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INSTITUT BIOLOGI SISTEM
INBIOSIS
INSTITUTE OF SYSTEMS BIOLOGY

SYSTEMS BIOLOGY INSIDER

VOLUME 3(1) 2021

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Greetings,


In this issue, we share a story of INBIOSIS alumnus, Ms. Siti Farah Mamat. We also highlighted our newly established Centre of Omics Data Analysis, CODA that provides consultation and assistance for big data analysis of different omics platforms.

Insights of this issue present four interesting topics from our newly appointed research fellows, Dr. Nurkhalida Kamal, Dr. Murni Nazira Sarian, Dr. Nisha T. Govender, and Dr. Ahmed Mediani.

Lastly, if you would like to share any interesting articles, opinions and thoughts related to systems biology, you are welcome to email them to me. We will do the best to include them in the future Systems Biology Insider bulletin.

Many thanks

Dr. Low Chen Fei
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Senior Lecturer / Research fellow
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Institute of Systems Biology Alumnus

I have spent almost five years at INBIOSIS, as a research assistant then a Masters student, majoring in Systems Biology (Biomolecular Sciences) under the supervision of Dr. Wan Mohd Aizat. Pursuing postgraduate study at INBIOSIS have opened a door to many opportunities and new experiences for me. During my time here, I have acquired lifelong lessons, experienced and learned a lot of new things, and made friends who I can call as a family.

My journey at INBIOSIS has equipped me with diverse technical and interpersonal skills that have helped me to adapt to my current position working in the industry. A postgraduate study is not only about the academic qualification, but there were a lot more that I have gained along the journey. UKM and INBIOSIS have provided various platforms to boost my professional and personal skills. For instance, I have developed the project management, teamwork,


communication, and problem-solving skills as I attended local and international conferences, presented my projects during the INBIOSIS Progress Seminars every semester, and involved in various activities with INBIOSIS students and staff where we have bonded with each other.

This set of transferable skills will be a great advantage to you when entering the society, no matter what kind of position you will hold or what type of industry you will be working. Hence, to my dearest juniors who will be entering the working society soon, enjoy your time as a student and collect as many skills and experience as possible. Keep in mind that as a job seeker, it is crucial to prepare yourself for the battle, especially during difficult times of this current economy that is greatly impacted by the Covid-19 pandemic. Our economic players are going through a lot of changes including the talent acquisition process.

Nowadays, LinkedIn has become a significant tool to showcase your professional profile, skills, and interest as it can be easily accessed by the recruiters. Over 65 million professionals use LinkedIn to build high-quality networking. Besides, it is crucial to learn the right way to showcase your skills and experience in the resume or career profile to make yourself more marketable. Learning new skills and upgrading your existing skills will be helpful to convince the recruiters that you are ready for new challenges and opportunities. Alhamdulillah, as for me, I have secured interviews and a position in a pharmaceutical company amidst the pandemic. I believe that a postgraduate student who went through so many kinds of challenges will be able to adapt to the new working world.

My final advice to you who are walking toward your dream, this path that you are taking may be bumpy and challenging. However, keep standing tall and trust the process. As Gold Meir says, "Make the most of yourself by fanning the tiny, inner sparks of possibility into flames of achievement". Remember, if you have the courage to begin, then you have the courage to succeed.

Ms. Siti Farah Mamat
Masters in Systems Biology
(Biomolecular Sciences) 2016-2019



Unlocking the full potential of secondary metabolites production in fungi via mimicking the natural physiological environment

There is an idiom saying 'no pain, no gain' and it is true enough when we relate to our life as we always face problems, hardships and trials. These events always induce stress in our life and it will be translated by our behaviors to cope with the stress. If the amount of stress is right enough for us which is known as eustress (good stress), it will alert us to be more energetic, motivated and could increase our focus and performance (Mills, Reiss and Dombeck, 2018). How does fungi behave if they are under stress conditions? Fungi will modulate the synthesis of secondary metabolites (SMs) to overcome this stress state for its survival, fitness, and pathogenicity, depending on their environmental protection or colonization needs (Hautbergue et al., 2018). In a review written by Bills and Gloer, they highlight that scientists in the past had limited knowledge on the stress

induction in fungi, and their study design for producing the SMs in fungi always in the laboratory standard control culture conditions whereby only several environmental parameters were studied such as the temperature, nutrient availability or light exposure (Bills and Gloer, 2017). This resulted in repetitive isolation of known and similar SMs from previous studies. Natural growth conditions, on the other hand, require a dynamic balance between various variables that can fluctuate separately as well as co-exposure to other fungi or bacteria and these responses enable various secondary metabolites to be produced. Several studies were designed in which the alteration of the growth environment was used as a method for the discovery of new secondary fungal metabolites.

