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reversing

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INFOGRAPHICS
WHAT YOU SHOULD KNOW ABOUT HEAD & NECK CANCERS

GROWING CANCER CELLS IN A DISH

IMMUNOTHERAPY: HOPE FOR CANCER PATIENTS

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Chairman's Message

YABhg Toh Puan
Dato' Seri Dr. Aishah Ong

Fifteen years ago, Cancer Research Initiative Foundation, or CARIF, was established by our patron, YAM Tan Sri Tunku Ahmad Tunku Yahaya and I as a company limited by guarantee to conduct cancer research to find a cure for cancer.

Today, CARIF has come-of-age and as Cancer Research Malaysia, it is now ready to take on bigger, bolder things. It fills me with a sense of pride to see CRM making its mark in the international stage. The capabilities of our scientists are acknowledged and their expertise and counsel are highly sought after by renowned collaborators from hallowed institutions such as Cambridge, Harvard, and others.

Therefore, more than ever, we need a supportive and involved community who strongly believes in and advocates the importance of research. We need your help and support to bear the finacial costs of research and innovations. Let's work together to keep the momentum and upwards trajectory so that our ambitious goal of #reversingcancer is made a reality.

A word or two from the Chief Executive

Prof. Dr.
Teo Soo-Hwang

Each year, 550,000 individuals are diagnosed with head and neck cancer. The majority of these cases occur in developing countries* in Asia.

The fight against cancer is a global one and CRM is internationally recognised as one of the partners from Asia

In this issue, you will read about developing the significant work that CRM is doing in finding the Achilles heel in head and neck cancer which includes immunotherapy and a mobile App for early detection.

We hope by reading reversing c, you will be inspired to talk about cancer research. Each one of us can play a proactive role to #reversecancer by donating to fund our research programmes.

We need your help now to continue to find solutions faster, especially for Asian-centric cancers. Donate to help us find treatments faster.

*Ferlay J, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer. 2015;136(5):E359-86.

OVERVIEW OF ORAL AND NASOPHARYNGEAL (HEAD AND NECK) CANCER TEAMS IN CRM

***Prof. Dr. Cheong Sok Ching** explains why giving priority to "Asian Cancers" is important in our fight to #reversecancer*

In Malaysia, more than 9,000 cases of head and neck cancers were reported from 2007-2011, which is ~9% of all cancer cases, making it the fourth most common cancer among Malaysians[i]. The annual incidence of head and neck cancers worldwide is more than 550,000 cases with around 300,000[ii] deaths each year. About 90% of all head and neck cancers are squamous cell carcinomas (HNSCC). HNSCC is the sixth leading cancer by incidence worldwide.

The fact is, head and neck cancers are fairly easy to detect early. In the case of oral cancer, for example, tissue changes in the mouth that might signal the beginnings of cancer can often be seen and felt easily[iii]. However, half of oral cancer patients die within 5 years of their diagnosis, mostly due to late presentation. Those who have been successfully treated, in turn, need to cope with the devastating consequences of their treatment such as alteration to their physical appearance and swallowing disorders. This is because, despite the fact that head and neck cancers are one of the most common cancers in South and South East Asian countries, the majority of cancer drugs developed for targeted therapy are for lung cancer, breast cancer, colon cancer and lymphomas as in the west, these diseases are more prevalent than oral cancer. Therefore, there is a huge gap in the development of targeted therapy for what is termed as "Asian Cancers".

This is why CRM prioritises its effort and resources in a robust head and neck cancer research programs to better understand the genetic changes that cause these cancers. This will give us the opportunity to develop drugs to treat this disease. Funding also needs to be set aside for an outreach program to teach the public about the early signs and symptoms of these cancers, as well as to equip health professionals with the right and easy-to-use screening tools in order to conduct screening programs particularly in remote areas of Malaysia where access to oncologists may require travelling for days at a time. The end goal is for us to use our knowledge to develop markers for the early detection of the cancers and develop novel therapeutic approaches for its prevention and treatment.

