式会社ケーエーナチュラルフーズ
〒181-0013　東京都三鷹市下連雀1-11-23
電話　0422-72-8120
営業時間　9：30～18：00（日・祝・年末年始休業）

エビデンスに基づいた医療機関専用サプリメント

露地栽培アガリクスKA21

太陽の下でも生えてくる生命力の強い露地栽培アガリクスKA21（アガリクスKA21）を主原料として配合。
アガリクスメーカー最多となる32本の国際論文に裏付けされた、信頼の製品をお役立てください。

主な研究施設
麻布大学、近畿大学医学部、慶應義塾大学SFC研究所、国立長寿医療研究センター、順天堂大学医学部、女子栄養大学生体防御学研究室、東京大学食の安全研究センター、東京薬科大学免疫学教室

エヌケーアップ・プレミアム
NKUP Premium

6袋入り　5,400円（税込）
30袋入り　27,000円（税込）

免疫増強、抗がん剤の副作用軽減

集中ケア用　高配合【β-グルカン+ビタミンD】

アガリクスKA21 80%配合

アガリクスKA21を高配合しているためβ1,3-1,6グルカンとビタミンDを豊富に含みます。集中ケア用サプリメントとしてご利用ください。
目安として1日1～2袋をお飲みください。

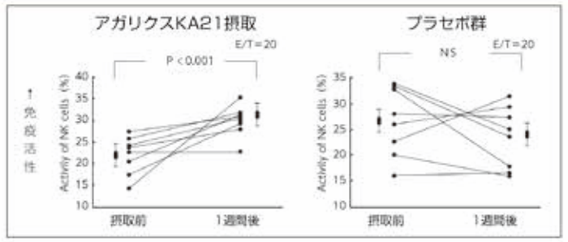
エビデンス　免疫増強、抗がん剤の副作用軽減

NK細胞活性化　（ヒト臨床　DOI:10.1093/ecam/nem016）

【試験実施機関】
順天堂大学免疫学講座

健常人(n=8)に露地栽培アガリクスKA21を1日3g、1週間経口摂取させ、NK細胞の有意な活性化が確認されました。

⇒ NK細胞の活性化をヒト臨床試験で確認

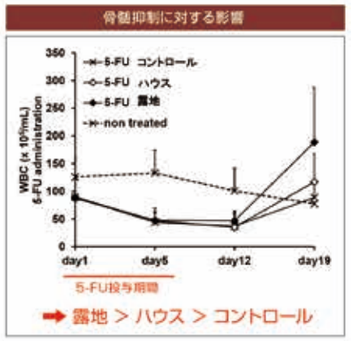


抗がん剤の副作用軽減作用　（マウス試験　DOI:10.1615/IntJMedMushrooms.2019033173）

【試験実施機関】
東京薬科大学免疫学教室

マウスに抗がん剤（5-FU）を5日間経口摂取させ、抗がん剤の副作用発現モデルを作製。
ハウス栽培と露地栽培アガリクスを摂取させ、副作用の発現状況を比較した結果、露地栽培群で骨髄抑制、脱毛、腎障害、消化管傷害、食欲低下、体重低下の軽減効果を確認しました。

⇒ 抗がん剤治療のサポート



商品サンプルと資料をお届けいたします　お申込み締め切り：2023年7月10日まで

お申込みはこちら　販売元：株式会社ケーエーナチュラルフーズへお申し込みください
〒181-0013　東京都三鷹市下連雀1-11-23

お電話　0422-72-8120
営業時間　9：30～18：00（日・祝・年末年始休業）

または右のQRのフォームからお申込み下さい

ブース番号	出展企業名
1	森田薬品工業株式会社
2	タヒボ e 株式会社
3	株式会社東京未病センター
4	ヒューマン・メタボローム・テクノロジーズ株式会社
5	セリスタ株式会社
6	株式会社ケーエーナチュラルフーズ
7	株式会社 Immprex
8	リジェネフォーティー株式会社
9	興和株式会社
10	株式会社ヘリックスジャパン

Floor guide Map