INTERNATIONAL SOCIETY FOR MEDICINAL MUSHROOMS

国际药用菌学会

International Society for Medicinal Mushrooms （ISMM）was founded in Vancouver, Canada. As a global non-profit organization, ISMM promotes the development of research, education, production, transportation, marketing and cultivation of medicinal mushrooms to have people to work towards common aspirations and goals. The integration will increase the impact of the international medicinal mushroom industry and benefit the health of people in the world.

Honorable President: Prof. S.T.Chang, Prof.S.P. Wasser
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国际药用菌学会（International Society for Medicinal Mushrooms），简称ISMM，在加拿大温哥华注册成立，由从事药用菌产业的科研、教学、生产、流通、市场、文化及相关产业链的单位、团体和个人自愿组成的为实现共同意愿的非营利性国际组织。本学会致力于促进国际药用菌产业各个领域的融合与发展，以提升药用菌行业在全球的影响力，造福人类健康。

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NEWSLETTER OF THE INTERNATIONAL SOCIETY FOR MEDICINAL MUSHROOMS

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News Reports

Do Mushrooms Really Use Language to Talk to Each Other? A Fungi Expert Investigates

By Alexander_Volkov/Shutterstock

Nearly all of Earth's organisms communicate with each other in one way or another, from the nods and dances and squeaks and bellows of animals, through to the invisible chemical signals emitted by plant leaves and roots. But what about fungi? Are mushrooms as inanimate as they seem – or is something more exciting going on beneath the surface?

New research by computer scientist Andrew Adamatzky at the Unconventional Computing Laboratory of the University of the West of England, suggests this ancient kingdom has an electrical "language" all of its own – far more complicated than anyone previously thought. According to the study, fungi might even use "words" to form "sentences" to communicate with neighbours.

Almost all communication within and between multi-cellular animals involves highly specialised cells called nerves (or neurones). These transmit messages from one part of an organism to another via a connected network called a nervous system. The "language" of the nervous system comprises distinctive patterns of spikes of electrical potential (otherwise known as impulses), which help creatures detect and respond rapidly to what's going on in their environment.

Despite lacking a nervous system, fungi seem to transmit information using electrical impulses across thread-like filaments called hyphae. The filaments form a thin web called a mycelium that links fungal colonies within the soil. These networks are remarkably similar to animal nervous systems. By measuring the frequency and intensity of the impulses, it may be possible to unpick and understand the languages used to communicate within and between organisms across the kingdoms of life.

Using tiny electrodes, Adamatzky recorded the rhythmic electrical impulses transmitted across the mycelium of four different species of fungi.

He found that the impulses varied by amplitude, frequency and duration. By drawing mathematical comparisons between the patterns of these impulses with those more typically associated with human speech, Adamatzky suggests they form the basis of a fungal language comprising up to 50 words organised into sentences. The complexity of the languages used by the different species of fungi appeared to differ, with the split gill fungus (*Schizophyllum commune*) using the most complicated lexicon of those tested.

The split gill fungus is common in rotting wood and is reported to have more than 28,000 sexes. Bernard Spragg/Wikipedia

This raises the possibility that fungi have their own electrical language to share specific information about food and other resources nearby, or potential sources of danger and damage, between themselves or even with more distantly connected partners.

Underground communication networks

This isn't the first evidence of fungal mycelia transmitting information.

Mycorrhizal fungi – near-invisible thread-like fungi that form intimate partnerships with plant roots – have extensive networks in the soil that connect neighbouring plants. Through these associations, plants usually gain access to nutrients and moisture supplied by the fungi from the tiniest of pores within the soil. This vastly expands the area that plants can draw sustenance from and boosts their tolerance of drought. In return, the plant transfers sugars and fatty acids to the fungi, meaning both benefit from the relationship.

The mycelium of mycorrhizal fungi enable symbiotic relationships with plants. KYTan/Shutterstock

Experiments using plants connected only by mycorrhizal fungi have shown that when one plant within the network is attacked by insects, the defence responses of neighbouring plants activate too. It seems that warning signals are transmitted via the fungal network.

Other research has shown that plants can transmit more than just information across these fungal threads. In some studies, it appears that plants, including trees, can transfer carbon-based compounds such as sugars to neighbours. These transfers of carbon from one plant to another via fungal mycelia could be particularly helpful in supporting seedlings as they establish. This is especially the case when those seedlings are shaded by other plants and so limited in their abilities to photosynthesise and fix carbon for themselves.

Exactly how these underground signals are transmitted remains a matter of some debate though. It is possible the fungal connections carry chemical signals from one plant to another within the hyphae themselves, in a similar way to how the electrical signals featured in the new research are transmitted. But it is also possible that signals become dissolved in a film of water held in place and moved across the network by surface tension. Alternatively, other microorganisms could be involved. Bacteria in and around fungal hyphae might change the composition of their communities or function in response to changing root or fungal chemistry and induce a response in neighbouring fungi and plants.

The new research showing transmission of language-like electrical impulses directly along fungal hyphae provides new clues about how messages are conveyed by fungal mycelium.

Mushroom for debate?

Although interpreting the electrical spiking in fungal mycelia as a language is appealing, there are alternative ways to look at the new findings.

The rhythm of electrical pulses bears some similarity to how nutrients flow along fungal hyphae, and so may reflect processes within fungal cells that are not directly related to communication. The rhythmic pulses of nutrients and electricity may reveal the patterns of fungal growth as the organism explores its surroundings for nutrients.

Of course, the possibility remains that the electrical signals do not represent communication in any form at all. Rather, charged hyphal tips passing the electrode could have generated the spikes in activity observed in the study.

What on Earth are they talking about? Katie Field, Author provided

More research is clearly needed before we can say with any certainty what the electrical impulses detected in this study mean. What we can take from the research is that electrical spikes are, potentially, a new mechanism for transmitting information across fungal mycelia, with important implications for our understanding of the role and significance of fungi in ecosystems.

These results could represent the first insights into fungal intelligence, even consciousness. That's a very big "could", but depending on the definitions involved, the possibility remains, though it would seem to exist on time scales, frequencies and magnitudes not easily perceived by humans.

Source: theconversation.com

Shroom FitBit: Processors in Tech Wearables Could Be Replaced With Fungi Mycelium, New Study Finds

By Tanuvi Joe

In a recent study titled 'Reactive fungal wearable', researchers explore the use of fungi as a potential candidate to produce sustainable textiles that can be used as eco-friendly bio wearables, for instance, the processors in tech wearables like Fitbits could be replaced by incorporating mushroom mycelium.

The joint research venture undertaken by the University of the West of England, Bristol, the U.K. (UWE Bristol) and collaborators from Mogu S.r.l., Italy, Istituto Italiano di Tecnologia, Torino, Italy and the Faculty of Computer Science, Multimedia and Telecommunications of the Universitat Oberta de Catalunya (UOC) has assessed the sensing potential of fungal wearables.

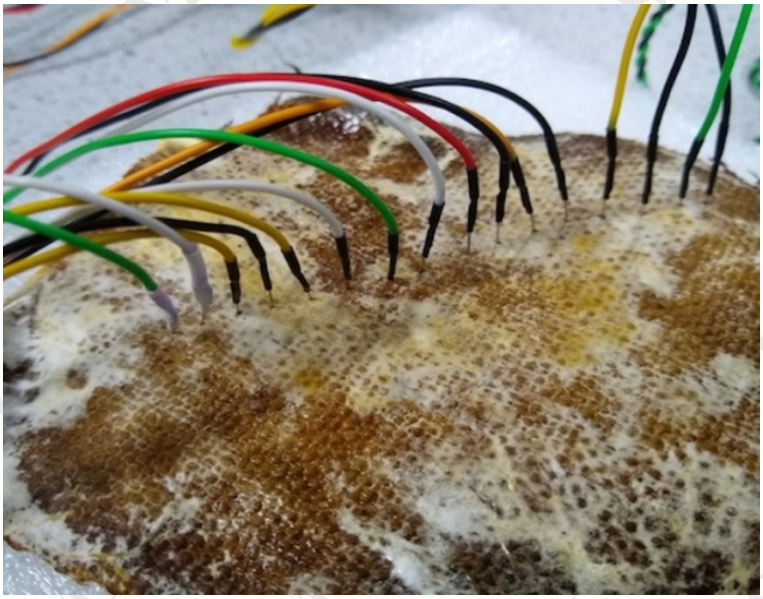
The researchers of the study conducted several laboratory experiments on the electrical response of a hemp fabric captured by oyster fungi by attaching it to computer sensors and stimulating it with attractants and repellents.

Wearable devices require complex and sophisticated circuits that connect to sensors having at least some computing power, thus making them 'smart'.

Oyster mushroom mycelium, the fibrous mainframe tissues of fungi that populate under the soil and from which mushrooms sprout was able to perceive several external stimuli like light, temperature, and moisture, as well as certain chemicals in the environment, and even electrical signals in a way that imitates the same function for sensors and processors.

To explain this concept further, we use an example of a heart rate monitor, and using the study's findings, **the mushroom's perceptions of the environment would become the data that gives you the beats-per-minute count on this device.**

Dr. Mohammad Mahdi Dehshibi, researcher with the UOC's Scene Understanding and Artificial Intelligence Lab (SUNAI), an author of the study said that fungi make up the largest, most widely distributed and oldest group of living organisms on the planet. "They grow extremely fast and bind to the substrate you combine them with and are even able to process information in a way that resembles computers. We can reprogramme a geometry and graph-theoretical structure of the mycelium networks and then use the fungi's electrical activity to realize computing circuits. Fungi do not only respond to stimuli and trigger signals accordingly, but also allow us to manipulate them to carry out computational tasks, in other words, to process information."



Close up of the fungal wearable incorporated into real cloth and locations of electrodes.

Source: 'Reactive fungal wearable' study

Prof. Andrew Adamtzky from UWE Bristol's Unconventional Computing Laboratory, another author on this study and who famously utilized slime molds to solve mazes and optimize city roadway planning in Tokyo and France, wrote in his new research paper. "**We have shown that it is possible to discern a nature of stimuli from the fungi electrical responses. The results paved a way towards the future design of intelligent sensing patches to be used in reactive fungal wearables**."

By nature, mycelium organizes itself into geometric structures in and throughout the soil and though fungal mycelium doesn't have many reasons for recognizing electrical signals in nature that we know of and Prof. Adamtzky wants to investigate whether reprogramming oyster mushroom mycelium genes to develop into different geometric structures would optimize the detection power of electrical signals.

According to Dehshibi, mycelium-based products are already used commercially in construction. "You can mold them into different shapes like you would with cement, but to develop a geometric space you only need between five days and two weeks. **They also have a small ecological footprint. In fact, given that they feed on waste to grow, they can be considered environmentally friendly**."

With this study's findings, the authors of the paper don't mean to replace silicon chips- fungal reactions are too slow for that. Rather, they think that the findings could help humans use mycelium growing in an ecosystem as a 'large-scale

environmental sensor' as fungal networks, are monitoring a large number of data streams as part of their everyday existence and if we could plug into mycelial networks and interpret the signals, they use to process information, individuals could learn more about what was happening in an ecosystem.

Mycelium can be used to make building bricks, coffins, canoes and there are several companies that are understanding the multifaceted uses of mushroom mycelium and incorporating it into their products. For instance, NetZero has developed a new type of 'mushroom ball' or orbs that leverage the carbon-sequestration ability of mycelium, derived from fungi, and can speed up the environment's natural carbon capture rate by two-fold thus empowering individuals to capture carbon from their backyard.

In the fashion industry, alt material startup Mycoworks recently bagged US$45 million in funding to use a mycelium-based material that can replace both emissions-heavy traditional cowhide as well as petroleum-based plastic vegan leathers.

Even the food industry has come forward and recognized the potential of this fungi with New Singularity, a plant-based seafood company based in mainland China developing their "1.0" microalgae-based vegan seafood analogues that will incorporate a mycelium fermentation technology to create their second iteration of seafood analogues.

Source: www.greenqueen.com.hk

Up-coming Events

Russian Mushroom Day-2022

September 14-16, 2022

ABOUT THE EVENT

The days of Russian Mushroom Day-2022 after a seven-year break will again be held in the format of a Mushroom Cruise.

New circumstances of doing business require a serious conversation about the reconfiguration of the entire Russian mushroom industry and the closed space of the ship is best suited for this.

Three days on board the comfortable four-deck motor ship "Leonid Krasin" will allow representatives of the mushroom industry to conduct a "collective brainstorming session" and answer topical issues on the agenda.

THEME

"The New Reality of Mushroom Growing in Russia: Adaptation or Transformation?"

TOPIC

- What will happen to the consumption of mushrooms in conditions of double-digit inflation?
- How will the priorities of Russians change - fresh or ready-to-eat mushrooms and mushroom products?
- How to increase the volume of sales of mushrooms in retail and is there an alternative to it?
- Which packaging will allow you to sell more mushrooms - cheap or environmentally friendly?
- Will the supply of foreign equipment and materials for mushroom growing be preserved?
- Is there an alternative to supplies from the West to the East and what can be produced in Russia?
- Will there be new sources of labor resources?
- On what, besides mushrooms, can a mushroom farm earn?
- Does the Russian mushroom industry need its own Association?

EXHIBITION

"Mushroom Innovations Expanding Opportunities"

On board the ship there is less space for an exhibition than in a hotel or exhibition center. Therefore, we will gather here companies with the most interesting and innovative proposals for the Russian mushroom industry.

The exhibition will be held in two halls.

Exhibition venue fee: 45000 R

If you want to book the exhibition venue, please register for mushroom Cruise

RUSSIAN MUSHROOM DAY PLAN

September 14

10.00 – 12.00 Registration.

12.30 Departure

12.30 – 13.30 Ceremonial departure.

13.30 – 14.30 Lunch.

15.00 – 18.00 Exhibition.

15.00 – 18.00 Conference.

19.00 – 20.00 Dinner.

September 15

08.30 – 09.30 Breakfast.

10.00 – 18.00 Exhibition.

10.00 – 12.00 Conference.

12.30 – 13.30 Lunch.

13.30 – 15.30 Parking in Myshkin

15.30 Sailing from Myshkin

16.30 – 17.00 Master class on cooking a dish from oyster mushrooms

17.00 – 18.00 Competition for the best dish of fast food from mushrooms.