One of the approaches is to mimic physiological conditions of the multispecies microorganism communities in ecosystem by co-culturing the fungi with other fungi or bacteria. Co-culture aims to activate the silent secondary metabolite gene clusters that codes for the biosynthesis of the secondary metabolites required in the communication and/or defense of fungi against other microorganisms. Co-culture study between *Aspergillus fumigatus* and *Streptomyces rapamycinicus* exposed an altered metabolome profile observed by High Performance Liquid Chromatography (HPLC) and HPLC-High Resolution Mass Spectrometry (HPLC-HRMS) (König et al., 2013). To gain insight of the regulation of the biosynthetic pathway, microarray approach was used to identify the SM gene cluster that is up-regulated

only in the co-culture. Deletion of the up-regulated PKS designated as FccA of the identified cluster resulted the silencing of the corresponding SMs which was observed by the HRMS-based metabolomics profiling in comparison to the wild-type culture. Further isolation and elucidation of the activated SMs was carried out and were identified as meroterpenoid derivatives which are mixed terpenoid-polyketide natural products known as fumicyclines A and B. Interestingly, the production of fumicyclines A and B achieved by direct physical contact between the bacterial and the fungal cells could be a proof that multispecies microorganisms cross-talk can induce the expression of silent genes.

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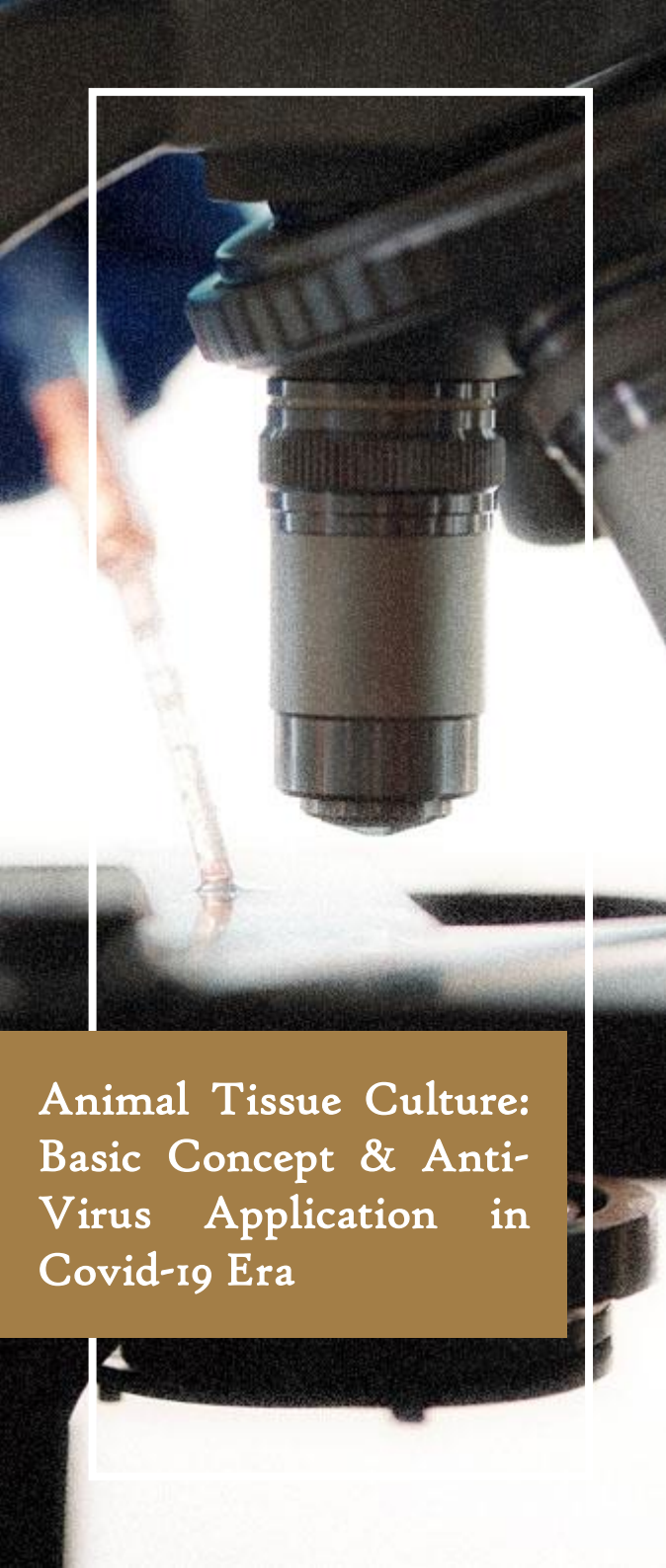


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Microscopy Lab @ INBIOSIS

Microscopy lab at INBIOSIS provides high technology of specialized optical instruments designed to produce magnified visual or photographic images of specimens. The laboratory is equipped with **Stereo-imaging microscope (Carl Zeiss / Stemi DV4)** that generates image at low magnification with light reflection on the surface of the specimens, and a **Fluorescence microscope (Carl Zeiss/Carl ZE)** that examines and analyses fluorescent-labelled specimens.