i Ministry of Health (Malaysia), 2016. Malaysian National Cancer Registry Report 2007-2011, Malaysia Cancer Statistics, Data and Figure.

ii Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. CA Cancer J Clin 2011; 61(2):69-90

iii https://www.nidcr.nih.gov/oralhealth/Topics/OralCancer/DetectingOralCancer.htm

Achievements by Head and Neck Cancer Team

54 Scientific Articles

2015-2016: 11
2013-2014: 15
2011-2012: 11
2005-2010: 17

47 Collective Awards

Ms. Yee Pei San,
Best poster award at the Annual Scientific Conference of the Malaysian Oncological Society, 2016

Dr. Vivian Tiong,
UICC Fellowship for attachment in Dr. Ultan McDermott 's laboratory at the Wellcome Trust Sanger Institute, Cambridge, UK, 2015

Professor Dr. Cheong Sok Ching,
Best Basic Science Paper at the 5th World Congress on Oral Oncology, Sao Paulo, Brazil, 2015

Ms. Chai San Jiun
Best oral presentation award at the 4th Nasopharyngeal Carcinoma Research Day, University Malaya, 2015

4 Ongoing Studies

- **Cancer Immunotherapy for head and neck cancer:** improve understanding on how cancer cells evade our immune system to survive, and develop vaccines to activate the immune system to prevent and treat cancer.
- **Drug repurposing for head and neck cancer:** using a combination of computational and laboratory science, identify existing drugs that, although not currently used for the treatment of head and neck cancer, can be repurposed for the treatment of this disease.
- **Identifying new therapeutic targets in head and neck cancer:** harnessing a powerful gene-editing technology called CRISPR-Cas9, we identify genes that are critical for the cancer to survive and find ways to kill these cancer cells.
- **Tele-Oncology Screening Initiative for Oral Cancer in Remote Areas of Malaysia (TRIM Study):** develop methods and tools that enable disease documentation and quick communication between the people who look after our patients. This will facilitate early detection of oral cancer and improve patient monitoring.

IMMUNOTHERAPY: HOPE FOR CANCER PATIENTS

***Dr. Lim Kue Peng** decodes ASCO's "Advance of the Year 2015" and describes the inroads CRM is pioneering in the area for head and neck cancers.*

In 2015 Dr. Julie Vose, the past president of American Society of Clinical Oncology (ASCO) declared, "No recent advance has been more transformative than the rise of immunotherapy, particularly over this past year, making immunotherapy the American Society of Clinical Oncology's (ASCO's) Advancement of the Year."

One of the flagship programs in CRM is the head and neck cancer immunotherapy development in the form of a **peptide vaccine.** Currently in pre-clinical testing stage, this pioneering project is made possible thanks to our discovery of unique proteins that are present in head and neck cancer cells that could be made into vaccines to activate the immune system – very much like how vaccines for infectious diseases are developed.

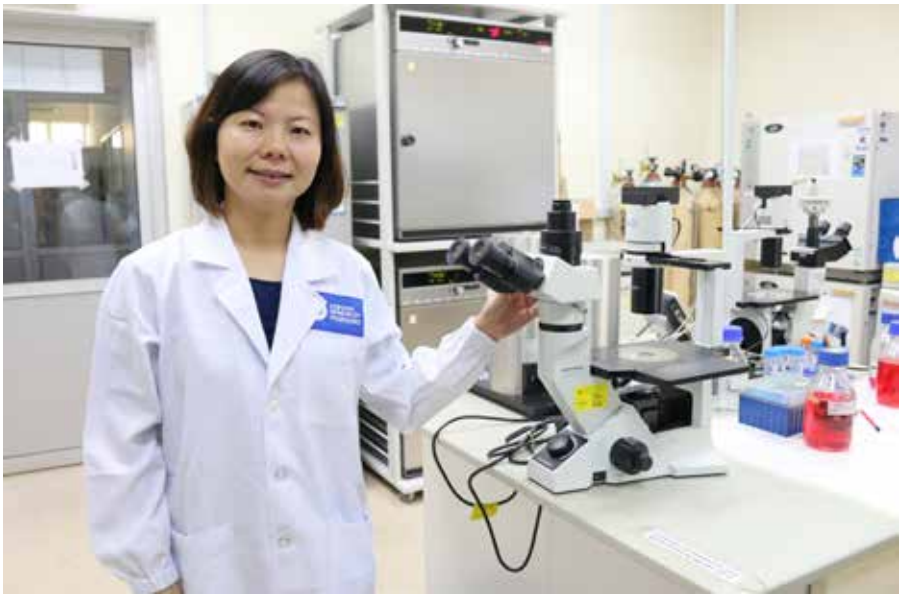
What is cancer immunotherapy?