18.30 – 19.30 Dinner.

September 16

08.30 – 09.30 Breakfast.

10.00 – 17.00 Exhibition.

10.00 – 13.00 Conference.

13.30 – 14.30 Lunch.

14.30 – 18.00 Free time

18.00 Arrival in Moscow

CONTACT

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The 11th International Medicinal Mushroom Conference 2022 3rd Circle

Welcome to the

IMMC11- The 11th International Medicinal Mushroom Conference

Belgrade, Serbia, Crowne Plaza Hotel

September 27-30th, 2022.

THE THEME OF THE CONFERENCE:

Medicinal Mushroom Science: Innovation, Challenges and Perspectives

Organized by:

International Society for Medicinal Mushrooms and University of Belgrade

Co-organized by:

Faculty of Agriculture – Belgrade
Mycological Society of Serbia
Faculty of Biology – Belgrade
Faculty of Natural Science -Kragujevac
IBISS- Institute for Biological Research "Siniša Stanković"
EHEDG – The European Hygienic Engineering & Design Group
Faculty of Science – Novi Sad
Faculty of Pharmacy – Belgrade

KEY TOPICS:

① Biodiversity of medicinal mushrooms (conservation, taxonomy and ecological distribution);
② Genetics and breeding of medicinal mushrooms (including molecular biology);
③ New trends in the cultivation, industrial production and fermentation of medicinal mushrooms
④ Biochemistry and pharmacology of medicinal mushrooms active compounds;
⑤ Medicinal mushrooms in veterinary and agriculture;
⑥ Medicinal mushrooms in clinical practice; antiviral and antimicrobial compounds;
⑦ Nutritional and medicinal value of mushroom products;
⑧ Industrialization of medicinal mushrooms products (including management, marketing, laws and regulations, standardization, ecotourism and mushroom hunting);

⑨ Psychedelic Mushrooms: Research, opportunities and the future for Psilocybe in medicine.

REGISTRATION

REGISTRATION FEES

Type	Early bird registration until 27.08.2022.	Late registration from 28.08.2022. until 20.09.2022.
PhD students	200 €	240 €
HINARI A & B * List countries	320 €	370 €
Regular attendees	420 €	490 €

*All prices are in Euros and include VAT 20%

*HINARI Group A&B: Participants residing in lower- and middle income countries. A list of HINARI countries can be found here.

*In order to increase accessibility to the IMMC11 Congress resources to all researchers and professionals coming from low resource countries, IMMC11 Organizing Committee decided to apply HINARI list of countries model for DISCOUNTED registration fees for those participants coming from ELIGABLE countries (HINARI Group A & B).

*PhD Student registration forms must be accompanied by a proof (a signed letter from the head of the department or other corresponding document) confirming the PhD student's status

Registration fee includes: access to all scientific sessions, access to poster sessions, access to exhibition and industry sessions, lunch and coffee breaks, welcome reception

IMPORTANT DATES & DEADLINES

- 15 May 2022 Abstract submission deadline
- 15 June 2022 Information to authors of abstract acceptance
- Withdrawal of Abstracts: 14 days after decision information
- Registration of presenter: 14 days after decision information
- 27 August 2022 Early bird registration deadline
- 28 August – 20 September 2022 Late registration
- 30 July 2022 Full registration cancelation
- 27-30 September 2022 IMMC11

PRELIMINARY PROGRAM

TUESDAY 27 September	
8:30	**Registration**
9:00-10.00	**Opening Ceremony**
Prof. Solomon P. Wasser, Israel/Ukraine - The History of Organizing IMMCs	
10:00-10:30	**Coffee break**

10:30-13:00	**Keynote 1:** **Prof. Shu-Ting Chang, Australia/China** Mushroom Biology: The impact on mushroom production and mushroom products **Keynote 2:** **Dr. Marina Soković, Serbia** Mushrooms, food, or medicine? Or both? **Keynote 3:** **Dr. Chrisopher Hobbs, USA** Mushroom Medicine: Latest News, Science, Clinical Uses, and Product Selection			
13:00-14:00	**Lunch break/Poster Viewings/Exhibition**			
14:00-17:00	**SESSION 1** **Biodiversity of medicinal mushrooms (conservation, taxonomy and ecological distribution);** **Chairpersons: TBD**		**SESSION 2** **Genetics and breeding of medicinal mushrooms (including molecular biology);** **Chairpersons: TBD**	
	Plenary lecture 1 **Prof. Georgios I. Zervakis, Greece** Current overview of Pleurotus species taxonomy, phylogenetic relationships and global distribution **Plenary lecture 2** **Prof. Guiseppe Venturella, Italy** Conservation, taxonomy, ecological distribution, and potential application of the culinary-medicinal mushroom *Leccinum scabrum*		**Plenary lecture 1** **Dr Boris Jakopovic, Croatia** Proteomic Research on the Therapeutic Properties of Medicinal Mushrooms	
	Dr. Le Tham Xuan, Vietnam	Biodiversity and comparative analyses of representatives of tomofaghus yellow gold lingzhi fungi (Ganodermataceae) – A rare source of precious materia medica	**Dr. Ivana Sofrenić, Serbia**	Metabolomics study of cultivated fruiting bodes od medicinal mushroom *Fomitopsis betulina*
	Giancarlo Angeles Flores, Italy	Diversity of *Pleurotus* spp. and their metabolites of nutraceutical and therapeutic importance	**Abraham Nkumah, Nigeria**	Molecular Identification, Cytotoxicity and Invitro Enzymatic Activities of Bioactive Peptide Rigidoosporous Microporus (Macro-Fungus) as Lead for Antidiabetic Agent.
	Jingliang Liang, China	Spatial Distribution of Suitability of Wild Chinese Caterpillar Fungus Resources in Qinghai Province	**Chuyu Tang Tang, China**	Metabolomic analysis of amino acids and their derivatives in three Ophiocordyceps sinensis strain
	Dr. Mustafa Kemal Soylu, Turkey	The Collection and Conservation of Wild *Hericium* species in Türkiye	**Guangyu Liu, China**	Study on the inhibitory mechanism of *Ganoderma lucidum* on pancreatic cancer based on network pharmacology and molecular docking methods
	Dr. Maja Karaman, Serbia	Diversity, Chemistry and Environmental contamination of wild growing Medicinal Mushrooms species as sources of biologically active substances	**Professor Jianzhao Qi, China**	Genome sequencing advances the development of medicinal-edible mushrooms

		(antioxidants, antidiabetics, AChE inhibitors and cosmeceuticals)		
	Ivan Dudaš, Serbia	Online ethnomycological research in Serbia	**Yating Dong, China,**	Random mutagenesis and genetic diversity of white rot fungus (*Phellinus igniarius*) by physical mutagens
	Ágnes Radnóti, Hungary	Taxonomic re-examination of Macrolepiota olivascens, a European taxon showing high similarity to parasol mushroom *M. procera* (Agaricaceae, Basidiomycota)		
17:00-17:30	**Coffee break**			
17:30-19:30	**Poster/short oral presentation session No 1 15-20 posters**		**Poster/short oral presentation session No2 15-20 posters**	
19:30-22:00	**Welcome Reception**			

WEDNESDAY 28 September				
9.00-10.30	**Keynote 4:** **Prof. Marin Berovic, Slovenia** Engineering Aspects in Cultivation of Medicinal Mushroom Biomass in Solid State and Submerged Bioreactors **Keynote 5:** **Dr Lillian Barros, Portugal** Mushrooms as a source of bio-based ingredients: food and cosmetic applications			
10.30-14.15	**SESSION 3 – A** **New trends in the cultivation, industrial production and fermentation of medicinal mushrooms** **Chairperson: Marin Berovic**		**SESSION 7 – A** **Nutritional and medicinal value of mushroom products;** **Chairpersons: Liiian Barrros**	
	Plenary lecture 1 **Franc Pohleven, Slovenia** Influence of substrate on growth and biological efficacy of Cordyceps militaris		**Plenary lecture 1** **Dr. Jovana Petrović, Serbia** Mushrooms as a source of functional food ingredients	
11:00-11:30	**Coffee break**			
11:30-14:15	**Dr. Angela Amazonas, Brazil**	Industrialization of medicinal mushrooms products in Brazil	**Professor Hui-Chen Lo, Chinese Taipei**	Effects of Medicinal Mushrooms on Hyperuricemia: Myths and Facts
	Jianbo Chen Chen, China	Study on the Quality of Fermented Mycelium of Chinese caterpillar fungus in Different Areas of Qinghai Province	**Ping Zhu, China**	Studies on the biosynthesis of ergot alkaloids
	Idan Pereman, Israel	Study on the Quality of Fermented Mycelium of Chinese caterpillar fungus in Different Areas of Qinghai Province	**Professor Milena Pantić, Serbia**	Potential application of selenium-enriched mushrooms in the food and pharmaceutical industry

	Dr. Valeria Ferraro, Italy	Preliminary results on the cultivation and the clinical use against human pathogens of *Pleurotus eryngii* var. thapsiae, a culinary-medicinal mushroom from Sicily	**Jovana Vunduk, Serbia**	Give me my dose-A researcher's and consumer's dive into the mushroom-based nutraceutical industry
	Rebeca Lavega González, Spain	Characterization of the composition, structure, enzymatic activity and bacterial metataxonomy of the sterile substrate used during Lentinula edodes growth and development.	**Dr. Roman Bleha, Czech Republic**	Isolation and structural analysis of polysaccharides from various medicinal mushrooms
	Saed Harsini, Iran, Germany	How mushroom can help us to achieve SDG 2 (Zero Hunger) and Optimal method of producing edible & Medicinal Mushrooms in hot and dry areas	**Dr. Liudmila Kalitukha, Germany**	Medicinal potential of the insoluble extracted fibers isolated from the Fomes fomentarius fruiting bodies. A review
14:15-15:15	**Lunch break/Poster Viewings/Exhibition**			
15.15-17.30	**SESSION 3 – B** **New trends in the cultivation, industrial production and fermentation of medicinal mushrooms** **Chairperson: Marin Berovic**		**SESSION 7 – B** **Nutritional and medicinal value of mushroom products;** **Chairpersons**: **Liiian Barrros**	
			Plenary lecture 1 **Professor Segula Masaphy, Israel** Aspects in morel mushrooms qualities and health promoting activities	
	Dr. Jaime Carrasco, Spain	Mechanism of biostimulation to prevent biotic disorders during mushroom cultivation	**Vanessa Grifoll, Spain**	Assessment of the in vitro antioxidant and anti-inflammatory potential of ethanol extracts of cultivable mushrooms
	Dr. Sandra Montoya, Colombia	Solid culture parameters for the production of fruiting bodies of the turkey tail fungus (*Trametes versicolor*) in tropical wheathers under controlled conditions	**Dr. Haseeb Anwar, Pakistan**	Hepatoprotective and hypocholesteromic effect of *LETINUS EDODES* (Shiitake mushroom) in alloxan induced diabetic rat model
	Iryna Bandura, Ukraine	Microbiota in mushroom fruting houses and the effect of isolated organisms on *P. ostreatus* mycelia growth and development in vitro	**Professor Victor Olusegun Oyetayo, Nigeria**	Mineral Element Enrichment of Mushrooms for The Production of More Effective Functional Foods
	Dr. Mustafa Kemal Soylu, Turkey	The Obtaining of The Pure Culture of Some Edible Ectomycorrhizal Mushrooms	**Dr. Attila Vanyolos, Hungary**	Hungarian macro fungi as promising source of bioactive natural products: summary of a decade research

	Professor Manuela Rollini, Italy	Growth of Medicinal Mushrooms (MMs) on maize cobs with different pigmentation: NovEl biotechnological approaches to valorize Maize by-Products (NETMAP)	**Professor Mi Kyeong Lee, Republic of Korea**	Lion's mane mushroom (*Hericium erinaceus*) as good source of bioactive constituents
	Dr. Wan Abd Al Qadr Imad Wan-Mohtar, Malesia	Bioreactor-produced *Ganoderma lucidum* Eats Wastewater	**Dr. Ranjit Singh, India**	In Vitro Culture Technology of *Ophiocordyceps sinensis*: A Boon for Nutraceutical & Pharmaceutical Industry
	Dr Elizabeth Morrison, USA	Newer and more economically viable methods of mushroom cultivation		
17:30-18:00	**Coffee break**			
18:00-19:45	**Poster/short oral presentation session No 3 15-20 posters**		**Poster/short oral presentation session No 4 15-20 posters**	
20:00-24:00	**Conference dinner**			

THURSDAY, September 29				
09:00-09:45	**Keynote 6: Prof. Zhibin Lin, China Multi-target antitumor effect of Ganoderma lucidum and its clinical application**			
09:45-14:00	**SESSION 4 – A Biochemistry and pharmacology of medicinal mushrooms active compounds; Chairpersons: TBD**		**SESSION 6 - A Medicinal mushrooms in clinical practice; antiviral and antimicrobial compounds; Chairpersons: TBD**	
	Plenary lecture 1 Prof. Ulrike Lindequist, Germany Interactions between medicinal mushroom components and conventional drugs - molecular basis and practical consequences		**Plenary lecture 1 Dr. Mikheil Asatiani, Georgia** Antifungal and Antioxidant Potential of Schizophyllum commune	
10:30-11:00	**Coffee break**			
	Dr. Anita Klaus, Serbia	Pink oyster mushroom *Pleurotus flabellatus* mycelium is a valuable source of biologically active components	**Dr. Andrej Gregori, Slovenia**	Cordycepin as a potential pharmacological inhibitor of pro-fibrotic pathways in systemic sclerosis
	Professor Martin Pavlik, Slovakia	Identification of triterpenes in *Ganoderma lingzhi* and *Ganoderma lucidum* and dynamics of fungal respiration during growth	**Dr. Vladimir Laudanović, Andorra**	Role of heteropolysaccharides derived from medicinal mushrooms in Chemoprevention and Carcinogenesis
	Dr. Andrej Gregori,	Extraction of cordycepin from *Cordyceps militaris* and its	**Professor Jingsong**	Study on active compounds of protecting nerve cells in *Ganoderma*

