#### Malaysian Society of Gastroenterology & Hepatology

# <u>BULLETIN MSGR</u>

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## PRESIDENT'S MESSAGE

Prof Sanjiv Mahadeva



Dear Members,

It is that time in our society again. 2 years have gone by since the current committee was elected (by you!) & their term has come to an end. As the out-going President of MSGH, I am proud to reflect on the activities and achievements of the society over the last 24 months. Our primary role in providing CME activities of the highest standard to our members has not faltered during this committee's tenure. Major events such as the APAGE/ MSGH IBD Forum in April 2014, together with our annual scientific meetings and endoscopy workshops have been resounding successes. This year, with the addition of the QE Endo Workshop in Kota Kinabalu in September, MSGH further expands its' "wings" to include a 2<sup>nd</sup> live endoscopy workshop of an international standard.

It has not just been CME activities, of course. With the advent of the new MMA fee schedule for private practitioners, MSGH has been at the forefront representing the fraternity and highlighting specific matters/problems with insurance companies and their reimbursements for GI procedures. For this, I have to thank Dr Akthar Qureshi, President-elect of MSGH, who has done most of the negotiations with MMA & the Director General of Health.

For the first time, following suggestions from our members, MSGH set up and funded a sub-committee to look into a unified training scheme for Gastroenterology in Malaysia. After several years and numerous meetings with relevant parties/authorities etc, I am pleased to say that this unified training scheme will finally take effect in the latter part of 2015. A joint committee for Gastroenterology/Hepatology training has been set up by MSGH to facilitate this training. It is anticipated in the full course of time, this role of training will be co-managed with the College of Physicians, under the auspices of the Academy of Medicine. MSGH has been ably supported by the secretarial staff of the Academy of Medicine all this while, so working together for purposes of postgraduate training should only be natural.

On a delightful note, the MSGH Bulletin has been totally revamped & developed a new look over the last 2 years. Edited by Associate Prof Raja Affendi, he has brought a dazzling, vibrant new image for the bulletin, with new sections such as "personal interviews" etc. The feedback we have received from members has been very positive & I hope Affendi will continue his great work for the ensuing editions. For your information, the bulletin, which is published twice a year, can be downloaded from the MSGH website. Hard copies are printed and distributed during our major CME activities.

I end with a note of gratitude and thanks to the current MSGH committee & the hard-working secretariat. All of us have our own "day jobs" & work done for the society is usually done in our spare time, for no financial gain, with the sole purpose of trying to do what is best for you, the members. I hope you will give the next President & his team the same trust & support as I have had over the last 2 years.

# **MESSAGE FROM EDITOR**

#### Dearest members,

Welcome to the second issue of MSGH Bulletin for 2015! In this issue, several brief reports including 'Endoscopy 2015', the routine MSGH activities held from round the country and also the exclusive report of 'Bringing Gastroenterology to the rural people of Sabah' is presented along with beautiful photos. The amazing and superb 'Gastro CSR' job was done for the rural people in Sabah lead by Dr M Vinod Kumar et al. from the Department of Surgery, Hospital Duchess of Kent, Sandakan, Sabah.



As an editor, I realize that the involvement of our entire gastro-hepatology community will help the Bulletin to grow and let us synergize together our clinical, endoscopic, teaching and research experiences to ensure the real expansion of our MSGH community.

The EndoQE 2015 - The 2<sup>nd</sup> Sabah International Endoscopy Workshop chaired by Datuk Dr Jayaram Menon is coming soon and I hope will be well attended by the members of MSGH. It is also a great pleasure to have a synopsis of a young and energetic gastroenterologist from the east coast, Dr Nazri Mustaffa to talk about his experience doing gastroenterology fellowship abroad and I sincerely hope the PhD in the field of gastroenterology will belong to him very soon and looking forward to his contribution to the society!

Mini review on the 'application of next generation sequencing in gastrointestinal diseases' was well written by the local scientist, Assoc Prof Norfilza M Mokhtar for all of us to read and digest and hope to apply in our clinical practice in the future.