Animal Tissue Culture: Basic Concept & Anti- Virus Application in Covid-19 Era

Concept

Animal tissue culture is the *in vitro* maintenance and propagation in a suitable artificial environment of isolated cell tissues or organs. When supplemented with a medium containing nutrients and growth factors, many animal cells may be induced to grow outside of their organ or tissue of origin under specified conditions. Scientists have been able to work with a wide range of cells under regulated conditions through the production of simple culture media; this has played an important role in advancing our knowledge of cell growth and differentiation, recognizing growth factors, and knowledge mechanisms underlying the normal functions of different types of cells. However, for *in vitro* growth of cells, the culture conditions may not mimic *in vivo* conditions with regards to pH, CO₂, O₂, nutrition and osmolality (Verma 2014). Furthermore, the cultured cells require sterility along with a steady supply of growth nutrients and sophisticated

conditions of incubation.

For decades, 2D cell culture has been regarded as a key tool in cellular and molecular biology due to its simplicity, reproducibility and reliability in nature. Nevertheless, it is now understood that 2D cell culture underrepresents the *in vivo* environment of living cells. The advancement and use of 3D scaffolds and biomaterials offer researchers an ability to more closely mimic the *in vivo* environment. However, many biomaterials are of animal origin, leading to variability, environmental and ethical concerns (Campuzano et. al. 2019).

In diverse fields, from basic to advanced science, animal cell culture has found its applications. For diverse research efforts, it has given a model system of:

1. The study of basic cell biology, processes of the cell cycle, specialized cell function, interactions between cell-cell and cell-matrix.
2. Testing for toxicity to study the efficacy of new medications.

3. Gene therapy for replacing non-functional genes with cells bearing functional genes.

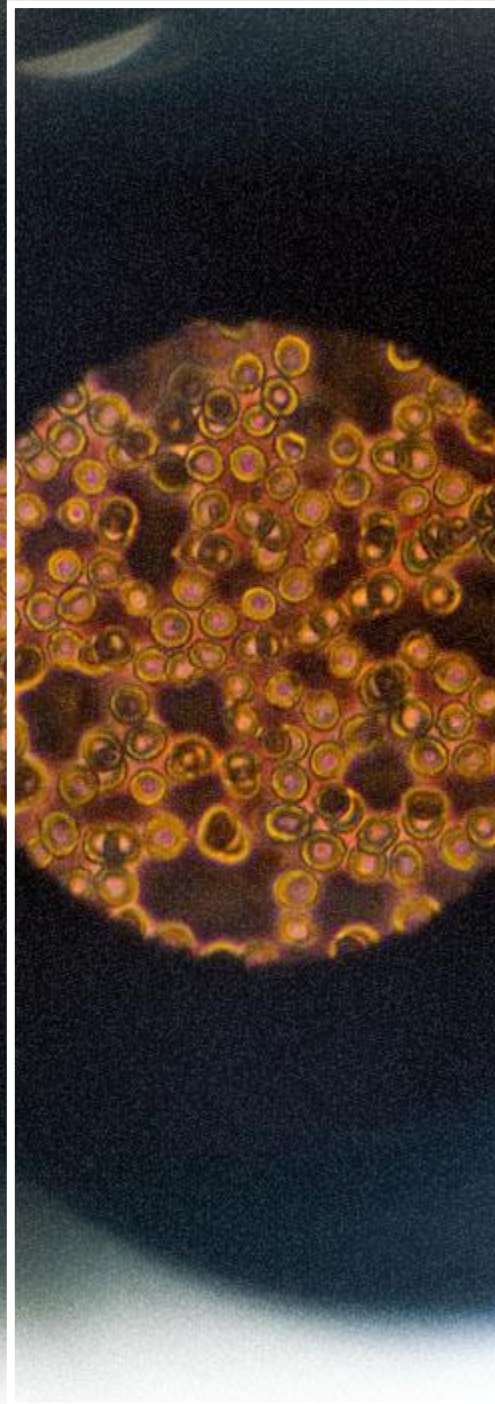
4. The characterization of cancer cells, the function of various chemicals in cancer cells, viruses, and radiation.

5. Production of vaccines, mABs, and pharmaceutical drugs.

6. Production of viruses for use in vaccine production (e.g., Covid-19, chicken pox, polio, rabies, hepatitis B, and measles).

Anti-virus application via cell culture

Many biotechnology products (such as viral vaccines) are fundamentally based on the mass cultivation of the cell lines of animals. While several simpler proteins are produced in bacterial cultures using recombinant DNA (rDNA), more complex glycosylated (carbohydrate-modified) proteins currently have to be produced in animal cells. Cell culture research is currently aimed at investigating the impact of culture



conditions on the viability, productivity, and persistence of post-translational changes such as glycosylation, which are essential for recombinant protein biological activity. Anticancer agents, enzymes, immunobiologicals [interleukins, lymphokines, monoclonal antibodies (mABs)], and hormones are biologics developed by rDNA technology in animal cell cultures.

To combat the current outbreak of Covid-19, a respiratory disease caused by the coronavirus SARS-CoV-2, researchers are investigating the virus intensely. As viruses do not replicate on their own, to allow scientists to isolate and study the viruses, cell lines are needed as hosts. Using the cell lines VeroE6 (kidney epithelial monkey cells), Huh7 (human liver cells) or human airway epithelial cells, SARS-CoV-2 can be isolated.