Cancer immunotherapy is a way to tell your immune system that cancer is an enemy and needs to be rid of. There are several types of cancer immunotherapy. For example, there are those that activate the immune system to attack cancer cells such as cancer vaccines; and there are those that take the 'brake' off from the suppressive arm of immune system such as checkpoint inhibitors.

Who will benefit from immunotherapy?

Immunotherapy has been tested on most types of cancers. However, not all cancer patients respond equally well and some types of cancers tend to produce better response (such as melanoma, a type of skin cancer).

Currently, the checkpoint inhibitors type of immunotherapy has been approved for the treatment of several types of cancer including melanoma, lung cancer and head and neck cancer. This is a huge milestone in terms of improving the survival of cancer patients. However, only a fraction of patients respond to these drugs. For example, for head and neck cancer patients, only 13-18% benefit from the treatment. We still don't know why this is so. What we do know is that there is a need to find better ways of activating the immune system in patients who currently do not respond to these drugs.



How does the CRM peptide vaccine work?

A crucial step towards understanding how cancer develops is to find out the differences between cancer cells and normal cells. Years of research on head and neck cancers have helped the team in CRM to identify several antigens (proteins) that are unique to these cancer cells. Further research then showed that cancer cells are dependent on these antigens to grow – which means when the peptide vaccine is injected into the body, our immune system can be educated to recognise them and then kill any cells that contain these proteins.

As the peptide vaccine is made to target cancer-specific proteins (which are not present in normal cells), your normal cells will be spared. This is a critical step during the development of cancer therapies in order to keep side effects to a minimum.

What's next?

We will evaluate the safety of the peptide vaccine before proceeding to clinical trials in humans. We have recently received two international grants from the Medical Research Council, UK to work collaboratively with the University of Southampton, to expand our cancer immunotherapy program to include the development of different types of cancer vaccines that would not only improve the treatment of head and neck cancer patients, but prevent the disease from occurring in the first place.

Much has been invested in this flapship research program. Here in Malaysia, in order to take it to the next stage, we need RM6 million to successfully complete critical testing of the vaccine as required by regulatory bodies (such as the Malaysian National Pharmaceutical Control Bureau (NPCB) and the USA FDA) before they can be used in clinical trials (the first testing in humans) by the anticipated date: end of 2018.

Together, we are looking at making a difference to ~900,000 head and neck cancer patients[1]. **If 2.2% out of the 30 million Malaysians donate RM10 to this cause, we would be done with the fundraising right now!**

Help us reverse cancer by going to www.cancerresearch.my/donate and follow the given steps. Each Ringgit takes us that much closer to realising our vision of a future free of the fear of cancer.

[1]Collective numbers for Oral, Lung, Breast and Prostate Cancers, Global Cancer facts and figures 2nd Edition (American Cancer Society).

GROWING CANCER CELLS IN A DISH

The first step to scientific discovery and novel cancer treatment

By Gan Chai Phei

Understanding cancer genes and developing drugs that hit these genes has led to new treatments for cancer. However, treatment for head and neck cancers remains a huge challenge. A major reason for this is up until very recently, the molecular mechanisms underlying head and neck cancer development is not well-known. Furthermore, the models for studying these cancers have been limited, particularly those associated with the risk habits (such as betel quid chewing) that are commonly seen in Asia.

Recognising the need, CRM started establishing a large panel of oral cancer cell lines in 2004 with the help of Professor Stephen Prime from the University of Bristol in the United Kingdom.

