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Editorial Board

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Ms. Siti Farah Mamat

Are You Up For New Challenges?

First of all, congratulations to all INBIOSIS students and graduates who already made it this far from your starting line! Now, you maybe start to think, where do you go after this? Should I pursue Ph.D.? Where do I want to work? Is there a suitable job I can apply for? As for me, I begin my career in a multinational pharmaceutical company, taking up a position that does not align with my academic qualification. I challenged myself to explore something new because I believe that every single opportunity will return something beneficial to you especially in the aspect of experience and skills that will open more opportunities in the future.

How to begin and where to start? First, you need to build your presence among the industry players and recruiters. Craft your professional profile in LinkedIn and update your online resume in Jobstreet, Indeed, SPA, Monster or any other job search portals. Set your direction, connect, and build networks with the professionals within your target industry. Next, learn how to create and customize the best resume, how to approach the recruiters, how to respond when you get approached, and how to follow up on your job application. Every single communication between you and the recruiters matters to give them a good impression of you.

Considering the current job market that is heavily affected by the Covid-19 pandemic, it is crucial to align your passion, strength, and qualification with the correct industry. It is advisable to go for the essential industry that can sustain for a long time throughout any challenges in the market. If you are aiming for a place outside your area of expertise, focus on the transferable skills that you can bring to the field. Showcase your skills and convince the recruiters that these skills will be beneficial for their companies. Once you are in the field, take every task and challenges that are given to you, and do your best to deliver your work on time with the best quality. Build the trust between you and your supervisor and colleagues. Once you demonstrated your capability, I believe that you will be empowered to work on more difficult tasks and take up bigger challenges.

When I first joined my current company in August last year, the biggest challenge was communication because everyone was working from home alternately. Once, I was assigned as a project leader where I had to communicate closely with my colleagues which I've never met before. I took the challenge and always refer to my supervisor and colleagues whenever I need guidance or assistance. When it comes to learning, 10% of knowledge comes from education, 20% comes from interaction with others and the biggest portion (70%) comes from on-the-job experience. Never be afraid to try, all you need is to trust the process and the outcome. It will be challenging, but if you are doing something you want to do, you will eventually find joy in it.

Understanding the production of glucosinolates from pathway analysis

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Glucosinolate is one of the secondary metabolites that can be found in broccoli, cabbage, and also in the model plant, *Arabidopsis thaliana*. Glucosinolates in their activated forms can be utilized to deter pests in the plant defense system. Several studies showed their capability in suppressing the tumor growth of various cancer cell lines of breast, brain, blood, bone, colon, gastric, liver, lung, oral, pancreatic, and prostate. We developed SuCCombase as a result of a continual effort to collect all molecular information linked to glucosinolate biosynthesis. Our recent review paper found glucosinolate genes with experimental evidence in the last 20 years, which can be divided into transcription factors, enzymes, and protein transporters. The increasing amount of molecular data produced from Arabidopsis thaliana facilitated us in constructing a comprehensive glucosinolate biosynthetic pathway in the model plant. The constructed pathway can be used as a reference in other plants that contained glucosinolates. Pathways in biology are interactions or reactions between chemicals, genes, proteins, and protein complexes that manage and sustain the energy and flow of information in a cell, allowing it to respond to internal and external stimuli. Signaling, regulatory, and metabolic pathways are the three primary types of pathways. A metabolic pathway is a set of chemical events that produce and break down molecules in a cell to provide the best possible environment for healthy cells in an organism. This pathway requires enzymes that catalyze the conversion of substances to metabolites or end products. Each pathway, whether signaling, regulatory, or metabolic, highlights the relationships between genes, proteins, and metabolites that are responsible for performing a certain task in an organism. By using bioinformatics approaches, we can analyze the pathway network constructed from transcriptome data using the graph clustering approach. The generated clusters will undergo several statistical analyses to assess the significant clusters for the next bioinformatics analysis such as pathway enrichment. The identified gene candidates will undergo molecular validation experiments such as qPCR to infer their role in glucosinolate biosynthesis.