	Slovenia	characterization by HPLC and potentiometric titrations	**Zhang,China**	*lucidum* based on spectrum-effect relationship method
	Dr. Elena Vetchinkina, Russian Federation	Antitumor activity of proteins and polysaccharides from medicinal basidiomycete *Lentinus edodes*	**Haiying Bao, China**	Research on Antitumor activity and mechanism of Mycomedicine
	Ralph Schmidt, Norway	Immunomodulatory and anti-inflammatory activity of the mushroom extract AndoSan	**Ntsama Mbani Genevieve, Cameroon**	Cervical Cancer: Knowledge, Attitudes, Practices of Women and Feasibility of Screening for Precancerous Lesions in a Health District of Cameroon.
	Professor Maja Kozarski, Serbia	Mushroom polyphenols as immune system balancers: What's the mechanism behind it and possible interactions with dietary fibers?		
14:30-15:30	**Lunch break/Poster Viewings/Exhibition**			
15:30 - 17:30	**SESSION 4 – B** **Biochemistry and pharmacology of medicinal mushrooms active compounds;** **Chairpersons: TBD**		**SESSION 6 - B** **Medicinal mushrooms in clinical practice; antiviral and antimicrobial compounds;** **Chairpersons: TBD**	
	Professor Yanfang Liu, China	Structure and conformation characterization of polysaccharide from *Ganoderma lucidum* and the structure-activity relationship on immunoregulation	**Soumaya Boudagga, Tunisia**	Using Biolog OmniLog system to determine nutritional phenome and antibacterial activity of Lion's Mane (*Hericium erinaceus*)
	Nathan Scott, United Kingdom	Antidiabetic effects of *Ganoderma lucidum* fruiting body polysaccharide extracts obtained through novel purification procedures	**Professor Segula Masaphy, Israel**	Fungal antagonism: morel mushroom infection by *Purpureocillium lilacinum*
	Professor Clementina Adenipekun, Nigeria	Screening of neuroprotective components based on *Ganoderma lucidum* oxidative stress injury theory and its mechanism	**Dr. Xiuzhang Li, China**	Potential analysis of Chinese cordyceps in the treatment of Covid-19
	Professor Wenhan Wang, China	Screening of neuroprotective components based on *Ganoderma lucidum* oxidative stress injury theory and its mechanism	**Dr. Siddharth Pramod Dubhashi , India**	A Randomized, Double Blind, Placebo Controlled Study to Evaluate the Efficacy and Safety of *Cordyceps* Capsules (Food Supplement) as an Add-On Therapy in Patients with Mild to Moderate COVID-19 Infection: from bench to bedside
	Sébastien Sinaeve,	Nephroprotective effect of a methanolic extract of two		

	Belgium	*Ganoderma* species and its association in an in vitro model of cisplatin induced tubulotoxicity		
	Vesna Lazic, Serbia	Antibacterial and antioxidative activity of chitosan and chitosan hydrochloride isolated from mushrooms		
17:30-18:00	**Coffee break**			
18:00-19:45	**Poster/short oral presentation session No 5 & No 7 15-20 posters**		**Poster/short oral presentation session No 6 & No 8 15-20 posters**	

Friday, 30 September		
09:30-10:15	**Keynote 7** **Prof. Omon S. Isikhuemhen, USA/Nigeria** Psychedelic Mushrooms: Research, Opportunities and Future Prospects	
10:15-11:45	**SESSION 9** **Psychedelic Mushrooms: Research, opportunities and the future for Psilocybe in medicine.** **Chairpersons: John Holiday, Omon S. Isikhuemhen**	
	Plenary lecture 1 **Dr. John Holliday, USA** Advances in cultivation over the last 20 years, and where cultivation is headed in the future	
	Prof.Dr. Hikmet Hakan Aydin, Turkey	Clinical trials and biopharmaceutical potential of psilocybin mushrooms.
	Gabriele Beltrame, Finland	Clinical trials and biopharmaceutical potential of psilocybin mushrooms.
11:45-12:15	**Coffee break**	
12:15-13:45	**SESSION 5** **Medicinal mushrooms in veterinary and agriculture;** **Chairpersons: TBA**	
	Plenary lecture 1 **Ewa Zapora, Poland** Tyromyces fissilis in the prevention and treatment of American foulbrood in honeybees	
	Prof. Dr. Wei Jia, China	Structural elucidation of a polysaccharide from *Flammulina velutipes* and its immunomodulation activities on mouse B lymphocytes
	Professor Paola Rossi, Italy	Hericium erinaceus neuroprotection of Choroid Plexus and Blood Brain Barrier in Wild-Type Frail Mice during Aging
13:45-15:15	**SESSION 8** **Industrialization of medicinal mushrooms products (including management, marketing, laws and regulations, standardization, ecotourism and mushroom hunting);** **Chairpersons: TBA**	
	Plenary lecture 1 **Assoc. Prof. Milena Stavrić, Austria** **Mycelium-based composites in the architectural scale**	
	Hana Vašatko, Austria	Growing Architecture - Towards mycelium-based products in architecture and design

	Professor Elena Savino, Italy	Selection of wood decay fungal strains with medicinal properties useful for development of myco-materials
15.15-15.30	**Closing Ceremony**	
15:30 - 16:00	**Farewell drink**	
16:00-19:00	**Visit to the exhibition of Wild mushrooms of Serbia at Botanical Garden Jevremovac**	

Overview of Oral Poster Presentations

Title	Presenter	Affiliation	Country	Ses. No
Identification and collection of medicinal mushrooms from DR Congo through an ethnomycological investigation	Prof. Manya Mboni Henry	University of Lubumbashi	Democratic Republic of the Congo	1
Ethnomycology, Sensory Analysis and Nutritional Composition of Eight Edible Mushrooms Consumed in the African Great Lakes Region	Assumpta Mukandera	ULB	Belgium	1
Biodiversity of the tropical species of the genus Ganoderma in Veracruz, Mexico	Prof. Alla Shnyreva	Department of Mycology and Algology, Moscow Lomonosov State University	Russian Federation	1
Culture degeneration and the role of cordycepin/pentostatin synthesis in the entomopathogen Cordyceps militaris	Dr. Andrej Gregori	MYCOMEDICA D.O.O.	Slovenia	2
Differences in metabolome of selected strains of Hericium erinaceus	Dr. Ivan Jablonský		Czech Republic	2
Variations in ITS region of medicinal fungal species Cerioporus varius and its phylogeographic analysis	Milena Rakić	University of Novi Sad, Faculty of Sciences	Serbia	2
A polysaccharide-protein complex isolated from Cultivated Chinese Cordyceps drives M1 phenotype polarization in macrophages	Xiaotong Yang	Institute of Microbiology and Immunology, College of life sciences, Shangai Normal University	China	2
BIOSCHAMP: Design of biostimulant alternative casing for the mushroom industry	Dr. Jaime Carrasco	Mushroom Technological Research Center of La Rioja (CTICH)	Spain	3
Effects of Oleic Acid on Metabolic Flux Distributions of Lanosterol Synthesized by Liquid Submerged Fermentation of Ganoderma Lucidum	Jie Feng	Institute of Edible Fungi, Shanghai Academy of Agricultural Sciences	China	3
Biology and Nutritional Contents in the Culinary-Medicinal Milky White Mushroom, *Calocybe indica* (Agaricomycetes), During Cultivation Involving Casing and Scratching	Omoanghe Isikhuemhen	North Carolina A&T State University	United States	3

Treatments				
Effects of *Pleurotus ostreatus* fermentation on the chemical composition of milo	Omoanghe Isikhuemhen	North Carolina A&T State University	United States	3
Supplementation of medicinal mushroom substrates with trace elements Se and Zn	Dr. Ivan Jablonský	Czech University of Life Sciences	Czech Republic	3
Bioactive compounds in Agaricus subrufescens grown in closed loop cultivation system – VegWaMus CirCrop	Dr. Agnieszka Jasinska	Lindum AS/ Poznan Univerity of Life Sciences	Norway	3

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Dutch Mushroom Days Cancelled

The Dutch Mushroom Days, scheduled for 6, 7 and 8 July, has been cancelled on April 15th, forced upon the organizers by the participation cancellation of many, mainly Dutch, market leading exhibitors.

Considerations like the war in Ukraine, rising inflation and costs for suppliers, a negative investment climate and COVID (in China) plus correspondingly expected lower amounts of visitors are among the reasons for doing so, and led to heated discussions behind the scenes. The cancellation of more than a few major players had a snowball effect, and the board of the Champignondagen Foundation, seeing itself confronted with many more cancellations coming in by April 14th, had to make the difficult and regretful decision to cancel the whole event: "We had to weigh up interests and the success of the Days was in danger. Without sufficient participants, the event can not serve as a the platform it should be, and revenues no longer outweigh costs, so we had no choice but to cancel the 2022 edition permanently."

At the time of going to press with this magazine, the board had just started to inform exhibitors and visitors and will be looking into the financial consequences of the decision for all those involved.

The Dutch Mushroom Days is the biggest international tradeshow for the edible mushroom industry worldwide, with normally some 100 exhibitors and 3000 visitors from 80 countries.

Source: https://mushroombusiness.com

4th International Congress and 5th National Conference on Biotechnology of Medicinal Plants and Mushrooms

October 18-19, 2022, Ramsar, Iran

Organised by: University of Zanjan, Sari Agricultural Sciences and Natural Resources University and Governorate of Ramsar

The Congress will provide an opportunity for students, entrepreneurs and technologists around the world to have a constructive dialogue and share their ideas about the scientific innovations in fields of biotechnology on medicinal plants and mushrooms.

Topics

- Genetic engineering, genetic diversity, tissue culture, gene expression, secondary metabolites and plant physiology
- Herbal and natural medicines based on biotechnology
- Biotechnology and biology of mountain, poisonous, edible and industrial fungi
- Trade of new biotechnologies in the field of medicinal plants, herbal medicines, mountain mushrooms and industrial
- Industries related to biotechnology medicinal plants and mushrooms
- Medicinal plants, rangeland protection and the environment
- Other research related to medicinal plants, fungi and medicinal derivatives

Papers are sought on all topics in biotechnology related to medicinal plants and mushrooms.

The deadline for submitting abstracts for oral or poster selection is August 21, 2022.

Congress expenses

The cost of registration, refereeing, issuing certificates and publishing articles for researchers outside of Iran is one hundred dollars, which can be arranged through Iranian embassies in those countries. Dear participants, after registration, inform the congress secretariat to coordinate with the Iranian embassy in that country.

Visit http://ic-bmpm.znu.ac.ir/ for more information.

Research progress

Taming the beast: a revised classification of *Cortinariaceae* based on genomic data

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Abstract: Family *Cortinariaceae* currently includes only one genus, *Cortinarius*, which is the largest *Agaricales* genus, with thousands of species worldwide. The species are important ectomycorrhizal fungi and form associations with many vascular plant genera from tropicals to arctic regions. Genus *Cortinarius* contains a lot of morphological variation, and its complexity has led many taxonomists to specialize in particular on infrageneric groups. The previous attempts to divide *Cortinarius* have been shown to be unnatural and the phylogenetic studies done to date have not been able to resolve the higher-level classification of the group above section level. Genomic approaches have revolutionized our view on fungal relationships and provide a way to tackle difficult groups. We used both targeted capture sequencing and shallow whole genome sequencing to produce data and to perform phylogenomic analyses of 75 single-copy genes from 19 species. In addition, a wider 5-locus analysis of 245 species, from the Northern and Southern Hemispheres, was also done. Based on our results, a classification of the family *Cortinariaceae* into ten genera—*Cortinarius, Phlegmacium, Thaxterogaster, Calonarius, Aureonarius, Cystinarius, Volvanarius, Hygronarius, Mystinarius,* and *Austrocortinarius*—is proposed. Seven genera, 10 subgenera, and four sections are described as new to science and five subgenera are introduced as new combinations in a new rank. In addition, 41 section names and 514 species names are combined in new genera and four lecto- and epitypes designated. The position of *tephanopus* in suborder *Agaricineae* remains to be studied. Targeted capture sequencing is used for the first time in fungal taxonomy in Basidiomycetes. It provides a cost-efficient way to produce -omics data in species-rich groups. The -omics data was produced from fungarium specimens up to 21 years old, demonstrating the value of museum specimens in the study of the fungal tree of life. This study is the first family revision in Agaricales based on genomics data and hopefully many others will soon follow.

Keywords: Agaricales, Fungariomics, Fungi, HybPiper, Museomics, Targeted capture sequencing, Whole genome sequencing

Fungal Diversity 112, pages89–170 (2022) DOI: 10.1007/s13225-022-00499-9

Roles of mushroom polysaccharides in chronic disease management

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Abstract: Chronic diseases have drawn much attention as the primary cause of death and disability. In exploring novel side-effect-free agents against chronic diseases, significant efforts have been devoted to mushroom polysaccharides due to their diverse biological activities. This work reviewed the structural features, biological performances and molecular mechanisms of mushroom polysaccharides in managing cancers, diabetes mellitus and cardiovascular diseases. The potentials of mushroom polysaccharides against chronic diseases highly depend on their structural features, including monosaccharide composition, molecular weight, the type and configuration of glycosidic bonds, degree of branching, the type of substituent pattern and chain conformation. Regarding their working mechanisms, shared and disease specific pathways were found. The three chronic diseases shared the regulation of specific signalling pathways and the adjustment of gut microbiota. In addition, the roles of transcription factors, receptors, enzymes, hormones and other functional proteins involved in the molecular mechanisms of mushroom polysaccharides against chronic diseases are first elaborated herein. The present review describes the state of the art of mushroom polysaccharides in treating chronic diseases and addresses the perspectives, and will further promote research on this topic.

Keywords: mushroom polysaccharide, chronic diseases, structural feature, biological performance, molecular mechanism

Journal of Integrative Agriculture 2022, 21(7): 1839–1866 DOI: 10.1016/S2095-3119(21)63871-6

Potential benefits and harms: a review of poisonous mushrooms in the world

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Abstract: Mushrooms have long been considered as delicacies as well as used as important dietary supplements and food. However, there are major concerns with poisonous mushrooms as these pose threats to public health and safety. In this paper, we provide a review focusing on poisonous mushrooms, their toxins, symptoms and utilizations. In addition, this paper establishes a poisonous mushroom list which includes 643 species from two phyla, 16 orders, 51 families and 148 genera. The toxicity of all these species was verified and 332 species were ranked as P1 signifying that these species have toxic studies and or clinical poisoning case records and 311 species were P2 meaning they had previously been recorded as poisonous in other studies. Furthermore, we discuss advances in technology including how genomic studies could be used as a breakthrough tool in the field of toxic mushrooms. With this comprehensive review, we aim to promote public awareness of poisonous mushrooms, including how to avoid mushroom poisoning, and how to better utilize poisonous mushroom resources.