What are cancer cell lines?

Cancer cell lines are, in its simplest explanation, cancer cells that we isolate from patients' tumors and then grow in a dish. These cell lines will keep dividing and growing, essentially 'living' forever in the dish under certain strict laboratory conditions.

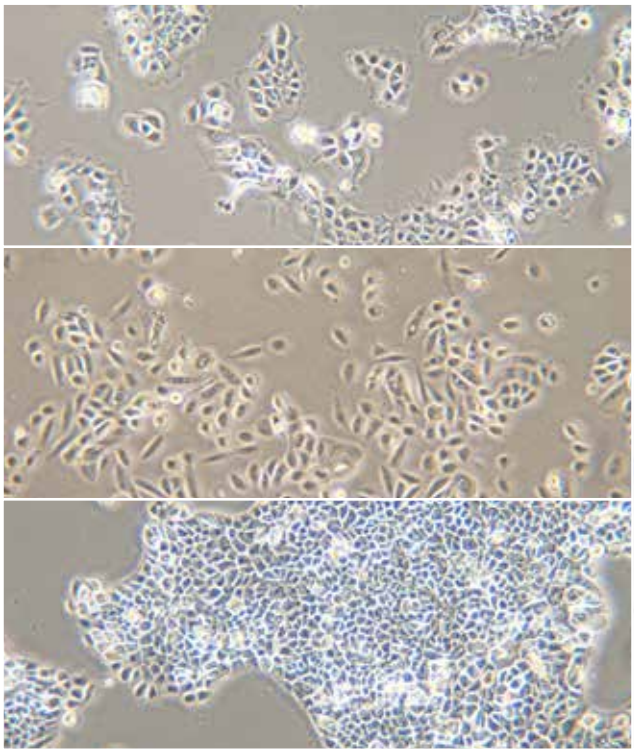
The concept of growing cancer cells in a dish sounds deceptively simple. The truth is this task is very challenging as we are required to grow them outside their natural environment – which is the human body. Once a cancer cell line is successfully established, they are used by scientists to study the biology of cancer and to test potential cancer treatments and drugs as these cell lines contain the same genetic make-up originating from the patient's cancer. It is often the first step to cancer drug testing as it is a reliable and cost-effective tool before we invest more money to conduct more complex studies such as the animal models and clinical trials. In fact, every cancer drug known to man that is currently used in the clinic was first tested on cell lines in the laboratory before they could be developed further for clinical use.

Oral cancer cell lines in CRM

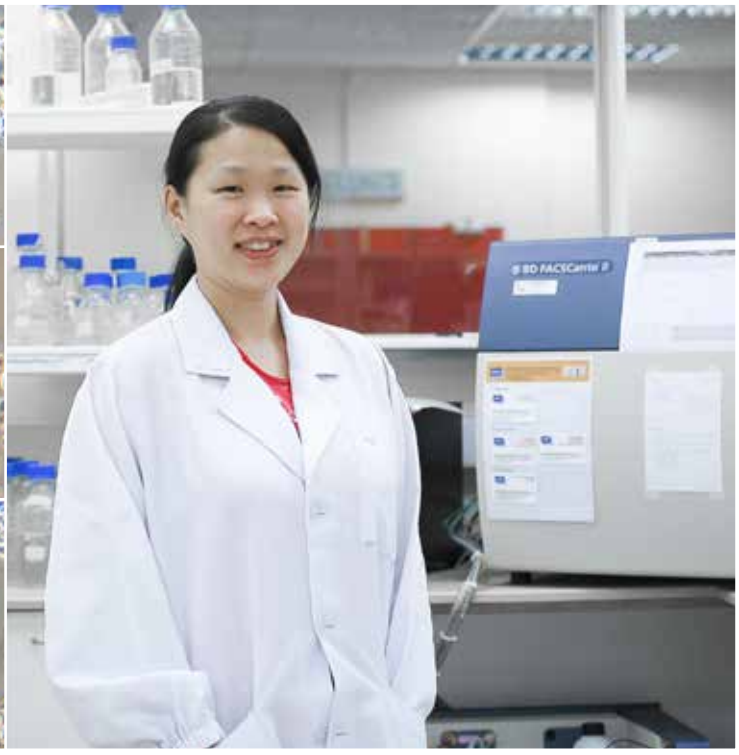
CRM currently hosts the **largest collection of Asian oral cancer cell lines.** They are used in more than 15 laboratories across 10 countries to help scientists understand various aspects of cancer development. We believe this global collaborative effort will advance our understanding of cancer development and how cancer spreads to other parts of the body (a process called metastasis) and result in finding ways to improve the survival of our patients.