I look forward to a more constructive and productive contributions as well as feedback from all the members to the MSGH Bulletin in the future and please do not hesitate to contact me at draffendi@ppukm.ukm.edu.my for your ideas and contributions!

Lastly, it is great honour and pleasure to work with the out-going MSGH president, Prof Sanjiv Mahadewa who shows great leadership skills, contributing plenty of great things for the MSGH and has a good 'craic' too along with the friendly committee members of MSGH for the 'premier league season of 2013-2015!

Yours Sincerely, Assoc Prof Dr Raja Affendi Raja Ali

# **MSGH COMMITTEE FOR 2013/2015**



**PRESIDENT** Prof Dr Sanjiv Mahadeva

**PRESIDENT ELECT** Dr Mohd Akhtar Qureshi

**IMMEDIATE PAST PRESIDENT** Dr Ramesh Gurunathan

HON SECRETARY Dr Tan Soek Siam

HON TREASURER Assoc Prof Dr Raja Affendi Raja Ali

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Dato' Dr Tan Huck Joo Dr Chan Weng Kai Assoc Prof Dr Hamizah Razlan Dr Raman Muthukaruppan Dr Tee Hoi Poh Prof Dato' Dr Goh Khean Lee Prof Dato' Dr P Kandasami

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#### Endoscopy 2015



Professor Dato' Dr KL Goh introducing each faculty during opening ceremony.

Jointly organised by Malaysian Society of Gastroenterology & Hepatology and University of Malaya, annual endoscopy workshop has been a proud tradition since 1993. This year, from 17<sup>th</sup> to 19<sup>th</sup> of April 2015, Endoscopy 2015 was held in the endoscopy suite and auditorium of South Wing of University of Malaya Medical Centre.

Themed "Maintaining quality in Endoscopy", Endoscopy 2015 was formally declared open by Deputy Vice-Chancellor of University of Malaya, Professor Dr Awang Bulgiba. The opening ceremony was also attended by Director of University of Malaya Medical Centre, Professor Dato' Dr Ikram Shah Ismail, Deputy Director of University of Malaya Medical Centre, Professor Dr Mustafa Ali Mohd and a hall packed with endoscopy-related health-care professionals. A short 10-minute video montage prepared by Dr Alex Leow excellently demonstrated the history of this workshop which can be dated back to two decades ago.

Like in the past, a top world class faculty was assembled by Professor Dato' Dr Goh Khean Lee. They were Professor Dr Kenneth K Wang (Mayo Clinic, Rochester, USA), Dr Christopher JL Khor (Singapore General Hospital), Dr Sundeep Lakhtakia (Asian Institute of Gastroenterology, Hyderabad, India), Professor Dr Hiroyuki Maguchi (Teine-Keijinkai Hospital, Sapporo, Japan), Dr Amit Maydeo



Professor Awang Bulgiba presenting a token of appreciation to Professor Kenneth Wang



Group photo for Endoscopy 2015

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(Global Hospital, Mumbai, India), Professor Dr Jong-Ho Moon (Soon Chun Hyang University, Bucheon, Korea) and Dr. Roy Soetikno (Singapore General Hospital). MSGH Special Lecture and University of Malaya Distinguished Lecture was delivered by Professor Dr Kenneth Wang entitled "Diagnosis and Endoscopic Treatment of Barrett's Esophagus". This then kick-started the workshop which interesting а series of cutting-edge live was demonstrations intertwined with state-of-the-art lectures. The highlights of both live demonstrations and lectures, just to name a few, were endoscopic ablation (using radio-frequency ablation technique) of Barrett's oesophagus, palliative RFA of cholangiocarcinoma followed by biliary metallic stenting, EUS-guided palliative RFA of biliopancreatic tumours, cholangioscopy and biliary intervention using 2<sup>nd</sup> generation SpyGlass system and per-oral endoscopic myomectomy (POEM). Participation of other key opinion leaders from across the globe were made possible by remote networking hosted by the combined effort of Telemedicine Development Center



Group photo for the participants of GIA course

(TEMDEC) of Kyushu University, Information Technology Department of University of Malaya Medical Centre and Malaysia Research and Education Network (MYREN). The said key opinion leaders were Associate Professor Dr Rajvinder Singh (University of Adelaide), Associate Professor Dr Pradermchai Kongkam (Chulalongkorn University) and Associate Professor Dr Shuji Shimizu (Kyushu University).