Traditional medicine registration at National Pharmaceutical Regulatory Agency (NPRA) in Malaysia

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All pharmaceutical items in Malaysia, including traditional medicines products, must be registered with the Drug Control Authority (DCA) under the Ministry of Health Malaysia before they can be marketed or promoted to consumers. National Pharmaceutical Regulatory Agency (NPRA) acts as the secretariat for DCA to issue and process product classification, product registration, licensing, monitoring as well as surveillance activities. Products that have been registered are assured in terms of safety, quality, and efficacy. However, without a proper knowledge on how to register these products, the registration process might be challenging. This article summarizes the registration process of traditional medicine in Malaysia.

Registration Process

To understand the process better, "DRUG REGISTRATION GUIDANCE DOCUMENT (DRGD)" serves as the reference guide for the registration process including quality control, inspection & licensing and post-registration activities of medicinal products including drugs, health supplements, natural product, and food-drug interphase products (Fig. 1). This DRGD shall be read in conjunction with the current laws and regulations together with other relevant legislations, where applicable, governing pharmaceutical and natural products for human use in Malaysia.

Traditional medicine can be defined as any product used in the practice of indigenous medicine, in which the drug consists solely of one or more naturally occurring substances of a plant, in the unextracted or crude extract form. There are some preparations of traditional medicine that are not allowed to be registered such as non-permissible or banned for natural products, contained ingredients listed under Poison Act 1952, traditional medicine that caused adverse effect and traditional medicine containing ingredient from human origin. In addition, raw herbs are exempted from registration.

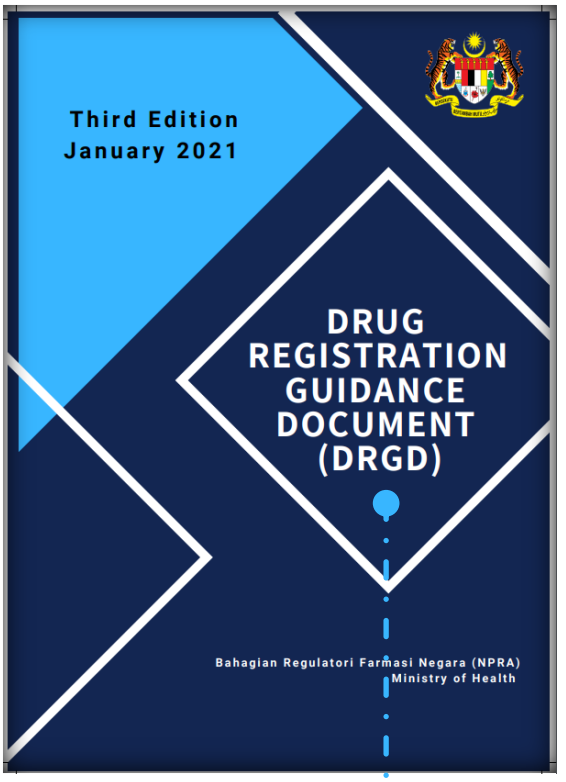
The cost for registering a general traditional product is RM1200. For a traditional product with therapeutic claim single ingredient is RM4000 whereas for 2 or more ingredients is RM5000. The turn-around time is around 116 working days for a single ingredient, 136 working days for a 2 or more ingredient and 245 days working days for a full evaluation product. There are four main steps to ensure product registration of traditional medicine is successful which are preparation, submission, regulatory outcome and post-registration process.

Step 1: Preparation

Product Classification application is not compulsory; however, it is advised to be done especially if applicants are not sure about the status of their product. Subsequently, a token needs to be purchased since the registration process will be performed via Quest3+ system that requires the token configuration (Fig 2a, 2b). All key documents, data and patent (if applicable) need to be available to proceed to the next step.

Step 2: Submission

Once all the required data and documents are prepared, the applicants need to key in and upload the documents. The required documents for traditional medicine are based on the category of claims and number of active ingredient (s). Depending on that, the application can be abridged or full evaluation.



- Part I - Administrative data and product information.
- Part II - Data to support product quality (Quality Document), and should be in compliance with Good Manufacturing Practice (GMP), with two batches of certificate of analysis, stability test, and other test(s).
- Part III - Data to support product safety (Nonclinical Document) and it should be in compliance with Good Laboratory Practice (GLP).
- Part IV - Data to support product safety and efficacy (Clinical Document). The guideline can be referred to internationally accepted guidelines.