Keywords: Macrofungi, wild mushrooms, oral poisoning, toadstool

Fungal Biology Reviews, 2022, DOI: 10.1016/j.fbr.2022.06.002

Beneficial interactions between bacteria and edible mushrooms

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Abstract: Mushroom-forming fungi establish mutual beneficial interactions with plants and degrade organic waste. These fungi also play an important role in human societies to produce mycelium materials, as a source of medicinal compounds, and as food. Bacteria interact with mushroom-forming fungi not only as competitors for nutrients and as pathogens but also to establish beneficial interactions. This review discusses the positive interactions of bacteria during the different stages of the life cycle of the white button mushroom *Agaricus bisporus* and other highly consumed mushroom-forming fungi. Bacteria are key in forming a selective substrate, in providing nutrients, in stimulating growth and mushroom formation, and in protection against pathogens. Implications for the mushroom industry are being discussed.

Keywords: Mushrooms, Agaricus, Pleurotus, Symbiosis, Growth-promoting bacteria, Mushroom induction, Disease suppression, Pseudomonas

Fungal Biology Reviews Volume 39, March 2022, Pages 60-72 DOI: 10.1016/j.fbr.2021.12.001

Research Trends in the Study of Edible Mushrooms: Nutritional Properties and Health Benefits

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[4]*Department of Biosystems and Agricultural Engineering, Michigan State University, East Lansing, Michigan, USA.*

Abstract: The consumption of edible-culinary mushrooms for the prevention and treatment of chronic disease has gained increasing attention. This review summarizes trends in the biotechnological and medicinal potential of edible mushrooms cultivated worldwide. Macronutrients (fatty acids, amino acids, and carbohydrates), bioactive compounds (phenolics, flavonoids, and carotenoids), and health benefits (antioxidant, antimicrobial, antifungal, anticancer, and pre-biotics properties) of mushrooms are described, including their cultivation, industrial processing, and consumption. In general, edible-culinary mushrooms present a rich nutritional composition with beneficial properties for human health. Indeed, the consumption of edible mushrooms is associated with a reduction in the risk of cancer and diabetes. Furthermore, mushrooms can be incorporated into different food formulations and used as a medicinal substance due to their mycochemicals with antioxidant capacity. Edible mushrooms are considered a "superfood" and can be recommended as a valuable constituent in the daily diet. In conclusion, this review describes trends, future decision-making, and guidance on the health benefits of edible mushrooms.

Keywords: edible and medicinal mushrooms, bioactive compounds, nutritional composition, biological activity

Volume 24, Issue 5, 2022, pp. 1-18, DOI: 10.1615/IntJMedMushrooms.2022043738

Valorization of mushroom by-products: a review

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[4] *School of Agriculture and Food, The University of Melbourne, Parkville, Australia*

Abstract: With the rapid growth of the global economy and the global population, the production of solid waste has increased remarkably. Mushrooms are gaining popularity among researchers for their ability to turn waste into nutrients. However, a large number of by-products are produced during the industrial processing of mushrooms. Traditional waste management, focusing on the utilization and disposal of mushroom by-products, has attracted the attention of researchers. Meanwhile, the circular economy has become a multidisciplinary research field, and the valorization of mushroom by-products is a very important part of circular economy research. Various mushroom by-products of mushroom are reviewed in this paper. By-products are used in food as raw materials or functional components, in livestock and poultry feed after grinding/fermentation, and as electrochemical materials and papermaking materials. The by-products can also be used to produce ethanol and other biological sources of energy, as absorbing substances in sewage treatment, and as fertilizer in soil amendment. Mushroom processing by-products can be applied in various fields. To improve production efficiency, new extraction technology (including supercritical fluid technology and microwave extraction technology) can be adopted to increase the bioactive substance content in the by-products.

Choosing appropriate processing temperature, time, and other processing conditions can also enhance product quality. Finally, more research is needed on the cost-effective utilization of the by-products and the feasibility of industrialization.

Keywords: mushroom by-products; innovative technologies; extraction; application; circular economy

J Sci Food Agric 2022 Apr 22. DOI: 10.1002/jsfa.11946

Magic mushroom extracts in lipid membranes

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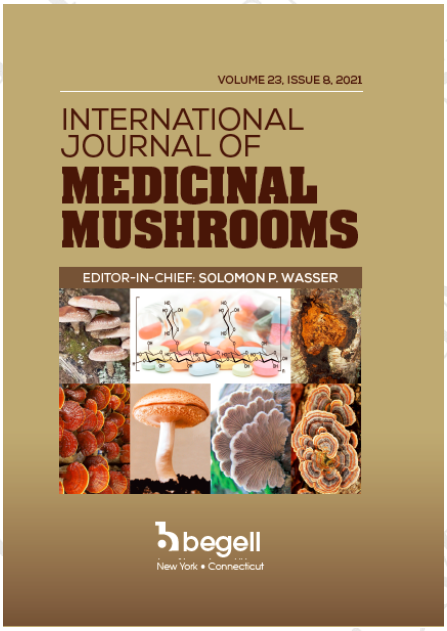
Abstract: The active hallucinogen of magic mushrooms, psilocin, is being repurposed to treat nicotine addiction and treatment-resistant depression. Psilocin belongs to the tryptamine class of psychedelic compounds which include the hormone serotonin. It is believed that psilocin exerts its effect by binding to the serotonin 5-HT2A receptor. However, recent in-vivo evidence suggests that psilocin may employ a different mechanism to exert its effects. Membrane-mediated receptor desensitization of neurotransmitter receptors is one such mechanism. We compare the impact of the neutral and charged versions of psilocin and serotonin on the properties of zwitterionic and anionic lipid membranes using molecular dynamics simulations and calorimetry. Both compounds partition to the lipid interface and induce membrane thinning. The tertiary amine in psilocin, as opposed to the primary amine in serotonin, limits psilocin's impact on the membrane although more psilocin partitions into the membrane than serotonin. Calorimetry corroborates that both compounds induce a classical melting point depression like anesthetics do. Our results also lend support to a membrane-mediated receptor-binding mechanism for both psilocin and serotonin and provide physical insights into subtle chemical changes that can alter the membrane-binding of psychedelic compounds.

Keywords: Psilocin, Magic mushrooms, Serotonin, Psychedelic drugs, Molecular dynamics (MD) simulations, Lipid-drug interactions

Biochimica et Biophysica Acta (BBA) – Biomembranes Volume 1864, Issue 9, 1 September 2022, 183957 DOI: 10.1016/j.bbamem.2022.183957

International Journal of Medicinal Mushrooms Call for Papers

About *International Journal of Medicinal Mushrooms*



International Journal of Medicinal Mushrooms is a journal covering the technologies/fields/categories related to Applied Microbiology and Biotechnology (Q3); Drug Discovery (Q3); Pharmacology (Q3). It is published by Begell House Inc.. The overall rank of *International Journal of Medicinal Mushrooms* is 10594. According to SCImago Journal Rank (SJR), this journal is ranked 0.471. SCImago Journal Rank is an indicator, which measures the scientific influence of journals. It considers the number of citations received by a journal and the importance of the journals from where these citations come. SJR acts as an alternative to the Journal Impact Factor (or an average number of citations received in last 2 years). This journal has an h-index of 30. The best quartile for this journal is Q3.

The ISSN of *International Journal of Medicinal Mushrooms* journal is 15219437. An International Standard Serial Number (ISSN) is a unique code of 8 digits. It is used for the recognition of journals, newspapers, periodicals, and magazines in all kind of forms, be it print-media or electronic. *International Journal of Medicinal Mushrooms* is cited by a total of 618 articles during the last 3 years (Preceding 2020).

International Journal of Medicinal Mushrooms Impact Score 2020-2021

The impact score (IS) 2020 of *International Journal of Medicinal Mushrooms* is 1.92, which is computed in 2021 as per its definition. *International Journal of Medicinal Mushrooms* IS is increased by a factor of 0.05 and approximate percentage change is 2.65% when compared to preceding year 2019, which shows a **rising** trend. The impact score (IS), also denoted as Journal impact score (JIS), of an academic journal is a measure of the yearly average number of citations to recent articles published in that journal. It is based on Scopus data.

Aims and Scope

The rapid growth of interest in medicinal mushrooms research is matched by the large number of disparate groups that currently publish in a wide range of publications. The *International Journal of Medicinal Mushrooms* is the one source of information that will draw together all aspects of this exciting and expanding field - a source that will keep you up to date with the latest issues and practice. The *International Journal of Medicinal Mushrooms* publishes original research articles and critical reviews on a broad range of subjects pertaining to medicinal mushrooms, including systematics, nomenclature, taxonomy, morphology, medicinal value, biotechnology, and much more. Papers on new techniques that might promote experimental progress in the aforementioned field are also welcomed. In addition to full-length reports of original research, the journal publishes short communications and interesting case reports, together with literature reviews. Letters to the editor on topics of interest to readers are also published.

For More Information and Submittion

https://www.begellhouse.com/journals/medicinal-mushrooms.html

International Journal of
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2022, Vol. 24, Issue no.8

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2022, Vol. 24, Issue no.10

International Journal of
Medicinal Mushrooms

2022, Vol. 24, Issue no.11

Points and Reviews

Short Review on Mushrooms and Their Utilization as Nutritional Supplements

Shuting (S.T.) Chang

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Mushrooms are fruiting bodies of macrofungi, which with other fungi are something special in the living world, being neither plants nor animals. They have been placed in a kingdom of their own called the kingdom of Myceteae. Mushrooms are without buds, without leaves, and without flowers. Yet they produce fruiting bodies [1]. They are without chlorophyll and also devoid of vascular, xylem and phloem. Although they cannot carry out photosynthesis, they can biosynthesize innumerable vital organic products. But their cell wall contain chitin rather than cellulose. A more recent report on mushroom fossilized indicated that a 440 million year-old fossilized mushroom may be the oldest organism to have lived in dry land [2].

NUTRITIONAL AND MEDICINAL VALUE OF MUSHROOMS

The greatest difficulty in feeding man is to supply a sufficient quantity of the body-building material – protein. The protein content of cultivated species ranges from 1.75 to 5.9% of their fresh weight – high compared to other common foods. The other three nutritional categories are: the source of energy food—carbohydrates and fats; accessory food factors – vitamins; and inorganic compounds which are indispensable to good health. Of course, water too, is essential.

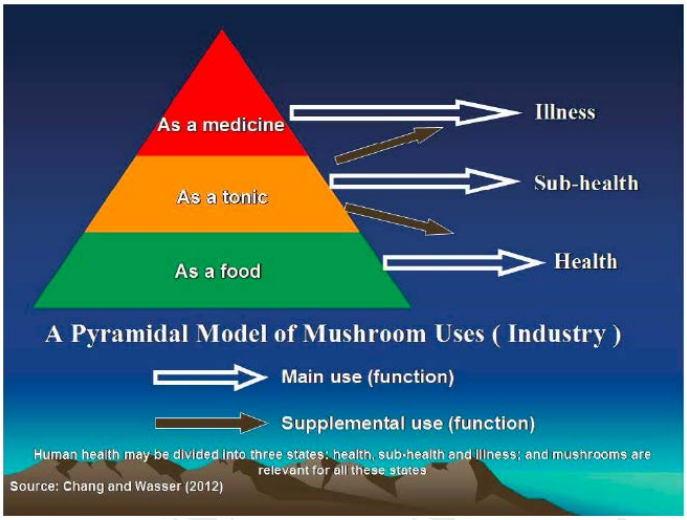

Figure 1: A pyramid model of mushroom uses (Industry). (Chang and Wasser, 2012; Chang and Buswell, 2022).

The second major attribute of mushrooms, their medicinal properties, has been drawn to a great attention during the last thirty years [3]. Of the 14,000—15,000 species of so-called mushrooms in the world, around 1,800 species of mushrooms have potential medicinal properties. Both these mushrooms and their root-like structure (called mycelium) produce several medicinal or nutracetical/ nutriceutical (general immune enhancing) compounds, central of which are the polysaccharides (high molecular weight strings of sugars), triterpenes and immunomodulatory proteins.

MUSHROOM BIOLOGY: THE IMPACT ON MUSHROOM PRODUCTION AND MUSHROOM PRODUCTS.

Principles of Mushroom Cultivation and production.

The cultivation of mushrooms ranges from a relatively primitive farming activity to a highly technological industry. In each case, however, continuous production of successful crops requires both practical experience and scientific knowledge. Mushroom cultivation is both a science and an art. The science is developed through research; and the art is perfected through curiosity and practical experience [2].

The Pyramid Model of the Mushroom Industry.

It has been noted that a nutritious balance of foods and an active lifestyle under a friendly environment can help achieve optimal health throughout life. The pyramidal model of mushroom uses (Figure 1) conforms fully to an old Chinese saying 'Medicine and food have a common origin". This statement is particularly applicable to mushrooms, whose nutritional qualities and tonic effects as nutriceuticals [4] or as dietary supplements (DSs) and medicinal attributes have long been recognized [5,8]. Human health may be divided into three states: health, sub-health, and illness. Mushrooms can used mainly as food for a healthy state, as a medicine for illnesses and as DSs for a sub-healthy state, as well as for both healthy and ill states as indicated [6,7].