This workshop also witnessed the launch of the 2<sup>nd</sup> generation SpyGlass cholangioscopy system in the South East Asia. Dr Amit Maydeo and Professor Dr Jong-Ho Moon captivated the audience during the live demonstration at the ease of use of this 2<sup>nd</sup> generation system compared with its predecessor. A lunch symposium was held on the last day of the workshop to further clarify on this new system and the enthusiasm shown

towards this new system was simply overwhelming. Immediately following this lunch symposium on the last day were 2 more special mini-workshops. One was given by Professor Dato' Dr KL Goh on the use of Hemospray in achieving hemostasis in luminal GI bleeding. The other one was a hands-on workshop on POEM using ex-vivo animal model conducted by Dr Amit Maydeo and his team. Under his guidance, this seemingly easy yet challenging procedure was carried out by the eager participants.



Group photo of Young Consultants and GI Fellows Forum

As in previous years, two other important events that took off a day earlier were the GIA Course and Young Consultants and GI Fellows Forum. GIA course was lined with interesting lectures pertinent to the GIA fraternity. It was organised by Mr Philip Gisan and Sister Malaiyarsi A/P Sellamuthu with the help of course coordinators Dr Chieng Jin Yu and Dr Ruveena Rajaram. Professor Dr Hiroyuki Maguchi was invited as guest faculty. On the other hand, Young Consultants and GI Fellows Forum was a success too. Coordinated by Associate Professors Drs Raja Affendi & Chan Wah Kheong and Dr Ho Shiaw Hooi, the forum drew the participation of close to 30 young consultants and GI fellows. Heated discussion was made even more



Professor Jong-Ho Moon performing SpyGlass cholangioscopy with Dr Sundeep Lakhtakia



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Dr Roy Soetikno performing colonic polypectomy while Professor Kenneth Wang, Dr Christopher Khor and Professor Dato' Dr KL Goh looked on

"fiery" by the presence of guest faculties, Dr Christopher Khor and Dr Roy Soetikno who were very critical with the management plan presented. The group truly benefited from the discussion and from the experience shared by the guest faculties.

Trade exhibition was another success. Held throughout the period of the workshop, more than thirty companies participated and showcased their products. On a lighter side of things, friendship was rekindled and made during the GIA "Get Together" Dinner and the Workshop Dinner. The participants truly enjoyed a wonderful evening of fine dining and great performance. Overall, Endoscopy 2015 achieved its purpose. Passion in therapeutic endoscopy was reignited and the participants went back with updated knowledge and skills. We sincerely owe our success to the distinguished faculty, the organising committee (including the many coordinators, moderators, doctors, nurses and support staff), the sponsors and last but certainly not least, the participants. We look forward to yet another successful workshop next year.

Report prepared by Dr Ho Shiaw Hooi Photos contributed by Dr Alex Leow



Dr Amit Maydeo demonstrating the technique of POEM during hands-on POEM workshop



Group photo of hands-on POEM workshop

## The MSGH Updates in Gastroenterology and Hepatology 19th October 2014, KL Hilton Hotel & 4th April 2015, Alor Setar

Once again the Society has successfully conducted two GI updates since the last bulletin. The GI Updates (aka Klang Valley meetings) provide a platform where both GI and surgical trainees come together to present and highlight interesting cases from their respective hospitals.

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The first GI update was held on the 19<sup>th</sup> October 2014 at KL Hilton Hotel. A total 7 presenters and 30 participants attended the meeting. Various cases were presented by the trainees with Datuk Ahmad Shukri sharing his experience in using the Over the Scope Clip (OTSC) in managing anastomotic leak and bleeding duodenal ulcer patients in Hospital Sultanah Nur Zahirah.