The National Institute of Infectious Diseases, Tokyo, Japan, has found that genetically modified VeroE6 cell lines

are highly susceptible to SARS-CoV-2 infection, according to a report by Matsuyama et al (2020), which would make them especially useful for isolating the virus. The cells are engineered to express large amounts of the transmembrane protease serine 2 (TMPRSS2) enzyme and are referred to as VeroE6 / TMPRSS2. To inoculate the VeroE6 / TMPRSS2 cells with the virus, the researchers used samples from seven Covid-19 patients. The cell cultures were then observed for structural changes that are signs of viral infection, virus titers were determined in cell cultures and electron microscopy was used to detect coronavirus particles (Matsuyama et. al. 2020).

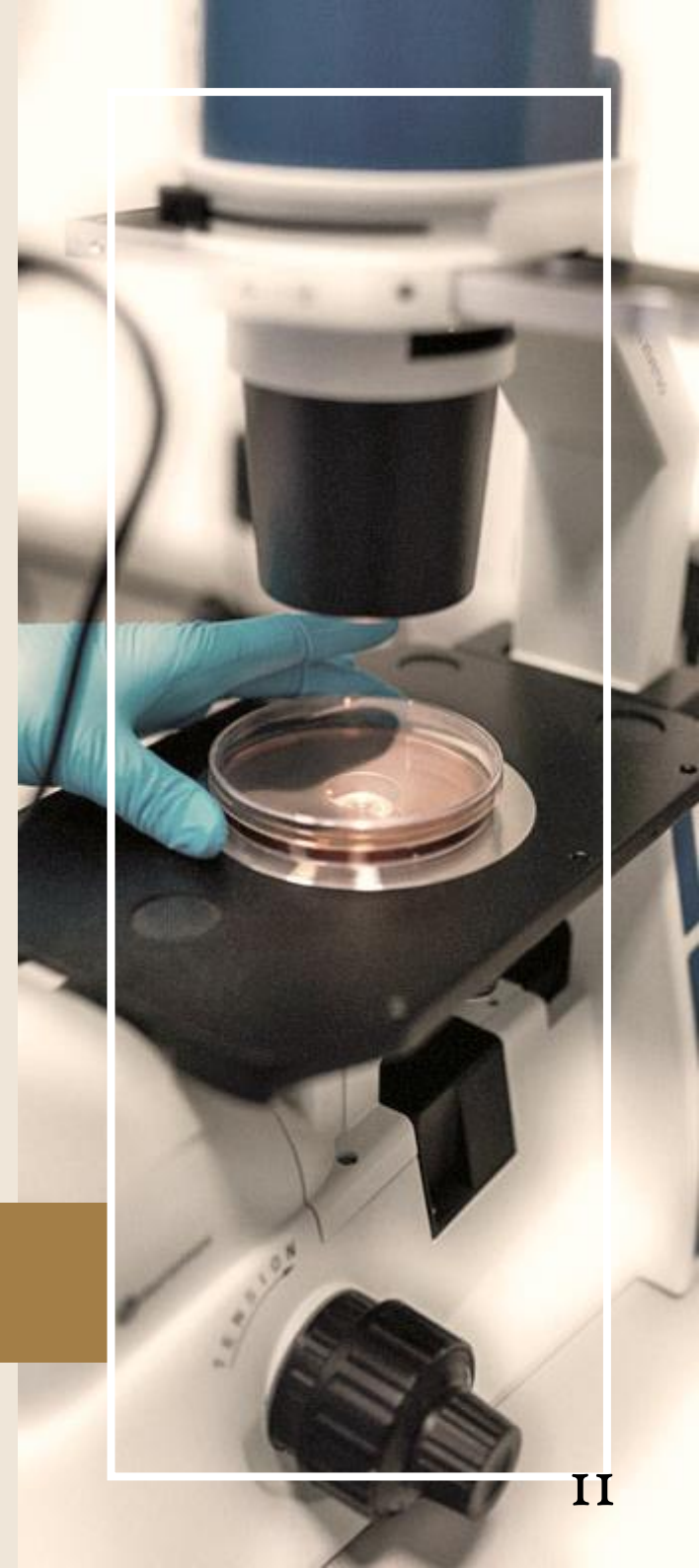
The research team has found that for SARS-CoV-2 isolation, VeroE6 / TMPRSS2 cells perform better than other cell lines. VeroE6 / TMPRSS2 showed a ten-fold greater number of cells contaminated with SARS-CoV-2 than unmodified VeroE6 cells (Matsuyama et. al. 2020). The study also indicates that TMPRSS2

can play an important role in the entry into the host cells of SARS-CoV-2. Studies on the SARS-CoV-1 associated SARS virus also support this inference. Thus, TMPRSS2 may be a drug development target against coronaviruses.

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D.I.Y Probiotics: Thinking outside and inside the box

Anyong haseyo! Globalization of the Korea has taken a toll on many of us. Today, Korean dramas, songs, dance-moves (K-pop), movies and food have popularly won the heart of Asians, especially Malaysians. Korean food stretches from mouth-watering bulgogi, kimbap, toekbakki, Korean fried chicken, samyetang and the all-time must have, kimchi.