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Open-Label Study of the Influence of Food Containing the Royal Sun Mushroom, *Agaricus brasiliensis* KA21 (Agaricomycetes), on β-Glucan-Specific Antibody Production in Healthy Human Volunteers

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ABSTRACT: The edible mushroom *Agaricus brasiliensis* contains a large amount β-glucan, which is mainly composed of a β-1,6-glucan structure. In this study, we investigated the effect of *A. brasiliensis* strain KA21 on the anti-β-glucan antibody titer in healthy humans and the role of antibodies as an immunomodulator. Twenty-two healthy volunteers were fed the dried fruiting body of *A. brasiliensis* (900 or 1500 mg/day) for 12 weeks. The anti-β-glucan antibody titer in the serum was determined by enzyme-linked immunosorbent assay. Immunoglobulin G (IgG) against β-glucan was significantly upregulated after intake of *A. brasiliensis*. Murine experiments demonstrated improvement of anti-β-glucan antibody production after intraperitoneal injection of *Agaricus*-derived β-glucan. To understand the role of antibody against β-glucan in exclusion of pathogenic fungi, we examined the interaction between HL-60 cells and antibody-treated heat-killed *Candida albicans*. Flow cytometry analysis indicated the upregulation of *Candida*-positive HL-60 cells after treatment with human IgG, whereas the competitive assay demonstrated that the main epitope of *Candida*-reacted IgG was the β-1,6-glucan structure. Binding between HL-60 and IgG-opsonized *C. albicans* was suppressed by anti-Fcγ receptor 1 (FcγRI) neutralizing antibody. Finally, using FcγRI-expressed cells with the nuclear factor of activated T-cell reporter assay, we demonstrated that higher titers of anti-β-glucan IgG can induce stronger Fc receptor-mediated cell activation through the formation of an antibody-β-glucan complex. In conclusion, oral ingestion of *A. brasiliensis* KA21 promotes anti-β-glucan antibody production and may contribute to preventing fungal infection through the activation of immune cells by forming antibody-β-glucan complexes via an FcγR-dependent pathway.

KEY WORDS: *Agaricus brasiliensis*, anti-β-glucan antibody, Fcγ receptor, β-glucan, medicinal mushrooms

ABBREVIATIONS: AgCAS, *Agaricus brasiliensis* cold alkaline-soluble fraction; **AgHWE**, *A. brasiliensis* hot water extract; **APC**, allophycocyanin; **ASBG**, *Aspergillus* soluble β-glucan; **BPBST**, 1% BSA-PBST; **BSA**, bovine serum albumin; **CSBG**, *Candida* soluble β-glucan; **DMEM**, Dulbecco's modified Eagle's medium; **DMSO**, dimethyl sulfoxide; **EF**, elongation factor; **EGFP**, enhanced green fluorescent protein; **ELISA**, enzyme-linked immunosorbent assay; **FBS**, fetal bovine serum; **FcR**, Fc receptor; **FITC**, fluorescein isothiocyanate; **GAPDH**, glyceraldehyde 3-phosphate dehydrogenase; **HKCA**, heat-killed *Candida albicans*; **HRP**, horseradish peroxidase; **Ig**, immunoglobulin; **IRES**, internal ribosome entry site; **mAb**, monoclonal antibody; **MCS**, multi- ple cloning site; **NFAT**, nuclear factor of activated T cells; **NHS**, *N*-hydroxysuccinimide; **PBS**, phosphate-buffered saline; **PBST**, PBS containing 0.05% Tween 20; **PE**, phycoerythrin; **PMA**, phorbol 12-myristate 13-acetate; **RTX**, rituximab; **sIgA**, secretory immunoglobulin A; **TMB**, 3,3′,5,5′-tetramethylbenzidine

I. INTRODUCTION

β-glucan is one of the main antigens produced by fungi. In the case of β-1,3-glucan, dectin-1 plays an important role in mammalian immune systems.[1] On the other hand, several pathogenic fungi, such as *Can- dida albicans*, produce not only β-1,3-glucan but also β-1,6-glucan.[2] Although several reports suggest the immunoenhancing effects of β-1,6-glucan,[3,4] the overall biological roles of the 1,6-β-glycosidic chain in immune systems are yet to be clarified. Previous studies demonstrated that a large number of anti-β-glucan antibodies exist in human and animal sera,[5–7] whereas the titer of anti-β-1,6-glucan antibodies is higher than that of anti-β-1,3-glucan antibodies in the majority of healthy humans.[8] However, there are individual differences in the titer of anti-β-glucan antibody in human serum,[8] which may be caused by genetic factors, lifestyle, occupation, eating habits, and living conditions. Furthermore, other reports have suggested that antibodies against β-glucan help to exclude infected pathogenic fungi.[9–13] Therefore, the intentional control of anti-β-glucan antibody production may be crucial for the prevention of opportunistic fungal infections.

Consumption of a nutritious diet composed of functional foods and dietary supplements easily contributes to improved health conditions and is becoming an increasingly important aspect in the field of preventive medicine. To date, we have investigated the pharmaceutical actions of royal sun mushroom, *Agaricus brasiliensis* S. Wasser et al. (*A. blazei* Murrill sensu Heinem., Agaricaceae, Agaricomycetes) strain KA21, which contains a large amount of β-glucan.[14,15] In a previous study, oral ingestion of *A. brasiliensis* KA21 was found to induce protective effects against acute hepatic injury in mice.[16] Interestingly, antioxidant and hepatoprotective activities of *A. brasiliensis* KA21 are stronger when the mushroom is grown in open air compared to indoors. In fact, a previous study found that outdoor cultivation significantly upregulated β-glucan content in *A. brasiliensis* KA21.[17] Based on these findings, we chose to focus our research on out- door-cultivated *A. brasiliensis* KA21. Analysis of this strain revealed that the structure of *Agaricus*-derived β-glucan is mainly composed of β-1,6-glucan with minor β-1,3-glucan content, which strongly activates innate immune cells via a pathway dependent on the C-type lectin receptor, dectin-1.[18] Moreover, a clinical study demonstrated that oral intake of fruiting bodies of *A. brasiliensis* KA21 significantly promoted activa- tion of natural killer cells.[15] These innate immune response-enhancing activities make *A. brasiliensis* useful for the prevention of infectious diseases.

In addition to its properties as a modulator of the innate immune response, *Agaricus*-derived β-glucan is also the epitope of anti-β-glucan antibody.[19] For this reason, *A. brasiliensis* may induce an increase in anti-β-glucan antibodies via activation of antigen-presenting cells. Therefore, in this study, we aimed to evalu- ate the effect of ingestion of *A. brasiliensis* on anti-β-glucan titer in healthy donors by investigating the role of daily diet in the regulation of adaptive immunology. Our results demonstrate that the β-glucan-specific antibody titer was upregulated as a result of daily intake of *A. brasiliensis*. Moreover, the immunoglobulin G (IgG)- β-glucan complex was found to strongly activate phagocytes via an Fcy receptor-dependent path- way. These findings indicate the potential of *A. brasiliensis* for use as a daily supplement to enhance levels of β-glucan-specific antibody.

II. MATERIALS AND METHODS

A. Clinical Study Design

The clinical portion of this study is part of another previous report that evaluated the effect of *A. brasil- iensis*

supplementation on the quality of life of a healthy human volunteer.[20] The open-label clinical study design (clinical study no. 22700) was reviewed by the study board of Nihonbashi Cardiology Clinic (Tokyo, Japan). All clinical tests were performed at Nihonbashi Cardiology Clinic upon approval (May 24, 2011). Assistance with subject selection and management, the verification of various test values, and the tabulation and statistical analysis of various test values were performed by Total Technological Consultants, Co. Ltd. (Tokyo, Japan). Test foods in the form of tablets made from 100% powder of outdoor-cultivated fruiting bodies of *A. brasiliensis* strain KA21 were provided by Terra Forte Co. Ltd. (Tokyo, Japan). Informed con- sent was obtained from all participants. Twenty-four healthy adult volunteers (12 men and 12 women) were administered tablets of 100% dried fruiting body of *A. brasiliensis* KA21 (low-dose group: 900 mg/day; high-dose group: 1500 mg/day) for 12 weeks. Twenty-two specimens of serum and saliva were collected at each point (before administration, after 6 weeks, and after 12 weeks; study period from May to November 2011) for use in an anti-β-glucan-specific enzyme-linked immunosorbent assay (ELISA). One volunteer in the high-dose group and another in the low-dose group did not complete the test. A summary of the protocol used for the clinical study is provided in Fig. 1. All clinical experiments were performed in accordance with the Declaration of Helsinki.

B. Animals and Materials

Male C57BL/6J mice were purchased from Japan SLC (Shizuoka, Japan). The mice were housed in a specific pathogen-free environment and used at 6-9 weeks of age. All animal experiments were performed in accordance with the guidelines[6] for laboratory animal experiments provided by the Tokyo University of Pharmacy and Life Sciences. Experimental protocols were approved by the Committee for Laboratory Ani- mal Experiments at Tokyo University of Pharmacy and Life Sciences (P17–48). Fruiting bodies of *A. brasil- iensis* KA21 cultivated outdoors were provided by Toei Shinyaku Co. Ltd. (Tokyo, Japan). Pustulan (soluble β-1,6-glucan polymer) from *Umbilicaria papullosa* (*Lasallia pustulata*) was purchased from Calbiochem (San Diego, CA). The 1,6-β-monoglucosyl branched β-1,3-glucan, laminarin from *Laminaria digitate*,[21] mannan (-1,6-/ -1,2, -1,3-mannan) from *Saccharomyces cerevisiae*,[22] bovine serum albumin (BSA), hexadimethrine bromide (polybrene), phorbol 12-myristate 13-acetate (PMA), and ionomycin calcium salt were purchased from Sigma (St. Louis, MO). Casein sodium, hygromycin B, 2-mercaptoethanol, and Im- munoStar peroxidase substrate were purchased from Wako Pure Chemical Industries, Ltd. (Osaka, Japan). We purchased blasticidin S hydrochloride from Kaken Pharmaceutical Co. Ltd. (Tokyo, Japan), rituximab (RTX; anti-human CD20 monoclonal antibody [mAb]) from Chugai Pharmaceutical Co. Ltd. (Tokyo, Japan), and the peroxidase substrate 3,3′,5,5′-tetramethylbenzidine (TMB) from KPL (Gaithersburg, MD). *C. albicans* NBRC 1385 and *Aspergillus niger* NBRC 6342 were obtained from NITE Biological Resource Center (Chiba, Japan). Recombinant human CD64 (extracellular domain; Met 1-Pro 288) polyhistidine (His) tag fusion protein was purchased from Sino Biological (Beijing, China). We purchased Imject Alum adjuvant and *N*-hydroxysuccinimide (NHS)-rhodamine from Thermo Fisher Scientific (Waltham, MA). We purchased TruStain FcX (Fc block), allophycocyanin (APC)-conjugated anti-human CD16 (B73.1), unlabeled and phycoerythrin (PE)-conjugated anti-human CD32 (FUN-2), unlabeled and fluorescein iso- thiocyanate (FITC)- or PE-conjugated anti-human CD64 (10.1), unlabeled and APC-, PE-, or FITC-conju- gated mouse IgG1 (MOPC-21), unlabeled and PE-conjugated mouse IgG2b (MPC-11), FITC-conjugated anti-human-IgG-Fc (HP6017), and horseradish peroxidase (HRP)-conjugated anti-His-tag mAb (J099B12) from BioLegend (San Diego, CA). PE-conjugated anti-human Dectin-1 (GE-2) was purchased from Gene- Tex (Irvine, CA). Nonfat dry milk and glyceraldehyde 3-phosphate dehydrogenase (GAPDH;

14C10) rabbit mAb (HRP conjugate) were purchased from Cell Signaling Technology (Danvers, MA).

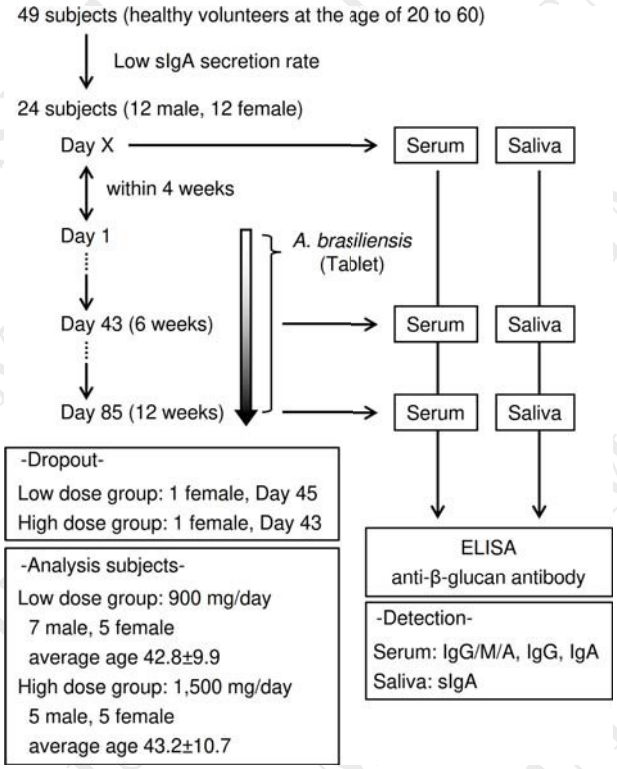

FIG. 1: Study protocol for *Agaricus brasiliensis* ingestion and ELISA to determine β-glucan antibody titer

C. Preparation of Polysaccharide Fractions

Polysaccharide fractions of the fruiting body of *A. brasiliensis* were prepared by repeated extraction with deionized water and cold sodium hydroxide.[18] Briefly, air-dried and powdered *A. brasiliensis* (25 g) was extracted with hot water (500 mL, 121°C for 2 h). The polysaccharide fraction was prepared from the extract by precipitation with 4 volumes of ethanol, followed by drying using acetone treatment (referred to hereafter as AgHWE). The residue was further extracted twice with hot water, as described above. The resulting residue was then extracted with cold alkali. The clear sodium hydroxide extracts became milky after neutralization to pH 7.0 with acetic acid and were then dialyzed against tap water and distilled water. The resulting solution was centrifuged before ethanol precipitation to obtain the water-soluble fraction (referred to hereafter as AgCAS). Purified solubilized β-glucan from the cell wall, *Candida* soluble β-glucan (CSBG) from *C. albicans* NBRC 1385, and *Aspergillus* soluble β-glucan (ASBG) from *A. niger* NBRC 6342 were prepared according to previous reports.[23,24] Low endotoxin levels of purified glucan fractions were confirmed. The glucans used in this study are listed in Table 1.