The second GI Updates was held on the 4<sup>th</sup> April 2015 at Sultanah Bahiyah Hospital in Alor Setar Kedah. This meeting was successfully conducted by Dato Muhammad Radzi and his team- Dr Kiew Kuang Kiat and Dr Zalwani. The GI update was held outside the Klang Valley for the first time to give trainees outside the Klang Valley an opportunity to participate in these meetings.

The meeting was an overwhelming success with a total of 12 presenters and over 50 participants. All the cases presented were both interesting and challenging. Various cases were presented which included pyloric intussusceptions, abdominal actinomycosis, intestinal amoebiasis and many more.

A comprehensive review of how to use manometery to interpret various oesophageal diseases was presented by Dr Ngiu Chai Soon from UKM Medical Centre whereas Dr Chan Ping Kiat gave a lecture and shared his experience on the Role of Interventional Radiology in GIT bleed.



Well done to all the trainees that participated in both these meetings. A very special thank you to Dato Muhammad Radzi and his team who helped conduct the meeting in Alor Setar successfully. We hope to conduct more of these meetings outside the Klang Valley in the near future!

Associate Prof Dr Hamizah Razlan



"Bringing Gastroenterology to the Rural People of Sabah" Bringing the Teropong to the Masses; The 4<sup>th</sup> Endoscopy and Ultrasound Camp 2014 - Telupid and Beluran District in Sabah 2014

> Reported by Dr M Vinod Kumar & Dr Ngo Choon Woon Department of Surgery, Hospital Duchess of Kent, Sandakan, Sabah



Frontal view of Primary Health Clinic at Telupid, with a back drop of setting Sun showing its hues.

A 70 year old Mark (true name concealed to protect his identity) had visited Hospital Beluran every 4 months for the last 10 years for his dugal. Dugal is Sabahan lingo for heartburn. ECGs were done at each visit and heart attack was ruled out. Other differentials were systematically dismissed before settling on dydpepsia for which he received oral antacids and histamine 2 receptor antagonists. The attending doctors had repeatedly counseled him for teropong or oesophagogastroduodenoscopy (OGDS) to investigate the cause for his dyspepsia. But Mark hadn't the resources for the trip to Sandakan to get it done at the specialist hospital - the Duchess of Kent Hospital (DOKH).

However from a fortunate turn of events, Mark and 61 other rural folks from both districts of Beluran and Telupid recently received expert consultations when general surgeons, Ms Salina Bt Aziz (DOKH), Mr Lai Chung Ket (DOKH), Mr Mohd Syahrir Sukarno (Tawau General Hospital) and Mr Abang Mohammad Affendi Bin Abang Yusop (Lahad Datu Hospital) led by Mr Vinod Mutyala Kumar, Head of Department of



Dr Afiza Hanun Binti Ahmad Family medicine specialist Telupid with Dr Supathiratheavy Rasiah Director Hospital Duchess of Kent, Sandakan sharing a pleasant moment. Onlookers Mr Ali Abdulla PPP Anaesthesia, Dr Dayaabaran SUMO, Mr Lai Chung Ket Specialist Surgeon.



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One of the patients blowing into the collapsed special balloon after deep inspiration, until its fully bloated for Urea Breath Test.

General Surgery DOKH visited the Beluran Hospital and Telupid Clinic. Dr Teo Han Liang from DOKH Radiology Dept joined the delegation to conduct hepatobilliary system ultrasound scans for all the patients.

The Telupid clinic edition on 28<sup>th</sup> August 2014 had 42 patients while the Beluran hospital edition on 29<sup>th</sup> August 2014 had 20 patients. Courtesy of the good people from Avro Medical Sdn Bhd who brought to the camp 5 of their Pentax OGDS systems, the surgeons enjoyed rapid turnover in scoping the patients enrolled. District medical officers face impossible challenges in referring rural folk to specialist hospitals given these patients have financial and transport difficulties. Hence they had delightfully enrolled the 62



Mr Vinod Kumar performing the upper endoscopy with patient sitting comfortably in a wheel chair.

patients of the camp for various indications from heartburn to vomiting blood.

The camp in its 4<sup>th</sup> edition is the brainchild of Mr VM Kumar. He had been at every one since its inception 2 years ago; at hand diligently guiding the surgeons through their scopes as well as providing expert opinions on management of the patients enrolled.