Kimchi is a probiotic lactic-acid bacteria (LAB) vegetable food. According to the World Institute of Kimchi, three key components present in kimchi are: i) leafy vegetable, ii) mix of spices and iii) by-products of lacto-fermentation. The general pickling procedure begins with the preservation of leafy or succulent vegetable in a brine

solution for a period of time (varies according to type of vegetable used). Next, the kimchi sauce or a mixed paste of rice flour, garlic, ginger, chilli flakes (*gojuchang*), sugar, shrimp paste, julienned leeks, spring onions, radish and carrot is rubbed all over the preserved vegetable and left to sit at room temperature for an overnight. It is during this time, the probiotic bacteria (*Lactobacillus* and *Leuconostoc* species) evolve and feed onto the carbohydrate and sugar compounds present in the substrate (the vegetables). Fermentation breaks down the carbohydrate into mainly lactic acid and a plethora of short chain fatty acids such as butyric acid, acetic acid and propionic acid.



Regular consumption of kimchi offers tons of health benefits; lowers the levels of “bad” cholesterol (LDL), promotes the functioning of heart, brain and immune system and delivers potent anti-inflammatory effect. The human digestive tract houses a range of bacteria, all of which are actively involved in digestion and the breakdown of chewed food into minute particles fitted for absorption into blood capillaries. A good balance of good and bad bacteria in the gut could be maintained with kimchi consumption. The word probiotics was derived from the Greek, *pro-bios* which means for life and an attractive immunomodulatory property would certainly warrant a

healthy life.

Over the years, Korea's probiotics market have grown by leaps and bounds – thanks to lactic acid bacteria extracted from their kimchi. Today, probiotics are available in the form of tablets and ampoules of food supplements tagged along a generous price.

Why purchase when you can do it yourself (D.I.Y)? The Korean Embassy in Malaysia organizes Hansik (Korean food in Korean language) Contest, a Korean food cooking competition as part of their programme, annually. This year, the event took place at UCSI University Kuala Lumpur on the 26th September 2020. An overwhelming variations of kimchi, each with

unique Malaysian touch competed for the winning prize. To name few, jackfruit kimchi, guava kimchi and mango kimchi, all made their way into hall of fame. These Malaysian-styled kimchi used various fresh grown local produce (vegetables and fruits) and the shrimp paste (an ingredient in the kimchi puree) was cleverly substituted with *chinchalok*, *belacan* and/or *budu*. They tasted great and most importantly did not trade off kimchi's authentic Korean taste and nutritive properties.

Are you still thinking of purchasing your probiotics supplement?
Do it today and do it yourself (D.I.T + D.I.Y)



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PC2 Greenhouse (RTPC2) @ INBIOSIS

RTPC2 is one of the facility at INBIOSIS that enables research on genetically modified plants to be carried out within a secure and controlled environment. RTPC2 is also available to all UKM researchers as well as open for service to other universities or companies. The existence of the RTPC2 facility conforms to the mandatory requirements of the Biosafety Act 2007, especially in research involving genetic manipulation studies. The facility helps to boost research in the field of biotechnology and crop improvement.

<https://www.ukm.my/inbiosis/en/rtpc2/>

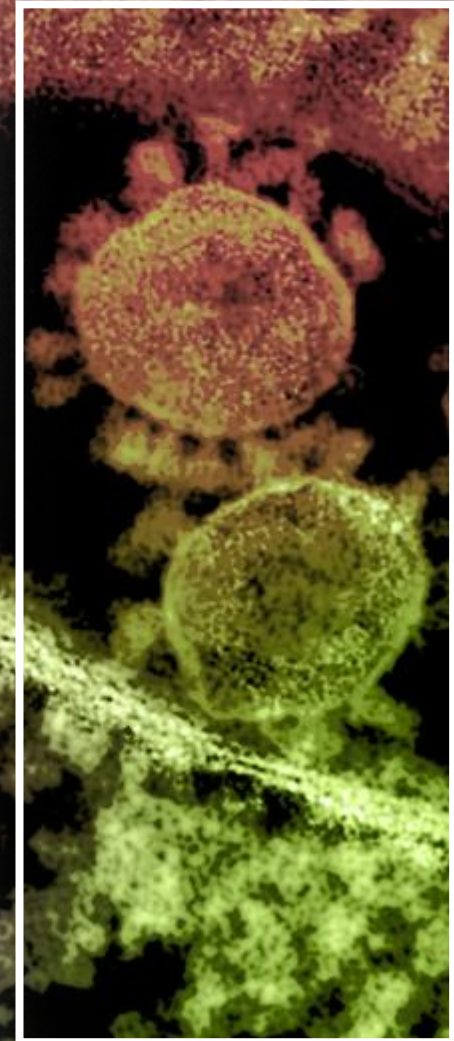


Metabolomics in studying Covid-19

A lot of Covid-19 research is currently attempting to explain the disease through the prism of the genome. Many immunologists and virologists are currently researching Covid-19 from the point of view of gene expression, and many studies concentrate on genetics and gene expression. The analogy "your DNA is a cookbook" is sometimes used by people and the product of the recipes and the eventual product of genes in body is made of protein. So, if anyone wants to search for the fact, the proteome should preferably be studied, but this is costly and difficult to do. As a result, transcriptomics, gene transcript analysis are typically done because it is the best way to get a detailed snapshot of the gene activity of a human, which is just a single step away from the reality of the protein. However, metabolomics can be preferred because it provides a view that is a step closer to fact than transcriptomics is.