The development of these cell lines was successful because of an on-going strong collaboration with University of Malaya (Oral Cancer Research and Co-ordinating Centre) and the Oral Health Division of the Ministry of Health, Malaysia. Further work to characterise these cell lines was conducted in collaboration with international partners including the National Institutes of Health, USA and University of Colorado, USA.

This work was supported by MOSTI, HIRG, core donors and supporters of Cancer Research Malaysia. Read more about the oral cancer cell lines developed and characterised by CRM here https://goo.gl/RBLDyG.



Cancer cell lines

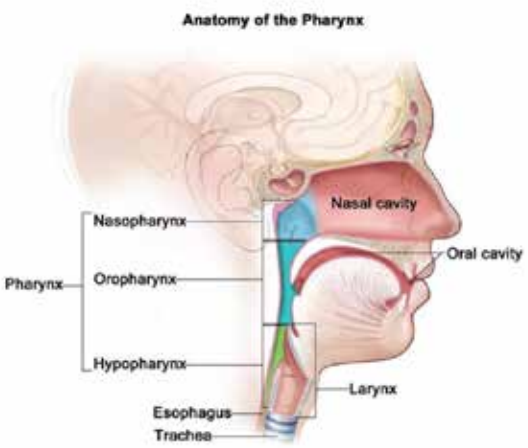


What You Should Know About Head & Neck Cancers

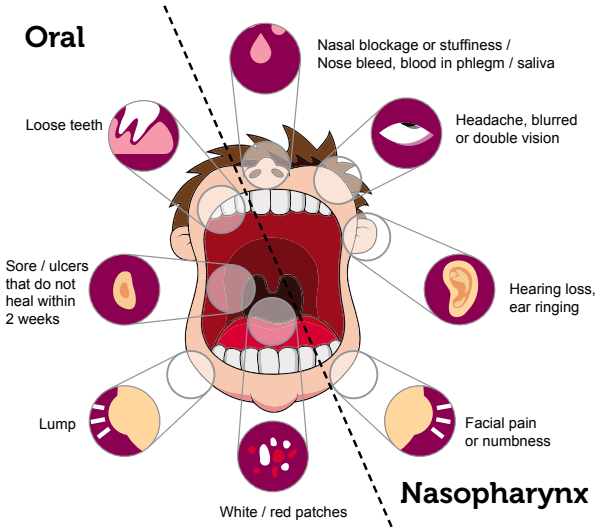
"Cancer didn't bring me to my knees, it brought me to my feet."

– **Michael Douglas,**
American actor and producer
Throat Cancer Survivor

DISTRIBUTION OF HEAD & NECK CANCERS



signs & symptoms



BE INFORMED ABOUT HEAD & NECK CANCERS

800K

In 2013 head and neck cancers resulted in more than 800,000 deaths globally*

The burgundy and ivory ribbon has been used to raise awareness for head and neck cancers.

Among Malaysians, oral, laryngeal and pharyngeal cancers are more common among Indians and nasopharyngeal cancers are more common among Chinese and Bidayuh.

Men are 3x more at risk and head and neck cancers are the 4th most common cancer in Malaysia.

85% are caused by an unhealthy lifestyle and diet. Reduce your risk by avoiding smoking, drinking alcohol, chewing betel quid and eating preserved foods.