D. Determination of Anti-β-Glucan Antibody

A 96-well plate (Greiner Bio-One, Frickenhausen, Germany) was coated with CSBG, ASBG, or AgHWE (25 μg/mL) in 0.1 M of sodium carbonate buffer (pH 9.5) and incubated overnight at 4°C. The plate was washed with phosphate-buffered saline (PBS) containing 0.05% Tween-20 (PBST) and blocked with 1% BSA-PBST (BPBST) at room temperature for 1 h. After washing, the plate was incubated overnight at 4°C with the appropriately diluted specimen (2000 for IgG/M/A and IgG and 200 for IgA) and the standard IgG from human serum (for IgG/M/A and IgG) or human serum (for IgA) for titer calculation. The plate was then washed with PBST and treated with peroxidase-conjugated anti-human total IgG/M/A-, IgG-, or IgA (□ chain)-specific antibody (Sigma) in BPBST. To evaluate salivary secretory immunoglobulin A (sIgA), 0.5%

casein-PBST was used as a blocking buffer and absorbance was measured using 20-fold diluted samples in the same plate. For the murine experiments, 100-fold diluted serum and peroxidase-conjugated anti-mouse IgG- or IgM-specific antibody (Sigma) were used. Binding of anti-β-glucan antibody to solid-phase glucans was monitored using TMB substrate, and color development was stopped with 1 M of phosphoric acid. Optical density was measured at 450 nm using a microplate reader (MTP450; Corona Electric, Ibaraki, Japan).

TABLE 1: Polysaccharides used in this study

Sample	Structure	Source
CSBG	β-1,6-/β-1,3-glucan	*Candida albicans*
ASBG	β-1,6-/β-1,3-glucan	*Aspergillus niger*
AgHWE	β-1,6-glucan (with slight β-1,3-glucan)	*Agaricus brasiliensis*
AgCAS	β-1,3-/β-1,6-glucan	*A. brasiliensis*
Pustulan	β-1,6-glucan (with slight β-1,3-glucan)	*Lasallia pustulata*
Mannan	α-1,6-/α-1,2-, α-1,3-mannan	*Saccharomyces cerevisiae*
Laminarin	Mono-β-1,6-/β-1,3-glucan	*Laminaria digitata*

E. Antibody Production in a Murine Model

β-1,6-glucan, pustulan (100 μg), or *Agaricus*-derived AgCAS (100 μg) were mixed with Imject Alum adjuvant (25 μL) and administered intraperitoneally in C57BL/6J mice. The first dose was administered on day 0, followed by administration on days 7 and 19. On day 22, blood was collected from the heart and the serum was diluted for use in ELISA.

F. Cell Culture

Human promyelocytic leukemia cell line HL-60 (RCB0041), the Jurkat (RCB3052) human T-cell line, and human embryonic kidney 293T (RCB2202) cells were obtained from RIKEN BRC (Ibaraki, Japan). HL-60 and Jurkat cells were maintained in RPMI 1640 medium (Gibco/Life Technologies, Carlsbad, CA) supple- mented with 50 μg/mL of gentamicin sulfate (Sigma) and 10% heat-inactivated fetal bovine serum (FBS; Equitech-Bio, Kerrville, TX). The 293T cells were maintained in Dulbecco's modified Eagle's medium (DMEM; Gibco) containing 10% FBS and 50 μg/mL of gentamicin. All cell cultures were maintained at 37°C in a humidified atmosphere of 5% CO and 95% air.

G. Preparation of HL-60 for Cell Culture

HL-60 cells were seeded at 1×10^6 cells per 5 mL of culture medium containing 20% FBS supplemented with 0.7% dimethyl sulfoxide (DMSO; Sigma) for 4 days at 37°C to induce mild differentiation into the neutrophil-like phenotype.[25] To analyze the related receptors on DMSO-treated HL-60 cells, the cellswere pretreated with TruStain FcX Fc receptor (FcR) blocking solution in FACS staining buffer. This pretreatment was followed by the addition of antibodies, including 1) APC-anti-human CD16 or APC-mouse IgG1, 2) PE-anti-human CD32 or PE-mouse IgG2b, 3) FITC-anti-human CD64 or FITC-mouse IgG1, or 4) PE-anti-human Dectin-1 or PE-mouse IgG1. After incubation at 4°C for 20 min, the cells were washed twice in staining buffer and fixed in formalin solution. Flow cytometry was performed using a FACSCanto flow cytometer (BD Biosciences, San Jose, CA), and data were analyzed by FACSDiva (BD Biosciences) and FlowJo (Tree Star Inc., Ashland, OR) software.

H. Preparation of Heat-Killed *C. albicans*

C. albicans strain NBRC 1385 was seeded in sterile yeast extract, peptone, and dextrose liquid medium (200 mL) in a Sakaguchi flask, shaken, and cultured at 27°C for 48 h. Then, the yeast form of *C. albicans* was treated by autoclaving. After centrifugation, cells were washed twice with deionized water, followed by the addition of 250 mL of water to dead cells with stirring for 1 day at 4°C. The easily extracted components were removed by centrifugation. Then, cells were washed twice with ethanol and dried using acetone. Dried heat-killed *C. albicans* (HKCA; 30 mg) was washed three more times with 100 μM of bicarbonate buffer (pH 8.5) and dissolved in 200 μL of the same buffer supplemented with NHS-rhodamine. After incubation at 20°C for 1 h, rhodamine-conjugated HKCA was washed twice with PBS before it was dissolved in 200 μL of PBS (rhodamine-labeled HKCA).

I. Antibody Opsonization of HKCA

The rhodamine-labeled HKCA suspension (50 μL) was preincubated with BPBST (950 μL) at 37°C for 30 min and divided into 5 equal volumes in microtubes. PBS, IgG from human serum (lot 010M4840; Sigma), or IgG1 control antibody (RTX) was added to each tube at 600 μg/mL (high concentration) and 120 μg/mL (low concentration), followed by incubation at 4°C overnight. Opsonized rhodamine-labeled HKCA was washed three times with sterile PBS before suspension in 500 μL of sterile PBS. To analyze the epitope of HKCA-binding antibodies, 100 μg of mannan, laminarin, and pustulan were added to each tube before incubation with both antibodies (600 μg/mL). The binding level of the human antibodies was monitored as follows: opsonized rhodamine-labeled HKCA (10 μL) was dissolved in FACS staining buffer (40 μL) and stained with FITC-anti-human-IgG-Fc (4 μL) at 4°C for 30 min. After washing, the binding level of human IgG was analyzed using a FACSCanto flow cytometer, as described above.

J. Coculture Study of HL-60 and HKCA

HL-60 cells were washed and suspended in culture medium containing 2% FBS and seeded at 2×10^5 cells/ mL into a 96-well flat-bottomed plate (Sumitomo Bakelite Co. Ltd., Tokyo, Japan) with or without anti- body opsonized rhodamine-labeled HKCA (25 μL/well) at 37°C (250 μL/well, final). After 2 h, the cells were gently suspended and the proportion of rhodamine-labeled HKCA-positive HL-60 cells was analyzed using a FACSCanto flow cytometer, as described above. To neutralize the FcRs, anti-human CD32 (mouse IgG2b) or CD64 (mouse IgG1) antibody and isotype-matched controls were added (1 μg/mL, final).

K. Plasmid Construction

The nuclear factor of activated T cells (NFAT) reporter gene plasmid was designed with pGL4.30[*luc2P*/ NFAT-RE/Hygro] (Promega, Madison, WI) as the backbone where the luciferase reporter gene *luc2P* was replaced with enhanced green fluorescent protein (EGFP) using an In-Fusion HD cloning kit (Takara Bio, Shiga, Japan). The lentiviral backbone pWPI, packaging plasmid psPAX2, and enveloping plasmid pMD2.G were purchased from Addgene (Watertown, MA) (Addgene plasmids 12254, 12260, and 12259 were gifts from Didier Trono). The EGFP-coding region in pWPI was removed and the DNA coding a blasticidin resistance gene was inserted into pWPI instead of EGFP (pWPI-elongation factor EF1 - IRES-Blast^R). Human Fcγ receptor 1A (CD64) and the FcR γ-chain coding gene were amplified by PCR using PrimeSTAR Max DNA polymerase (Takara Bio) from template cDNA prepared from HL-60 cells with the following primer sets: pBud-CD64-F (5′-TCGTGAACACGTGGTACCATGTGGTTCTTG-3′) and pBud-

CD64-R (5′-GTGATGATGACCGGTCGTGGCCCCCTGGGG-3′), and pBud-FcR γ-chain-F (5′-TCACTATAGGGAGACAAGATGATTCCAGCA-3′) and pBud-FcR γ-chain-R (5′-GTGATGATGACCGGTCTGTGGTGGTTTCTC-3′). The amplified DNA was inserted after the cytomegalovirus and EF1□ -promoter sequence of pBudCE4.1 (Thermo Fisher Scientific) with the multiple cloning site (MCS)-*myc* and MCS-V5 coding sequence removed to obtain the C-terminal His -tag-fused FcR sequence. DNA coding the sequences for CD64-His (with Kozak sequence, without stop codon) and FcR γ-chain-His (without start codon, with stop codon) was amplified by PCR from pBud vector using the following primer sets: pWPI-CD64-F (5′-CTAGCCTCGAGGTTTACCATGTGGTTCTTGAC-3′) and pWPI-CD64-P2A-R (5′-AGAGAAGTTCGTGGCATGGTGATGGTGATGATGACC-3′), and pWPI-P2A-FcR γ-chain-F (5′-GAAAACCCCGGTCCCATTCCAGCAGTGGTCT-3′) and pWPI-FcR γ-chain-R (5′-GAAAATAACCGGATCTCAATGGTGATGGTGATG-3′). The P2A self-cleaving peptide[26] sequence (ATNFSLLKQAGDVEENPG/P) coding oligo double-stranded DNA was synthesized, and two DNA fragments (CD64 and FcR γ-chain) were combined across P2A peptide and inserted between the sequences in the EF1□ -promoter and internal ribosome entry site (IRES) of pWPI-EF1□ - IRES-Blast^R to generate the lentivirus expression vector (pWPI-EF1□ -CD64-P2A-FcR γ-chain-IRES- Blast^R). All DNA sequences were confirmed using a BigDye Terminator version 3.1 cycle sequencing kit (Thermo Fisher Scientific) and an ABI3130xl DNA analyzer (Applied Biosystems, Foster City, CA).

L. Lentivirus Production

The 293T cells were plated onto 24-well plates (Sumitomo Bakelite Co. Ltd.) at a density of 1×10^5 cells in 500 μL per well. The next day, pWPI-EF1□ -CD64-P2A-FcR γ-chain-IRES-Blast^R (1 μg), psPAX2 (0.75 μg), and pMD2.G (0.5 μg) were mixed with 3 μg of polyethyleneimine (Polysciences, Warrington, PA) in DMEM and incubated for 30 min at room temperature. The cells were incubated for 5 h after transfection with a mixture of the plasmids. The medium was then replaced with DMEM containing 30% FBS. After 3 days, the culture supernatants were filtered and used for transduction.

M. Preparation of FcR-Expressing Jurkat Cells

We confirmed that the Syk gene in the Jurkat cells (RCB3052) was not mutated in the mRNA sequence, as discussed in a previous study.[27] Jurkat cells (5×10^5 cells/mL) were transfected with *Pvu*I-treated linearized reporter gene plasmid (5 μg) with 7.5 μL of Lipofectamine 3000 (Thermo Fisher Scientific) in 2 mL of culture medium. After selection by hygromycin treatment (1000 μg/mL), cells were stimulated by PMA/ionomycin and EGFP-positive cells were sorted (Cell Sorter SH800; Sony, Tokyo, Japan). The supernatant of 293T cells (50 μL) containing lentivirus-carrying FcRs was added to the NFAT-EGFP coding gene-transduced Jurkat cells (1.5×10^5 cells in 1 mL of RPMI 1640 medium with 30% FBS) in the presence of polybrene (4 μg/mL). Cells were selected by blasticidin (1 μg/mL) and the stable expression of CD64 and FcR γ-chain in blasticidin resistance cells (Jurkat-FcR) was confirmed using a Accuri C6 flow cytom- eter (BD Biosciences) and immunoblotting. Jurkat-FcR or parental Jurkat cells were treated with PE-anti-CD64 antibody or PE-mouse IgG1 isotype control and analyzed by flow cytometry. The same number of Jurkat-FcR and parental Jurkat cells were lysed using Laemmli sample buffer with 2-mercaptoethanol and boiled for 5 min. The proteins were separated by 11% polyacrylamide gel electrophoresis and transferred onto a nitrocellulose membrane (GE Healthcare, Bloomington, IL). After blocking with 0.05% Tween 20/ Tris-buffered saline containing 0.5% dry milk, the membranes were incubated with anti-His-tag mAb-HRP or anti-GAPDH mAb-HRP, detected using peroxidase substrate (ImmunoStar). The resulting images were scanned using a C-DiGit Blot Scanner (LI-COR Biotechnology, Lincoln, NE).

N. Reporter Gene Assay

A 96-well plate (Nunc MaxiSorp; Thermo Fisher Scientific) was coated with 50 µL of IgG1 control antibody (RTX, 0-500 ng/mL) or CSBG (10 µg/mL) in sodium carbonate buffer and incubated overnight at 4°C. The plate was washed with PBS and blocked with BPBST at room temperature. After washing with PBS, the CSBG-coated plate was further incubated with two-fold serial dilutions (×5–160) of human serum IgG (Sigma). For the experiment assaying FcR-mediated NFAT activation, Jurkat-FcR cells (2×10^5 cells/ mL) were seeded in RTX-coated plates or human IgG-treated CSBG-coated plates and cultured at 37°C for 20 h in culture medium containing ionomycin (1 µM, final). To assess the response of Jurkat-FcR cells to soluble antibodies, RTX (0-10 µg/mL) was added to Jurkat-FcR cells cultured in uncoated plates. For the competition assay, recombinant soluble CD64 protein (0-1 µg/mL) was added to the Jurkat-FcR cells cultured in RTX (1 µg/mL)-coated plates. After incubation, NFAT-dependent EGFP expression was deter- mined using flow cytometry (Accuri C6; BD Biosciences). All buffers and reagents were filter-sterilized before use in reporter gene assays.

O. Statistical Analysis

Significance of the differences between mean values was assessed using the one-sample *t* test in the clinical study and the Student's *t* test in the basic study.