Step 3: Regulatory Outcome

Once the Authority registered a product, the product registration holder will be notified and a product registration number (MAL number) will be issued via Quest3+ system. A legitimate registration number starts with "MAL," then continues with eight digits before ending with T alphabet that indicates the registration category is traditional medicine shall be released for each product. The registration number is specific for the product registered with the name, identity, composition, characteristics, origin (manufacturer) and product registration holder, as specified in the registration documents. It shall not be used for any other product.

Step 4: Post Registration Process

A product's registration status is valid for five (5) years or for the time mentioned in the Authority database (unless the registration is suspended or cancelled by the Authority). Applicants must follow all obligations and requirements set by the Authority during the approval of product registration as they are responsible for maintaining the product in terms of quality, safety, and efficacy during the validity period of registration. Failure to do so might result in the application for product registration renewal being rejected.

Conclusion

In short, the registration process for traditional medicine products can be accomplished via four main steps. There is no shortcut to market these products without undergoing the registration process. NPRA staff are always available to assist the applicants. In-depth information on registration traditional medicine can be found in the guideline of DRGD which is available on the website of NPRA.

Reference

[1]https://www.npra.gov.my/index.php/en/industry.html

Proteomics as a tool to understand the mechanisms of Alzheimer's disease

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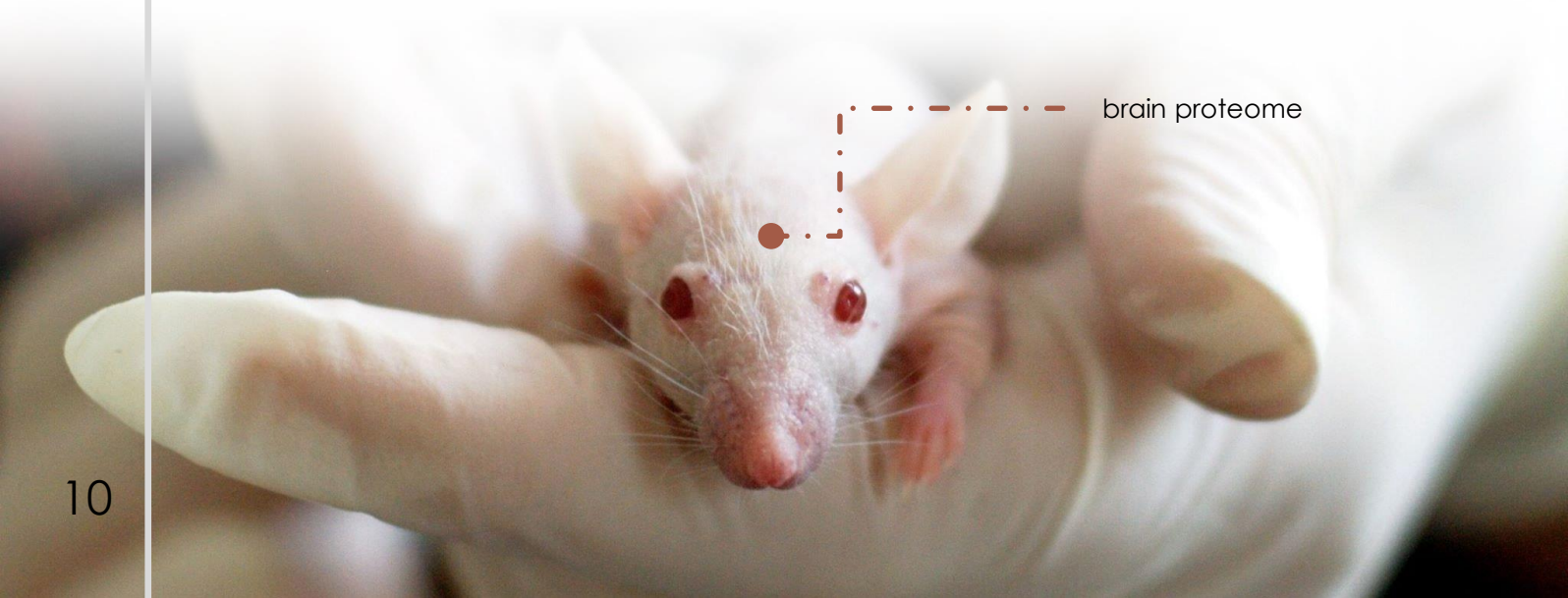
Have you ever run into someone you know and his or her name slipped your mind? Do you often engage in a frantic search for misplaced keys, purses, or other everyday items? Do you walk into a room only to forget what brought you there?