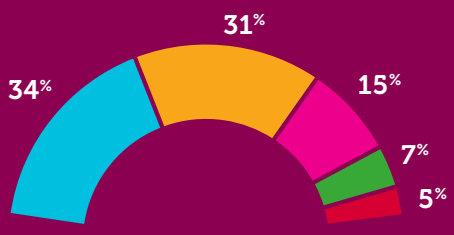
Early detection is within your grasp. Be aware by knowing the signs and symptoms and seek medical attention upon discovering any suspected signs and symptoms.

**Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet. 2015 January 10; 385(9963): 117–171)*

1. Tobacco & Smokeless Tobacco
2. Poor Nutrition
3. Socio-Economic Status
4. Chemical Exposures and Inhalants (Formaldehyde, Wood Dust)
5. Betel Quid Chewing
6. Consumption of Preserved Food
7. Virus Infection (EBV, HPV)
8. Alcohol

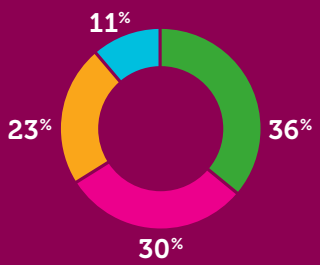
FACTS

Most Frequent Head and Neck Cancers in Malaysia*



- Nasopharyngeal Cancer
- Thyroid Cancer
- Oral Cancer
- Laryngeal Cancer
- Salivary Gland Cancer

2/3 of Nasopharynx and Oral Cancer Patients Were Diagnosed at Late Stage*



- Stage I
- Stage III
- Stage II
- Stage IV

The five years survival rate is 80% to 90% for early cancers, and this decreases to 40% for late stage cancers.

Head and Neck Cancers in Malaysia*

"Like with every form of cancer, early detection is what it is all about. I urge everyone to learn the facts about this condition. It can be prevented with testing, and it can be beaten if caught early!"

– Rod Stewart,
British Rock Singer and Song Writer
Thyroid Cancer Survivor

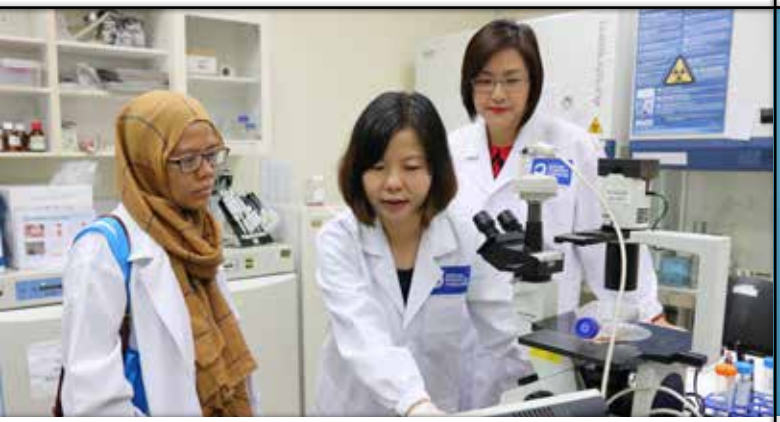
**National Cancer Registry Report, Malaysia Cancer Statistics - Data and Figures, 2007*

RECAP OF EVENTS

Here are some of the many interesting events that took place in and around CRM recently. Be sure to follow us on our social media platforms for updates on our upcoming events!

Pink Picnic in the Park

Visit by UK Women's Delegation led by HE Vicki Treadell, British High Commissioner to Malaysia



One-on-One Interview with BERNAMA

Media Roundtable with our collaborator from the Wellcome Trust Sanger Institute, UK

Live Radio Interview on BFM

Visit from Akademi Sains Malaysia

TELE-ONCOLOGY SCREENING INITIATIVE FOR ORAL CANCER IN REMOTE AREAS OF MALAYSIA (TRIM) STUDY

*Outreach Executive, **Nabihah Haron**, shares her experience running the pilot study for TRIM in Limbang, Sarawak.*

What is the TRIM Study all about?