III. RESULTS

A. Daily Intake of *A. brasiliensis* Promotes Anti-β-Glucan Antibody Production

In the clinical study, we evaluated the effect of oral intake of *A. brasiliensis* (900 or 1500 mg/day) on β-glucan-specific antibody titer in the serum of a low-dose group of 12 volunteers and a high-dose group of 10 volunteers. Various soluble β-glucans, including CSBG composed of β-1,3-/β-1,6-glucan from *C. albicans*, β-1,3-glucan with short β-1,6-glycosidic side branches, ASBG from *A. niger*, 1,6-glycosidic chain rich β-glucans, and AgHWE from *A. brasiliensis*, were used as glucan antigens in this experiment (Table 1). After 6 weeks of supplementation with *A. brasiliensis* fruiting bodies, the titer of total serum anti-CSBG-IgG/ IgM/IgA (both low- and high-dose groups) increased significantly, whereas specific IgG was increased after 12 weeks in the high-dose group (Table 2). In addition, anti-ASBG-IgG and total serum anti-AgHWE-IgG/ IgM/IgA were significantly upregulated from 6 weeks and at 12 weeks, respectively, in the high-dose group. On the other hand, significant changes in the titer of serum IgA specific for β-glucan were not observed in all types of glucan antigens.

The individual regulation (rate of variability) is shown in Fig. 2. The total anti-CSBG antibody in all subjects in the high-dose group (*n*=10 of 10) at 12 weeks was increased compared to before the experiment. The same upregulation was observed in the low-dose group, except for four subjects (*n* = 8 of 12). On the other hand, total antibodies against ASBG for approximately half of the subjects were increased (*n*=5 of 12 and 6 of 10 in the low- and high-dose groups, respectively), whereas AgHWE-specific total an- tibodies were mainly increased (*n*=10 of 12 and 10 of 10 in the low- and high-dose groups, respectively) by *A. brasiliensis* ingestion for 12 weeks. The IgG titer showed a similar tendency to the total anti-β-glucan antibodies, but IgA classes were not consistent with these results.

As for sIgA, we evaluated the effect of *A. brasiliensis* ingestion on mucosal immunity and found no effect on the salivary sIgA secretion rate (Table 3). In addition, although salivary anti-CSBG-sIgA was slightly decreased after 6

weeks of *A. brasiliensis* intake, ultimately no definitive changes were observed (Table 3). Taken together, continuous daily intake of *A. brasiliensis* fruiting bodies strongly improved production of anti-β-glucan antibodies in the blood.

B. *A. brasiliensis*-Derived Glucan Has the Ability to Induce Antibodies against *Candida* Cell-Wall β-Glucan

Next, we investigated whether *A. brasiliensis*-derived glucan could induce antibodies against *Candida* cellwall β-glucan in mice. *A. brasiliensis*-derived β-glucan (AgCAS), purified β-1,6-glucan (pustulan), or PBS (control) was administered intraperitoneally in mice, along with Alum adjuvant three times. Then, levels of anti-CSBG or anti-ASBG antibodies in the serum were measured by ELISA. The study design is shown in Fig. 3A. Administration of AgCAS significantly increased the amount of IgG and IgM against CSBG and IgM against ASBG compared to the control group (Fig. 3B and C). On the other hand, pustulan significantly increased IgG levels against CSBG but was not effective against ASBG (Fig. 3B and C). These results indicate that *A. brasiliensis*-derived β-glucan is fully capable of inducing antibodies against both *Candida* and *Aspergillus* cell walls.

TABLE 2: Anti-β-glucan antibody titer during the mushroom ingestion experiment

Subject	Group	Before	6 weeks	12 weeks
CSBG-IgG/M/A	Low dose	4083.30 ± 2213.00	4457.73 ± 2237.19*	4497.98 ± 2288.97*
	High dose	2654.77 ± 2164.75	2778.48 ± 2067.67*	2948.24 ± 2356.97**
CSBG-IgG	Low dose	4669.62 ± 2546.05	4967.08 ± 2428.40	4952.33 ± 2578.48
	High dose	2965.01 ± 2018.26	2998.41 ± 1720.61	3164.69 ± 2026.23**
CSBG-IgA	Low dose	61.32 ± 33.71	58.61 ± 31.46	61.73 ± 30.20
	High dose	42.17 ± 39.38	43.13 ± 41.61	56.93 ± 53.71
ASBG-IgG/M/A	Low dose	1701.41 ± 2029.02	1604.16 ± 1656.86	1669.50 ± 1880.78
	High dose	685.66 ± 234.39	699.64 ± 251.72	704.15 ± 238.56
ASBG-IgG	Low dose	2451.90 ± 3007.82	2294.86 ± 2209.04	2345.18 ± 2507.87
	High dose	1004.09 ± 366.57	1064.23 ± 384.63*	1062.08 ± 347.93*
ASBG-IgA	Low dose	57.88 ± 31.54	54.84 ± 26.89	53.07 ± 26.24
	High dose	79.63 ± 89.95	79.51 ± 92.99	87.64 ± 87.18
AgHWE-IgG/M/A	Low dose	2252.84 ± 1786.55	2314.68 ± 1577.32	2412.61 ± 1758.05
	High dose	1212.55 ± 898.35	1252.90 ± 751.65	1381.49 ± 962.45**
AgHWE-IgG	Low dose	2353.44 ± 1815.89	2397.98 ± 1482.60	2270.97 ± 1535.78
	High dose	1369.91 ± 994.00	1422.32 ± 979.22	1379.51 ± 912.57
AgHWE-IgA	Low dose	77.37 ± 54.00	78.73 ± 47.97	73.64 ± 48.19
	High dose	56.04 ± 73.88	54.12 ± 57.99	65.69 ± 74.03

Values represent the mean ± SD (n=12 for the low-dose group and 10 for the high-dose group). *P < 0.05 and **P < 0.01, one-sample t test compared to before intake.

C. Anti-β-Glucan Antibody Improves *Candida* Recognition via CD64 on HL-60 Cells

Both the human and murine studies demonstrated that *A. brasiliensis* has the potential to upregulate anti-β-glucan antibodies, particularly antibodies against *Candida*-β-glucan. As such, we carried out several basic experiments to evaluate the effects of anti-β-glucan antibody in the exclusion of *C. albicans* using human promyelocytic leukemia HL-60 cells. Rhodamine-labeled HKCA (yeast form) was treated with human serum IgG or RTX (IgG1 control) to analyze the binding of IgG by FACS. As a result, HKCA was opsonized by human serum IgG but not control IgG in a dose-dependent manner (Fig. 4A), and the competitive assay using representative soluble glucans demonstrated that the

main epitope of *Candida*-reactive antibodies was β-1,6-glucan, followed by β-1,3-glucan and α-mannan, respectively (Fig. 4B). Furthermore, the adhesion of HL-60 cells to rhodamine-labeled HKCA was drastically improved by pretreatment with serum IgG in a dose-dependent manner, whereas control IgG had no effect (Fig. 4C and D). In addition, pretreatment of soluble β-1,6-glucan (pustulan) during opsonization strongly inhibited *Candida* recognition by HL-60 cells (Fig. 4E).

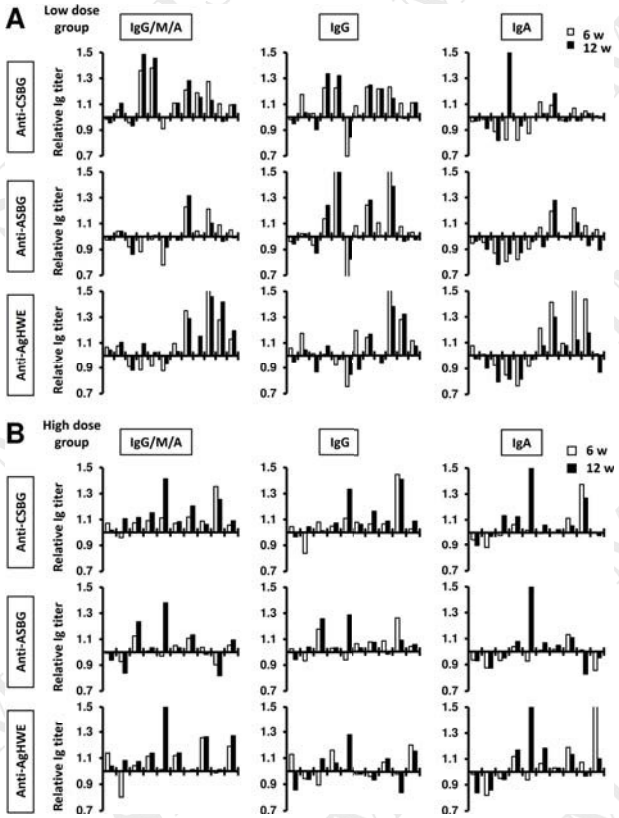

FIG. 2: Rate of variability of antibody titer in individual subjects. Changes in anti-CSBG, ASBG, or AgHWE anti- body titers before and after 6 or 12 weeks (6 or 12 w, respectively) of *Agaricus brasiliensis* intake. (A) The low-dose group ingested 900 mg of *A. brasiliensis*/day. (B) The high-dose group ingested 1500 mg of *A. brasiliensis*/day. Three different types of antibodies were used to detect total IgG/M/A, IgG, and IgA.

TABLE 3: β-glucan-specific secretory immunoglobulin A in saliva during mushroom ingestion

Subject	Group	Before	6 weeks	12 weeks
CSBG-sIgA	Low dose	1.42 ± 0.73	1.28 ± 0.74	1.18 ± 0.73
	High dose	1.36 ± 0.66	1.16 ± 0.53*	1.17 ± 0.49
ASBG-sIgA	Low dose	1.52 ± 0.83	1.40 ± 0.83	1.30 ± 0.86
	High dose	1.55 ± 0.92	1.35 ± 0.76	1.38 ± 0.67
AgHWE-sIgA	Low dose	1.09 ± 0.79	0.98 ± 0.84	0.93 ± 0.85
	High dose	0.97 ± 0.78	0.83 ± 0.62	0.86 ± 0.70

Values represent the mean ± SD (n=12 for the low-dose group and 10 for the high-dose group). *P < 0.05, one-sample t test compared to before intake.

Next, we examined the involvement of FcRs and dectin-1 on the surface of HL-60 cells in improving IgG-dependent *Candida* recognition. As shown in Fig. 5A, similar levels of CD32 and CD64 were expressed on HL-60, whereas no

expression of CD16 and dectin-1 was observed. In this case, although pretreatment of anti-CD32 antibody did not interfere with *Candida* adhesion (Fig. 5B), CD64-specific blockage significantly suppressed *Candida*-positive HL-60 cells (Fig. 5C). Taken together, these results indicate that upregulation of circulating anti-β-glucan IgG, especially IgG for β-1,6-glucan, promotes *Candida* recognition from the phagocytes via a CD64-dependent pathway.

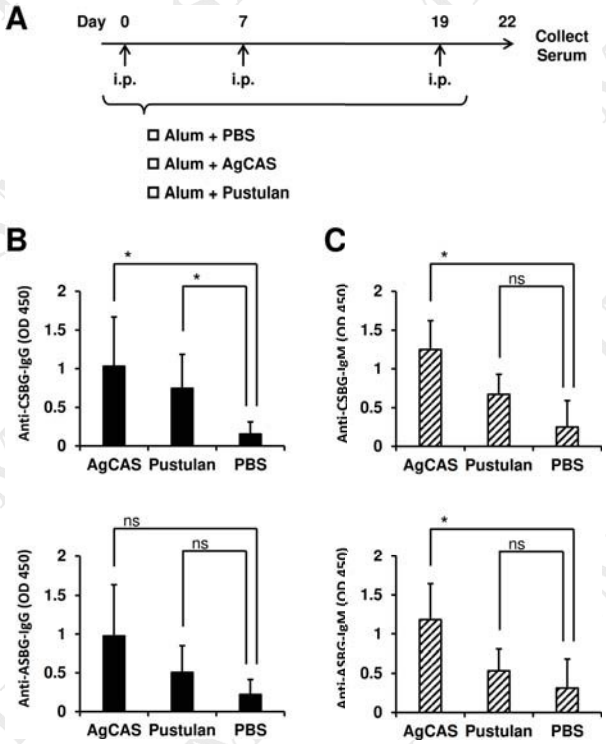

FIG. 3: *Agaricus*-β-glucan induced antibody cross-reaction with *Candida* cell-wall β-glucan. (A) Experimental protocol to evaluate the effect of *Agaricus*-β-glucan (AgCAS) on the induction of antibody production in mice. Pustulan (β-1,6-glucan) and PBS were also injected with Alum adjuvant for use as the control. On day 22, blood was collected and used for ELISA. (B and C) Measurement of anti-β-glucan antibody in murine serum. Serum was diluted 100-fold and IgG (B) and IgM (C) in response to CSBG or ASBG were analyzed by ELISA. Values represent the mean ± SD ($n = 4$). *$P < 0.05$, significant difference from PBS-injected group. ns, not significant.

D. Anti-β-Glucan Antibody Induces Signal Transduction in CD64-Expressing Cells by Forming a Complex with β-Glucan

To evaluate the effect of anti-β-glucan antibody on CD64-dependent cell activation, we established a CD64/ FcR y-chain stably coexpressing the Jurkat T-cell line with the transfected NFAT reporter-EGFP gene (Fig. 6A-C) and used this system (Jurkat-FcR-NFAT-EGFP) to assess antibody-induced NFAT activation. Cell activation was strongly induced by immobilized IgG (RTX) in the presence of calcium ion but not soluble IgG (Fig. 6D). NFAT activation was significantly inhibited by the treatment of recombinant soluble CD64-His protein (Fig. 6E), indicating antibody-CD64-dependent cell activation. Finally, we examined whether the antibody-β-glucan complex could activate CD64-expressing cells. The β-glucan-coated plate was blocked and treated with human serum IgG, followed by washing and the addition of Jurkat-FcR- NFAT-EGFP. As shown in Fig. 6F, surface β-glucan and IgG complex significantly induced NFAT-dependent EGFP expression on Jurkat cells in a dose-dependent manner. These results indicate that stronger cell activation is

induced via a CD64-dependent pathway, depending on the amount of antibodies forming a complex with fungal β-glucan.