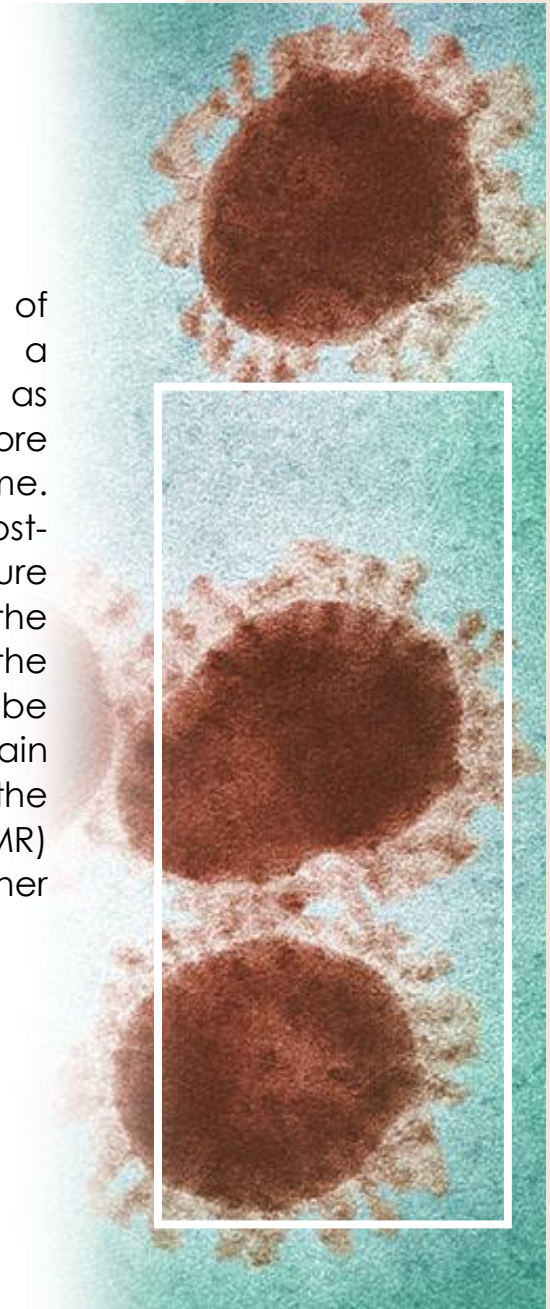
Metabolomics is a large-scale analysis of metabolites in biofluids, tissue extracts or

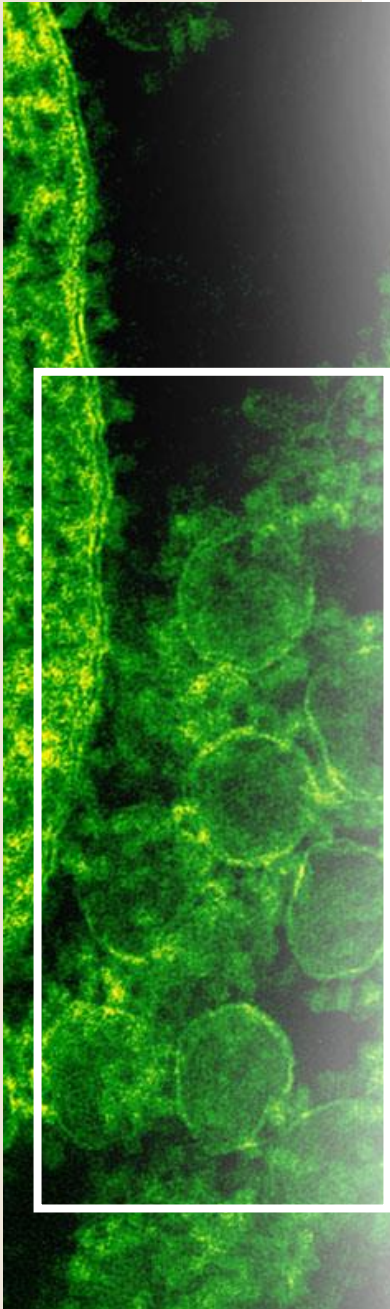
organisms. Biologically active molecules, such as glucose, cholesterol, creatinine, hormones, lipids, and more are small (< 1000 Da) metabolites. It gives useful insight into the underlying cell functions, illnesses, and human health in turn. Metabolites are the ultimate effectors of the cellular machinery and represent the penultimate stage in the progression from the genome to the proteome, to the metabolome, to the phenotype. In other words, metabolomics represents the downstream biology of systems and has attracted considerable interest in researching cell-to-organism metabolic networks. Through examining the metabolome, we may calculate the dynamics of the cell response to internal or external disorders in order to gain a deeper understanding of the underlying biology from the cell level to the level of the organism. This information promotes the identification of biomarkers and biological pathways that are active or inactive during illness or health conditions. Cell metabolomics is an evolving area that answers basic biological questions and enables metabolic phenomena in cells to be studied.