We all forget things once in a while. Forgetting stuff is a part of life and it often becomes more common as people age. However, serious memory problems make it difficult to do everyday tasks like finding your way home, tie a shoe, driving, or using a phone. Dementia is the term applied to a group of symptoms that negatively impact memory and it is not a normal part of aging. Other than memory impairment, people with dementia may also have problems with visual perception, decision making, language skills, and personality changes. Alzheimer's disease (AD) is the most common form of dementia, which is characterized by a progressive decline in memory and cognitive capabilities, accompanied by neuropathological hallmarks, such as aggregates of amyloid beta in plaques and neurofibrillary tangles that are formed by hyperphosphorylation of a microtubule-associated protein tau. AD is an age-related, non-reversible brain disorder that develops over a period of years before the symptoms appear, and commonly occurs in people over 65 years of age. The worsening breakdown of the connections between neurons responsible for learning and memory in the brain is another hallmark associated with the disease. In advanced cases, the brain tissues initially cause focal atrophy of specific regions and then gradually progress to generalized atrophy involving the entire brain, which ultimately results in death.



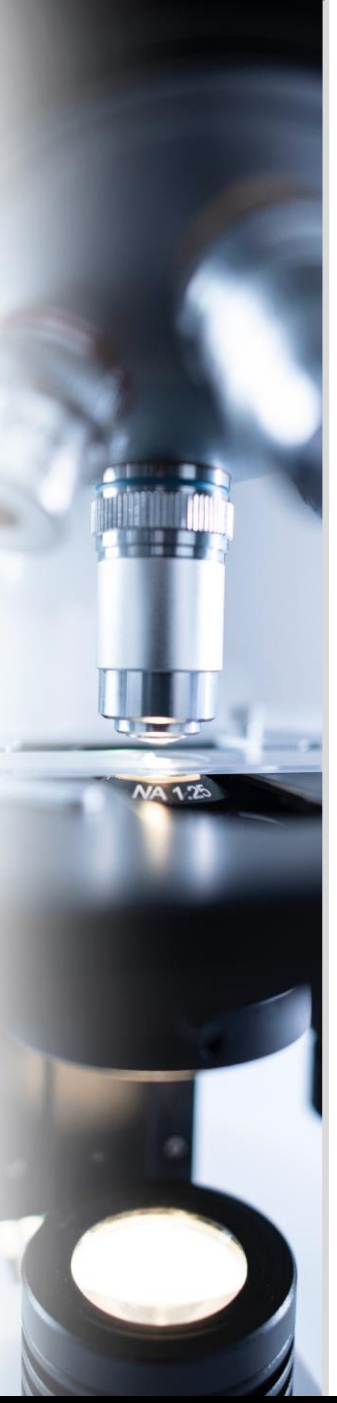
Our understanding of the molecular mechanisms that underlie the pathogenesis of AD is still incomplete. For instance, we do not know what factors drive the AD neuropathology development, what factors lead to the memory impairment in AD, what factors are responsible for considerable heterogeneity in the progression rate of AD patients, and what molecular mechanisms appear to distinguish AD from other neurodegenerative diseases such as frontotemporal dementia and Parkinson's disease, as well as the normal brain aging. A greater understanding of all these factors is essential for the development of effective therapeutics and the discovery of new biomarkers for AD. There are mounting evidence indicate that amyloid beta and tau represent only a fraction of the complex and heterogeneous biology of AD. The previous record for AD clinical trials has been very poor: 99.6% of AD clinical trials have failed, and currently, no disease-modifying treatment is available, suggesting that new therapeutics are particularly needed for AD. This high failure rate has been attributed to various factors including having the wrong drug targets, starting treatment too late in the disease progression, or relying too much on results from preclinical studies that use animal models of AD that poorly reflect the conditions in human disease. Therefore, the number of proteomic studies that examine protein changes in AD brain tissue has been increasing. The unbiased, mass-spectrometry-based proteomic studies has emerged as a powerful tool for unraveling the intricate biology underlying AD.