The Tele-Oncology Screening Initiative For Oral Cancer In Remote Areas Of Malaysia or TRIM (formerly known as Malaysian Oncogrid Programme) is a project to improve early detection of oral cancer by using a mobile phone App. This App enables us to take photos of suspicious lesions in a patient's mouth and then send these pictures to specialists or oncologists in hospitals nearby for review. If the lesions are suspected to be cancerous, patients can quickly be referred for treatment and follow-up in a seamless manner.

What impact would this programme make?

The public and cancer patients will benefit from early detection, and referral procedures that are more efficient that could result in better survival rates in the longer term.

Like other cancers, early detection is the key to nipping the disease in the bud. However, in rural areas of Malaysia, getting a diagnosis may mean that the patient has to travel beyond their means. This barrier could result in a delay in diagnosis. For example, when we did the pilot study for TRIM in Limbang, the nearest hospital to the area is in Miri. This means villagers will have to travel and pass through four border gates, 2 in Malaysia and 2 in Brunei, just to get suspicious lesions looked at! Hardship in travelling may mean it would be days or even months before a diagnosis can be made, if at all.

With the App, we hope to be able to treat patients in a more cost-efficient and timely manner. The usage of the App can be integrated with routine services offered by Klinik Kesihatan or Klinik Desa.

Who else is involved in this programme?

The success of this program hinges on the strong collaborations between Cancer Research Malaysia other institutions including University of Malaya, Oral Health Division of the Ministry of Health, Malaysian Dental Association, Malaysian Private Dental Association and University Kebangsaan Malaysia.

Where are we now with this programme and what's next?

When we asked the dentists and specialists who participated in TRIM study, 78% stated that they would like to continue using the App beyond the study as they are motivated by the believe that it could assist in detection of oral mucosal lesions by providing a direct link between dentists and experts.

The completed pilot study showed high accuracy in identifying lesions within the mouth using the App. We also identified the challenges that we may face in using the App in rural areas and all these lessons will be taken into consideration towards improving the App. We are now planning for the next phase of the study which is to conduct further testing before working towards implementing the use of this App in a larger scale to benefit more healthcare providers and patients.

The first phase of the TRIM Study was made possible by the generous donation received from Berjaya Cares Foundation. The second phase which will include integration of a GPS-enabled map system and real-time messaging is currently in development. If you would like to donate and support this App, write to us at info@cancerresearch.my for more information. To read Nabihah's study, please visit online.liebertpub.com/doi/abs/10.1089/tmj.2016.0128?journalCode=tmj&

DRUG DISCOVERY AT CANCER RESEARCH MALAYSIA

The Drug Discovery Team focusses on identifying targeted anti-cancer compounds from natural resources and several innovative platforms integrating chemistry and bioassays have been established.

We are using human cancer cell lines as well as zebrafish, which has ~70% genetic similarity to humans, to identify potential cancer drugs that target only cancer cells and not healthy normal cells. Currently, the team has identified several Malaysian natural-derived compounds that potentially inhibit important features in cancer such as proliferation and blood/lymphatic vessel growth and the team is now validating these hits. In addition, we are establishing platforms to evaluate the pharmacokinetic properties of these interesting compounds, mainly to understand how these compounds behave when they are introduced into the body.

We are also establishing methods to inject human cancer cell lines into the zebrafish to directly observe how cancer cells behave and interact with the microenvironment *in vivo*. This exciting new *in vivo* platform will be used in the future to validate cancer drugs we discovered, and to identify novel anti-cancer drugs that have a high chance to work in the mammalian system.

INTERNSHIP OPPORTUNITIES

Cancer Research Malaysia is committed to training the next generation of cancer researchers and accepts undergraduate and graduate students for training under its industrial training and internship programmes. During the training period, students will have the opportunity to:

- enhance their scientific knowledge;
- gain professional experience;
- obtain hands-on research experience;
- interact with faculty, postdoctoral fellows, and graduate students;
- attend group meeting sessions to learn about in-progress projects at Cancer Research Malaysia;
- present their research at a special session at the end of the training.