Mark unfortunately turned out to have gastric cancer vividly revealed on the screen during his OGDS. He was promptly transferred to DOKH where he underwent further imaging, gastrectomy and is now undergoing chemotherapy.



At the end of the day a group photo with all smiles for the successful completion of the camp, exposing all to harsh realities of village life.

# EndoQE 2015 - The 2<sup>nd</sup> Sabah International Endoscopy Workshop

#### 10<sup>th</sup> - 13<sup>th</sup> September 2015

The Gastroenterology unit of the Department of Medicine, Queen Elizabeth Hospital, Kota Kinabalu, Sabah will be organising EndoQE 2015, the second Sabah International Endoscopy Workshop from 10<sup>th</sup> September 2015 till 13<sup>th</sup> September 2015. The first Sabah International Endoscopy Workshop, ie EndoQE 2014, was a resounding success last year with a "Hands-on" Workshop that focussed on teaching Gastroenterology Fellows the finer points of ERCP and EUS.

EndoQE 2015 will whet the appetite of Gastroenterologists, Gastroenterology Fellows, Gastrointestinal Assistants (GIAs), Physicians and Surgeons alike for all that's new in Endoscopy. At the same time it will emphasise the basic principles of sound endoscopic practice. It is being held in collaboration with the MSGH, EUS-TAP (EUS Task Force Asia-Pacific) and WIGNAP (Women in Gastroenterology Asia-Pacific), all of which are leading drivers for Gastroenterology and GI Endoscopy in this region. Our theme is "The Borneo Endoscopy Adventure" and we promise that it will be both educational and exciting.

Our stellar Faculty is our main draw. Headlining the show will be two living legends in GI Endoscopy and Gastroenterology ie Nageshwar Reddy from Hyderabad and David Carr-Locke from New York. Dr Reddy is current President of WEO (World Endoscopy Organisation) and Dr Carr-Locke was Past President of the ASGE (American Society for Gastrointestinal Endoscopy). Their mastery of ERCP is internationally acknowledged. We also have an array of outstanding experts in EUS. Dr Benedict Devereaux from Brisbane, Dr Payal Saxena from Sydney, Dr Roy Soetikno from Singapore, Dr Ryan Ponnudurai and Dr Sharmila Sachithananthan from Malaysia will headline the EUS cast. We also have a special workshop on advanced endoscopy imaging helmed by Dr Rajvinder Singh from Adelaide who is reknowned for his work on optical-enhanced endoscopy imaging.

The programme will be spread over 4 days. On 10<sup>th</sup> September 2015 we begin with the GIA Conference which is strongly encouraged for all GIAs. It covers a wide spectrum of areas of particular relevance to GIAs. They will have the distinct privilege of being lectured by our Faculty members. This will be followed by the GIA Dinner in the evening.

On 11<sup>th</sup> September we will have a series of State-of-the-Art Lectures by our Faculty. This will focus on key areas in Endoscopy and Gastroenterology. It will also feature a WIGNAP symposium. In the afternoon we will have a "Hands-on" EUS and ERCP Workshop for the GI Fellows. All GI Fellows are strongly encouraged to participate in this invaluable training session mentored by some of the luminaries of GI Endoscopy.

On 12<sup>th</sup> September we will have LIVE Endoscopy featuring a wide-spectrum of cases and therapeutic endoscopic procedures performed by our Faculty. In the evening there will be a Workshop Dinner featuring a not-to-be-missed lecture on the future of Endoscopy by Nage Reddy himself.

We will round it up on 13<sup>th</sup> September with a Workshop on Advanced Endoscopy Imaging Workshop focussing on Colonic polyp imaging as well as advances in Barret's oesophagus. It will be helmed by Dr Rajvinder Singh, an expert on optical-enhanced imaging. It will be of great benefit to GI Fellows and endoscopists alike.

We would strongly encourage everyone in the GI Endoscopy fraternity to attend EndoQE 2015 and avail themselves of the various tourist attractions of the Land Below the Wind. Selamat Hari Raya!