Traditionally, most AD studies have used a targeted, hypothesis-driven approach that focuses on the selected proteins of interest. For example, amyloid beta, tau, and apolipoprotein E proteins have been identified as the major protein present in amyloid plaques, neurofibrillary tangles, and late onset AD, respectively. Using a targeted approach, however, limits the ability to understand these protein changes in the broad context of AD and precludes the discovery of novel disease-associated proteins. There are many advantages of using mass-spectrometry-based proteomics to study AD pathogenesis. First, the unbiased nature of this approach permits the discovery of novel proteins involved in the disease. Second, thousands of protein differences can be quantified simultaneously using minuscule amounts of brain tissue. Third, proteomics can detect post-translational modifications on proteins such as phosphorylation, oxidation, and ubiquitination, which are known to have an important pathological role in AD. The large amount of data generated in proteomic studies may provide a comprehensive view of all protein differences that occur in AD, which can provide insight into the molecular mechanisms that cause AD at a network or systems level, which is particularly useful when studying complex diseases like AD. The technical and financial constraints are among the limitations in mass-spectrometry-based proteomics in the past. However, these factors have recently become less restrictive, and consequently, the number of proteomic studies using AD brain tissue has increased. Overall, the capability of proteomic studies in providing a roadmap of protein changes that are associated with AD will hopefully assist in the identification of novel biomarkers of the disease as well as the development of medicine to cure the disease.

Dr. Ng Chyan Leong's research interests are to unveil the structure and function of conserved hypothetical proteins (human and pathogenic bacteria), secondary metabolites biosynthesis enzymes, and toxin and epitope of allergen molecules. His group determines the atomic resolution protein structure using X-ray crystallography, and applies biochemistry, biophysics, molecular biology and bioinformatics for structural and functional analysis. Together with national and international collaborators, the group has determined the first crystal structure of the human CZIB protein, house dust mite allergen, nerol dehydrogenase and thermophilic amylase, and characterized several secondary metabolites biosynthesis enzymes and proteins with unknown function. Dr. Ng's research interest is also extended to understanding the impact of carbon sources (glucose vs triglyceride) in fungi metabolite biosynthesis, and plant alkaloid biosynthesis pathway using systems biology approaches, which may lead to the development of alternative microbial fermentation platform and drug discovery. His group has received various university and national research grants, and actively collaborates with industry partners. Their research output has been published in peer-reviewed indexed journals (https://orcid.org/0000-0001-8590-7418) including Nature Communications, Scientific Reports, Plant Physiology and Biochemistry, Phytochemistry, Peer J and Microbial Cell Factories.

Please feel free to contact Dr. Ng (clng@ukm.edu.my) for research and industrial projects collaboration. Research students are welcomed to join the group.

Assoc. Prof. Dr. Ng Chyan Leong is a structural biologist. He completed his PhD in York Structural Biology Laboratory (YSBL), Chemistry Department, University of York, UK in 2007. He then worked as a postdoctoral fellow at the Medical Research Council, Laboratory of Molecular Biology, Cambridge, UK, focusing on protein translation and ribosome research.



Dr Goh Hoe Han's research applies multi-omics approaches, encompassing transcriptomics, proteomics, and metabolomics aided by bioinformatics analysis for holistic understanding of biological systems. Such integrated approach is exemplified by his studies on *Nepenthes* pitcher plants to uncover the effects of plant hybridisation on the molecular expression in the pitcher tissues and fluids of three local *Nepenthes* species. Transcriptomics analysis with sequencing was applied to describe the molecular events during *Garcinia*-type seed germination in mangosteen that forms a new plantlet in the absence of an embryo.