We are looking for motivated individuals who have CGPA (or equivalent) of 3.5 and above. The training period should be at least 10 weeks (exceptions apply).

Doctors and medical students are encouraged to apply.

Please apply to us by filling up the **application form downloadable from** www.cancerresearch.my/join-us/

Applications will be reviewed 4 times in a calendar year. The review cycle is as follows:

Review Cycle	Deadline to submit application
1	31 January
2	30 April
3	31 July
4	31 October

Only successful candidates will be notified, within one month from the date of application deadline.

Wong Zheng Wei (right) had the opportunity to put his knowledge into practice through an eight-week industrial attachment at Cancer Research Malaysia.

Valuable internship

PHARMACEUTICAL Chemistry students at International Medical University (IMU) have the opportunity to put their knowledge into practice through an eight-week industrial attachment.

The attachment allows students to gain valuable industrial experience and build their professional network for their careers.

Wong Zheng Wei was given the opportunity to undertake his attachment at Cancer Research Malaysia (CRM), which is the leading cancer research organisation in Malaysia.

Wong relates his experience undertaking this attachment.

"Within the training period, I was expected to complete a project to test the anti-proliferative effect of a previously approved breast cancer drug on oral cancer cell lines.

"I was taught the basics of cell culturing procedures to prepare cell proliferation assay, as well as immunoblotting for the project, plasmid extraction and basic animal work.

"Apart from laboratory work, it was mandatory to attend weekly meetings, gatherings, product presentations and talks by professionals from other institutes.

"I would say these exposures have kept me up-to-date with the advancement of science and technology, and at the same time, piqued my interest in research.

"The experience would not be complete without the awesome colleagues and people I interacted with while I was there.

"Moreover, they were amiable and down-to-earth, thus it was easy to get along and I could rely on them when I had doubts.

"The modules that I have learnt in the Pharmaceutical Chemistry programme such as Biological Science, Pharmaceutical Biotechnology and Pharmaceutical Engineering assisted me in coping with the project work during the attachment.

"The practical sessions introduced me to appropriate skills and use of laboratory instruments, while the lectures gave me insight into the field of cancer, communication skills, teamwork and problem solving, aided me when I was adjusting to the working environment and I owe it to the Social Responsibility module that I have gone through in IMU.

"Despite it being only three months, I was fortunate to experience life in research, which turned out to be both challenging and enjoyable.

"At the end of it, I learnt that it pays to try new things and never to let go of an opportunity."

The pharmaceutical chemistry degree from IMU is accredited by the Royal Society of Chemistry (RSC), UK.

The course is undertaken entirely at IMU and completed in three years or six semesters.

After obtaining the IMU BSc (Hons) Pharmaceutical Chemistry degree, those who meet the academic criteria can also continue to pursue the Master of Pharmacy programme at the University of Sydney or Curtin University in Australia.

They are given credit exemptions in the Master of Pharmacy programmes.

The graduates of the Master of Pharmacy degrees from these universities can register as practising pharmacists in Australia and Singapore, but not in Malaysia currently.

Upon completion of the degree, graduates can enter the workforce and begin their career as chemists in pharmaceutical and other chemical industries.

Those with pre-university results, have a passion for chemistry, and the interest of working in the pharmaceutical industry can apply online and pursue this interesting and rewarding career in pharmaceutical chemistry.

Those who have just completed their SPM and do not have pre-university qualification can consider enrolling in the one-year IMU Foundation in Science (FiS) programme, the direct route for entry into any of the IMU's local degree programmes.

■ For details, visit www.imu.edu.my; e-mail

Lim Wei Wen
(Monash University)

Felix Mea
(Taylor's University)
Tan Jun Hao
(Universiti Sains Malaysia)

Su Kar Yan and **Ngu Ee Ling**
(Sunway University)

SPLASH & DASH

Cancer Research Malaysia thanks all participants, volunteers, sponsors, and partners for their support in making our inaugural Splash & Dash Fun Run a success!

See you at the next race!

Would you like to organise your very own Splash & Dash? Drop us a line at **info@cancerresearch.my** to find out how.