The study of metabolic variations between Covid-19 patients with severe symptoms and those with moderate symptoms and tests is important to determine whether any of the metabolic markers are correlated with disease period and mortality. Differentiating between serious and moderate conditions allows high-risk patients to get better-targeted treatment and it also enables medical professionals to leverage their abilities and resources more effectively. This is where metabolomics can offer a compromise; it lies somewhere between the snapshot

of gene expression and the core of proteomics. It does not result in a complete and detailed picture as transcriptomics does, and much more information is still given by the proteome. But NMR metabolomics is a very cost-effective and easy way to capture many things that are important to the health of an individual. And perhaps the key reason metabolomics can be acceptable is that there are certain biomarkers, such as GlycA, in the nuclear magnetic resonance (NMR) panel that can not be tested with other techniques.





The NMR is the only platform for glycoprotein acetylation quantification, GlycA. GlycA is a very interesting biomarker used to study inflammation. It outperforms many traditional inflammatory biomarkers, including C-reactive protein (CRP). GlycA tends to capture baseline inflammation much better than CRP. The CRP being a single molecule is very volatile. It is going up and down quickly, and sometimes it's not there, even though you would expect it to be existed. GlycA, on the other hand, is even more stable since it is a hybrid biomarker made up of many molecules. This means that GlycA has baseline levels as opposed to CRP. The best part of the study of NMR metabolomics is that while one key biomarker, such as GlycA may exist, it is accompanied by 200 other biomarkers that are a very rich source of complementary knowledge. For

example, researchers are also looking at lipoprotein particles, fatty acids, amino acids and several other options that are shown to have a strong connection with inflammation in the study. And in broader cohort settings where the aim is to predict outcomes, a combination of biomarkers typically outperforms models based on single measurements.

In conclusion, the baseline health of the patients plays a major role in the outcome of vaccine studies or a clinical trial for Covid-19 treatment. We generally need access to all of their clinical data if we want to profile the patient, and if we want to describe the state of their immune systems. Using metabolomics, a clear overview of the baseline health of the patients can be obtained.



Centre of Omics Data Analysis (CODA)

Centre of Omics Data Analysis is a one stop solution research centre for the analysis of different omics research data. Quantitative research and data analysis are becoming increasingly important for multidisciplinary research of systems biology, thus it drives CODA to offer consultation and assistance that cover high-throughput data analysis and interpretation associated with systems biology to the public, particularly the scientific community that includes researchers and students.

Genomics & Transcriptomics

- Offers service from single gene to genome-wide analysis for standard and next generation sequencing (NGS), genotyping, and quantitative PCR, followed by data analysis including preliminary analysis of data, analysis of NGS data using Trinity and statistical analysis.
- The core for genomics and transcriptomics cater NGS data management and analysis for transcriptome profiling, transcriptome *de novo* assembly and other applications.

Proteomics

- Provides state-of-the-art LC-QTOF-MS analysis including protein ID, proteomics profiling and targeted proteomics analysis for clients.
- The service covers sample preparation, data collection and data analysis.

Metabolomics

- Provides comprehensive non-targeted metabolite profiling and targeted analysis of small molecules using gas and liquid chromatography (GC/LC) instrumentations.
- Supports consultations on topics from study design to data analysis, statistics, data visualization and interpretation of metabolomics data.

Bioinformatics

- Provides project design and data analysis for next generation sequencing analysis that includes consultation on the selection and optimal application of software tools for data analysis.
- The code of bioinformatics caters sequence based analysis, structural bioinformatics, network analysis and development of biological database.