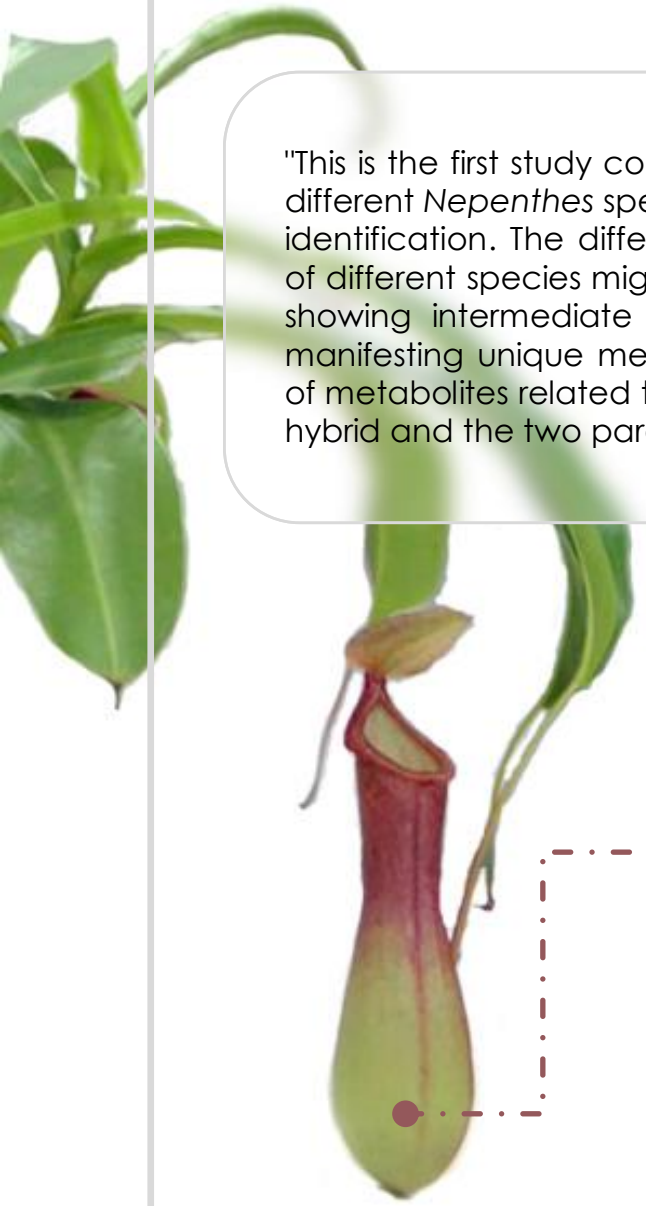
Dr Goh's expertise in functional genomics has been recognised as a frequent invited speaker at international conferences and participating in national roundtable discussions. Dr Goh was the Head of Centre for Plant Biotechnology whom contributed to the commissioning of the first PC2-certified greenhouse at UKM, before becoming the Head of Centre for Bioinformatics Research (2016-2019) when he established the Centre of Omics Data Analysis (CODA) as a one-stop service provider for omics data analysis.

Dr Goh is keen on industrial collaboration in precision biotechnology for tropical plant improvement and also the commercialisation of novel recombinant plant enzymes. If you are interested to collaborate or be part of the plant functional genomics group, please email to gohhh@ukm.edu.my and refer to his website https://gohlab.weebly.com/

Assoc. Prof. Dr. Goh Hoe Han is a plant molecular biologist who obtained his PhD from the University of Sheffield, United Kingdom in 2011 before starting his first academic position at the Institute of Systems Biology, Universiti Kebangsaan Malaysia. He pioneered the Plant Functional Genomics Research Group, focusing on molecular exploration of tropical plants and crop improvement using functional genomics approaches.

Spotlight : CODA - Metabolomics

The Centre of Omics Data Analysis, CODA – Metabolomics provides comprehensive non-targeted metabolite profiling and targeted analysis of small molecules using gas and liquid chromatography (GC/LC) instrumentations. CODA – Metabolomics also supports consultations on topics from study design to data analysis, statistics, data visualization and interpretation of the metabolomics data.



"This is the first study comparing metabolites in the carnivory organs of different *Nepenthes* species with comprehensive profiling and putative identification. The differential metabolite compositions in the pitchers of different species might have ecological implications with the hybrid showing intermediate phenotype between the parents as well as manifesting unique metabolites. However, there is no clear evidence of metabolites related to the differences in dietary habits between the hybrid and the two parent species."

Rosli, M. A. F., Mediani, A., Azizan, K. A., Baharum, S. N., & Goh, H.-H. (2021). UPLC-TOF-MS/MS-Based Metabolomics Analysis Reveals Species-Specific Metabolite Compositions in Pitchers of *Nepenthes ampullaria*, *Nepenthes rafflesiana*, and Their Hybrid *Nepenthes* × *hookeriana*. Frontiers in Plant Science, 12(573).

https://doi.org/10.3389/fpls.2021.655004

Number of publication (Jan-June 2021)

47 Indexed journal

26 Q1/Q2 journal

5 Top 10% journal

3 Industrial collaboration

29 National collaboration

11 International collaboration

Number of registered postgraduate student (June 2021)

29 PhD

24 MSc

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