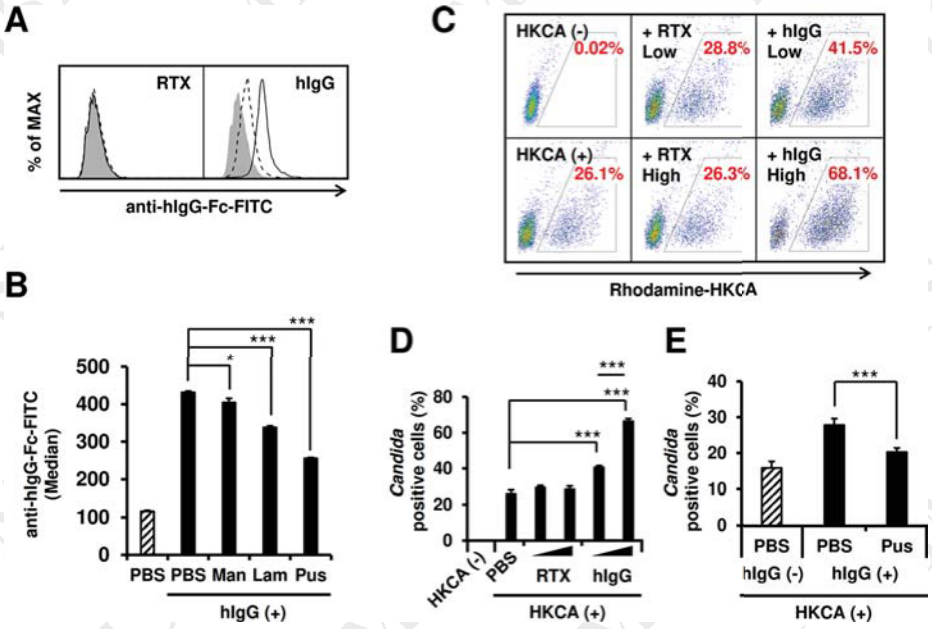

FIG. 4: Anti-β-1,6-glucan antibody promotes *Candida* recognition by HL-60. (A) Detection of *Candida* cell-wall binding IgG using flow cytometry. HKCA was treated with human serum IgG (hIgG) or RTX (IgG1 control) and stained with anti-IgG-Fc-FITC. The filled gray area represents PBS, the dashed line indicates low-dose IgG, and the solid line indicates high-dose IgG. (B) Analysis of glyco-epitopes of anti-*Candida* antibody by flow cytometry. HKCA was treated with hIgG in the presence or absence of β-1,6-glucan (pustulan; Pus), β-1,3-glucan (laminarin; Lam), or □ -1,6-/□ -1,2-/□ -1,3-mannan (yeast mannan; Man). Cell-wall binding IgG was detected by anti-IgG-Fc-FITC. Values represent the mean of median (FL-1) ± SD (n = 3). $^{*}P < 0.05$, $^{***}P < 0.001$. (C, D, and E) Effect of anti-β-1,6-glucan antibody on *Candida* recognition. HL-60 was coincubated with rhodamine-HKCA pretreated with PBS, RTX, and hIgG (C and D) or hIgG plus pustulan (E). After 2 h, the proportion (%) of rhodamine-positive HL-60 was analyzed by flow cytometry. Values represent the mean ± SD (n = 3). $^{***}P < 0.001$, significant differences from PBS-treated HKCA between the low-dose hIgG- and high-dose hIgG-treated HKCA (D) or between hIgG- and hIgG plus pustulan-treated HKCA (E).

IV. . DISCUSSION

In this study, we demonstrated that oral ingestion of *A. brasiliensis* promoted anti-β-glucan antibody production and the complex of antibodies and *Candida* cell-wall β-glucan could strongly activate immune cells via a CD64-dependent pathway.

Since *A. brasiliensis* is rich in β-1,6-glucan, it may be used as a vaccine to amplify anti-β-glucan anti- body levels in the body. Previous studies have shown that *A. brasiliensis*-derived polysaccharides activate innate immune cells through pattern-recognition receptors, such as dectin-1, as well as Toll-like receptors 2 and 4.[18,28–30] On the other hand, the effects of *A. brasiliensis* on the induction of antibody production and the biological significance of induced anti-β-glucan antibodies have not been studied sufficiently. It is well known that activation of the innate immune system is necessary to induce effective antibody production, and that *Agaricus*-derived β-glucan acts both as an epitope and as

an activator of the innate immune system. In particular, the β-1,6-glucan structure may accelerate the production of antibodies, since triple-helical soluble β-1,3-glucan (e.g., grifolan from *Grifola fronfosa*[31] and sonifilan from *Schizophyllum* commune,[32] which only have a β-1,6-monoglycosidic side chain) is less potent as an antibody epitope.[11] Interestingly, *Agaricus*-derived β-glucan has both β-1,3- and β-1,6-glucan structures,[33,34] which may induce antibody production more strongly.

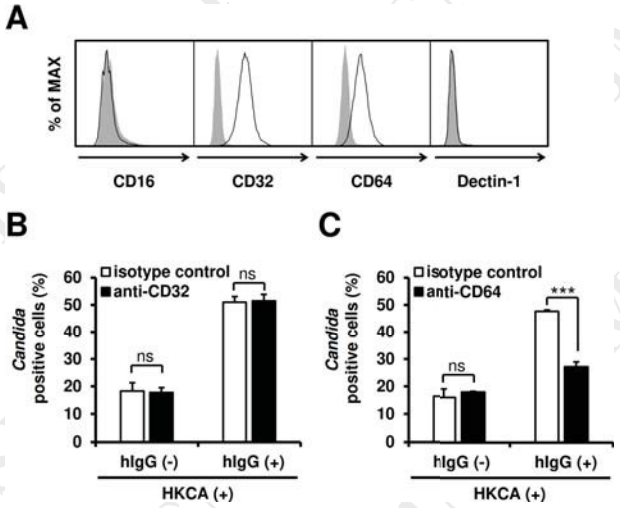

FIG. 5: Involvement of CD64 in improving *Candida* recognition by anti-β-glucan antibodies. (A) Flow cytometric analysis of related receptors expressed on the cell surface of HL-60. The filled gray area represents cells with the control antibody, and the solid line indicates cells with the functional antibody. (B and C) Effect of neutralizing antibodies for FcRs on the promotion of *Candida* recognition of HL-60 by anti-β-glucan antibody. HL-60 was coincubated with human IgG-treated rhodamine-HKCA in the presence of anti-CD32 antibody (B) or anti-CD64 antibody (C). Then, rhodamine-positive HL-60 was analyzed by flow cytometry. Values represent the mean ± SD (n = 3). ***P < 0.001, significant differences from cells with the isotype control. ns, not significant.

We recently reported a highly common antigenicity between *Agaricus*-derived β-glucan and β-glucan derived from clinically isolated *Candida* species.[19] In fact, oral ingestion of *A. brasiliensis* significantly increased the amount of antibody against *Candida* β-glucan (Fig. 2). On the other hand, the increase in the antibody titer against *Aspergillus*, which is mainly composed of β-1,3-glucan, was less marked. This tendency was also proven by the results of animal studies that showed the potential of *Agaricus*-derived β-glucan to induce antibodies against β-1,6-glucan more easily than antibodies against β-1,3-glucan (Fig. 3). Although Alum adjuvant was coadministered to confirm the epitope of induced antibodies, the single administration of AgCAS also induced the production of antibodies against *Candida*-β-glucan (data not shown), supporting the role of AgCAS as an innate immune stimulant.

We recently reported that many pathogenic *Candida* species have the β-1,6-glucan structure on their cell surface.[35] The majority of epitopes of human blood IgG that bound to HKCA had a B-1,6-glucan structure (Fig. 4). Because the inhibition of B-1,6-glucan synthesis or the neutralization of β-glucan by anti-β-glucan antibodies suppresses *Candida* infection,[12,13,36,37] increasing the amount of anti-β-1,6-glucan antibodies may be beneficial against *Candida* infection. As we showed, anti-β-1,6-glucan antibodies and CD64 regulated *Candida* recognition (Fig. 5), and subsequent cellular activation was induced by the β-glucan-IgG complex in a CD64-dependent manner (Fig. 6). Although the receptors and

the underlying mechanisms that control the immunomodulatory effects of β-1,6-glucan have not yet been fully elucidated, our results indicate, at least in part, that antibodies and FcRs play a role as an alternative β-1,6-glucan receptor. Accordingly, both β-1,3- and β-1,6-glucan in *A. brasiliensis* may contribute to its immunoenhancing activities through inter- actions with dectin-1 or antibody/FcR on innate immune cells.

Intentionally increasing the production of anti-β-glucan antibodies via the diet can contribute to the prevention of fungal infectious diseases, especially in individuals or groups with lower anti-β-glucan antibody titers. To induce stronger production of antibodies, further research conducted from different perspectives is needed, such as with the combination of food with other foods. Interestingly, it was recently shown that anti-β-1,6-glucan antibodies bind to certain types of tumor cells, suggesting that circulating anti-β-1,6-glu- can antibodies may be useful in preventing not only infection but also tumor development.[38] Therefore, the enhancement of antibody production by *A. brasiliensis* may be part of the mechanism(s) of the antitumor effects that *A. brasiliensis* has shown thus far.[14,39,40] Moreover, the mechanism of *A. brasiliensis* KA21 as a functional food has been elucidated further by clarifying that it enhances anti-β-glucan antibody pro- duction. In addition, culturing *A. brasiliensis* outdoors is proven to enhance β-glucan content as well as antioxidant and hepatoprotective activities and vitamin D content.[15–17] Numerous studies have indicated the various pharmacological effects of vitamin D, which is also known to activate both the innate and adaptive immune systems.[41] Therefore, we believe that various factors, including these beneficial molecules, influ- ence the overall pharmacological action of *A. brasiliensis* KA21.

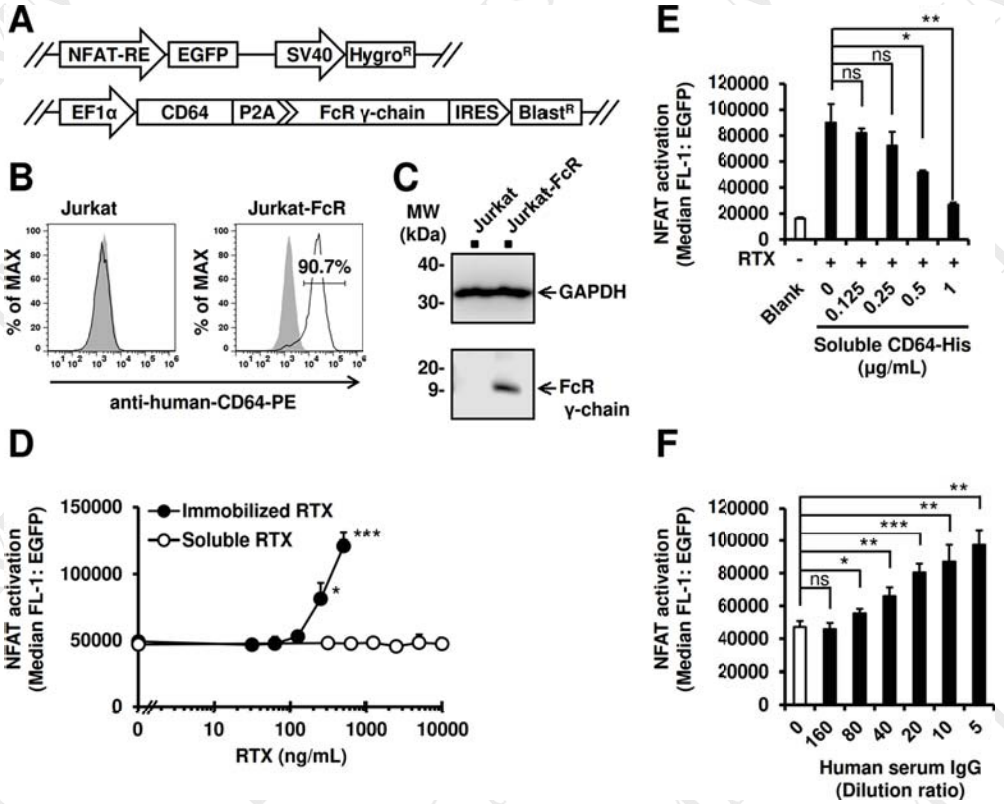

FIG. 6: Involvement of FcRs in NFAT activation induced by anti-β-glucan antibody. (A) Schematic representation of plasmid (NFAT-EGFP/hygromycin resistance gene) and lentiviral (FcRs/blasticidin resistance gene) vector for the reporter gene assay. (B and C) Stable expression of CD64 and FcR y-chain on the Jurkat T-cell line. (B) Cell surface expression of CD64 was analyzed using flow cytometry. Gray shading represents cells with the control antibody,

and solid lines represent cells with the PE-anti-CD64 antibody. (C) Intracellular expression of the FcR γ-chain was detected by immunoblotting. The whole cell lysate was transferred to nitrocellulose membrane and immunoblotted with anti-FcR γ-chain antibody. The same membrane was also blotted with anti-GAPDH antibody to confirm equal loading. (D, E, and F) Antibody-induced NFAT-dependent EGFP expression on Jurkat-FcR was analyzed by flow cytometry. NFAT activation on Jurkat-FcR was induced only by plate-coated RTX (IgG1 control, 0-500 ng/mL), not by soluble RTX (0-10 μg/mL) (D), and was inhibited by the addition of soluble CD64-His protein (E). (F) A microplate was coated with CSBG, blocked, washed, and treated by two-fold serial dilutions of human serum IgG (×5-160). After washing, Jurkat-FcR was added, and NFAT-dependent EGFP expression was analyzed after 20 h of incubation. Data are presented as the mean of median (FL-1) ± SD (n = 3). *P < 0.05, **P < 0.01, and ***P < 0.001, significant difference from normal control. ns, not significant.

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Call for Papers

Aiming to build the relationship between the members and the Society, the publication of the newsletters was proposed before the launching of the Society. The newsletters represent one of the key official publications from the Society. Contents of the newsletters will include notifications of the decisions made by the committee board, reviews or comments contributed by ISMM committee members, conferences or activities to be organized, and the status updated in research, industrialization, and marketing for medicinal mushrooms. The newsletters will be released quarterly, by the first Monday of every January, April, July, and October, with possible supplementary issues as well. The Newsletter is open to organizations or professionals to submit news, comments, or scientific papers relating to medicinal mushroom research, marketing, or industry.

Contact information

For any inquiry in membership enrollment, subscribing to ISMM newsletters, upcoming activities and events organized by ISMM, or submitting news reports, statements, or manuscripts to the Society, please contact the secretariat's office in Beijing, China.

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