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2020 INBIOSIS Achievements

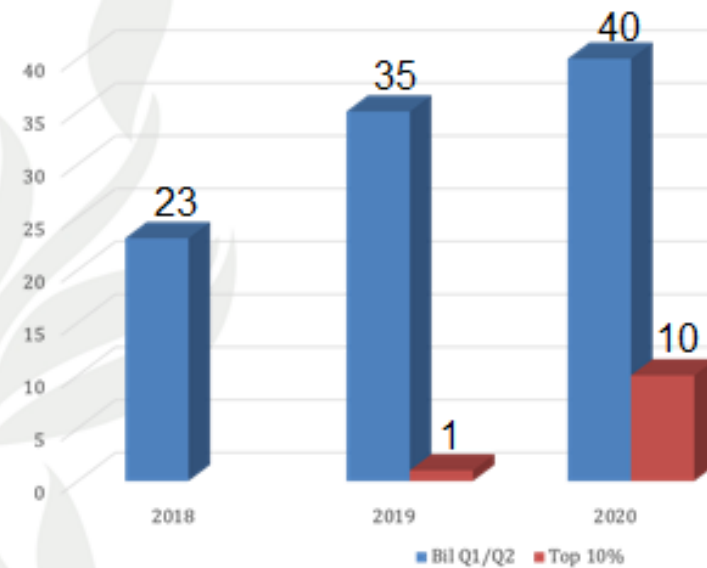
GRANT RECEIVERS

Nama Felo	Jenis Geran	Jumlah Geran	Tajuk Geran	Tempoh Projek
GERAN UNIVERSITI				
Prof Madya Dr Goh Hoe Han	Dana Impak Perdana (DIP)	RM100,000.00	Reference database for functional genomics analysis of mangosteen	01-08-2020 - 31-07-22
Dr Hamidun Bin Bunawan	Dana Impak Perdana (DIP)	RM100,000.00	Functional Analysis of P4 Protein as RNA Silencing Suppressor in Rice Tungro Bacilliform Virus	01-08-2020 - 31-07-22
Dr Murni Nazira Binti Sarian	Geran Galakan Penyelidik Muda (GGPM)	RM37,500.00	In vitro anticholinesterase effect of Polygonum minus Huds ethanolic extract on SH-SY5Y human neuroblastoma cells.	01-10-20 - 30-09-22
Dr Maizom Binti Hassan	Geran Universiti Penyelidikan (GUP)	RM65,000.00	Identification and Characterization of juvenile hormone genes from oil palm pest, <i>Metisa plana</i> Walker for potential insecticide discovery via comparative genomic approaches	01-08-20 - 31-07-22
GERAN ANTARABANGSA				
Dr Low Chen Fei	International Development Research Centre (IDRC), Canada	RM200,000.00	Integrated quorum quenching strategies to reduce antimicrobial resistance in shrimp aquaculture (i-QAS)	01-01-20 - 31-12-21
GERAN KPT				
Dr Maizom Binti Hassan	LRGS MRUN	RM180,800.00	Tajuk Program: High Performance Big Data Analytics Platform for Optimizing Oil Palm Yield via Breeding by Design Tajuk Projek: Omics Guided Insecticide Development for Use in Precision Agriculture	10-03-20 - 09-03-23
Dr Emelda Rosseleena Rohani	Geran Penyelidikan Fundamental (FRGS)	RM100,100.00	Applying cyto-histology and metabolomics approaches to understand the effects of desiccation and low temperature on mangosteen as a recalcitrant seed model	1-11-2020 - 31-10-2023
Dr Kamalrul Azlan Azizan	Geran Penyelidikan Fundamental (FRGS)	RM110,000.00	Assessing the phytotoxic terpenes in <i>Wedelia trilobata</i> essential oil (EO) for potential sustainable weed management strategy	1-11-2020 - 31-10-2023
Dr Wan Mohd Aizat Bin Wan Kamaruddin	Geran Penyelidikan Fundamental (FRGS)	RM99,932.00	Encapsulation of kesum essential oil containing β -caryophyllene into carbon microsphere for stability enhancement against whitefly pests	1-11-2020 - 31-10-2022
Dr Sarahani Binti Harun	Geran Penyelidikan Fundamental (FRGS)	RM100,800.00	Identification of key regulatory genes connected to insect hormone pathways using gene co-expression network analysis in oil palm pest, <i>Metisa plana</i>	1-11-2020 - 31-10-2022
Dr Nor Azlan Bin Nor Muhammad	Geran Penyelidikan Fundamental (FRGS)	RM149,800.00	Elucidation of oil palm pest, <i>Metisa plana</i> insect development pathways via whole genome sequencing	1-11-2020 - 31-10-2023

2020 PUBLICATIONS

JENIS PENERBITAN	SASARAN	Perbandingan	
		JAN-DIS 2020	JAN - DIS 2019
JURNAL TERINDEKS	60	55	59
JURNAL (Q1 - Q2)	40	40	35
JURNAL Q3 - Q4)	20	5	9
BUKU PENYELIDIKAN	3	4	3

PENINGKATAN Q1/Q2 DAN TOP 10%



Tahniah

DR HAMIDUN BUNAWAN

Felo yang Menerbit Paling Banyak Artikel dalam Tahun 2020

6 Jurnal

3 Q1 1 Q2 2 Q4



Tahniah

Felo yang Menerbit Artikel sebagai Penulis Pertama Tahun 2020



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DR. KAMALUL AZLAN AZIZAN

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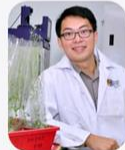
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1 Buku



PROF. MADYA DR. GOH HOE HAN
2 Buku



PROF. MADYA DR. ZETI AZURA MOHAMED HUSSEIN
1 Buku

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Pegawai yang Menerbit Artikel Sebagai Penulis Pertama dan Penulis Bersama dalam Tahun 2020



MOHD FAIZ MAT SAAD
2 Artikel Q1 & Q4

NUR SYATILA AB GHANI
2 Artikel Q1

HAZIM SYAHMI ELIAS
1 Artikel MyCite

SARAH IBRAHIM
1 Artikel Q1

RAFIDAH AHMAD
1 Artikel Q2

Tahniah

Felo yang Menerbit Artikel dalam Jurnal Q2 Tahun 2020



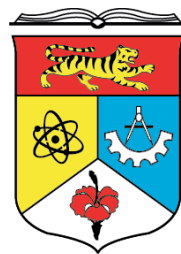
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