Datuk Dr Jayaram Menon Organising Chairman EndoQE 2015 Queen Elizabeth Hospital, Kota Kinabalu



## My Gastroenterology Fellowship Experience - A Tale of Two Cities By Dr Nazri Mustaffa, Consultant Gastroenterologist, HUSM

It all started at APDW 2010 in Kuala Lumpur.

I had always wanted to do a Gastroenterology-related PhD. I however was worried that doing so would interfere with my Gastroenterology training, as this would mean that I would not be able to properly complete this and proceed with the Gastroenterology Subspecialty registration process later on. Nevertheless, after much consultation with several senior Gastroenterologists I decided to continue my pursuit of obtaining a PhD in order to boost my academic credentials. Luck was on my side as Dr Tee Hoi Poh from Kuantan mentioned that his previous supervisor Prof Rupert Leong, a Gastroenterologist from Sydney was looking for a candidate to take up an inflammatory bowel disease-themed PhD. It so happened that Rupert would be attending the upcoming APDW to be held in Kuala Lumpur, and after several emails he agreed to meet me there to discuss my plans in further detail.



Photo with Prof Ida Normiha Hilmi and Prof Rupert Leong

From September 2010 we fast forward to August 2011. Through Rupert, an arrangement was made where I would initially spend time in Sydney followed by a Gastroenterology Fellowship in University Malaya under the general supervision of Prof Dato KL Goh, with Prof Ida Hilmi supervising the IBD-related content of my training. This would then culminate with a laboratory-based period where I would focus on analysing the IBD samples I had collected, generating data for my PhD.

Thus began my adventure. From August 2011-2012 I was attached to the Gastroenterology and Hepatology Department of the Concord Repatriation General Hospital (CRGH) in Sydney, New South Wales, Australia. As I was doing a PhD on IBD, I focused on patients who attended the IBD clinic at CRGH as well as those who needed ward admission for IBD-related issues. I was also exposed to daycare patients who had infliximab infusions as part of their IBD treatment regime. Apart from this I also attended the weekly combined Gastroenterology meeting on Thursday mornings (where there would be input from the radiology and histopathology teams), as well as the Gastroenterology and Hepatology CME presentations which would be held immediately after the morning meeting. Interestingly, for the CME meetings there would always be two presenters: a short introduction by the Consultant Gastroenterologist, followed by a more in-depth talk on the selected topic by their Gastroenterology Fellow. Prof Peter Katelaris for example, started out by talking about the

history of CRGH itself, how it began as the Thomas Walker Convalescent Hospital which then became the Yaralla Military Hospital. Also known as 113 Australian General Hospital, it was the largest hospital in the Southern Hemisphere during the Second World War. Following the war, it became a repatriation hospital for returned servicemen and thus the hospital's name was changed to reflect this. Unfortunately I have no recollection of what his trainee talked about on that day. I would also be present during Rupert's endoscopy list on Fridays. After obtaining my IBD samples I would then travel to my laboratory at the Centenary Institute, located within the Royal Prince Alfred Hospital grounds in Sydney city itself. The rest of the day would be spent processing and storing the samples for analysis later on.

From September 2012 until December 2013 I was attached to the Gastroenterology and Hepatology Unit at the University Malaya Medical Centre (UMMC), Kuala Lumpur. As mentioned earlier, Prof Dato KL Goh, as Head of Unit was my overall supervisor whilst Prof Ida Hilmi specifically supervised my IBD-related training. Apart from the usual endoscopic and ward duties, I also attended the Gastroenterology and Hepatology Clinics specifically focusing on patients with IBD. Occasionally on Tuesday afternoons after clinics there may be short talks on medical devices or related newer medical therapy. On Wednesday afternoons during lunchtime there would be the Gastroenterology and Hepatology Radiology meeting where both the surgical and medical teams would come together and decide on further patient management, based on input from the Radiologists. Thursday mornings there would be short CME presentations by either one of the Consultants or Fellows prior to starting the therapeutic endoscopy list. If there were samples collected I would then proceed to the Medical Microbiology Laboratory, located in the adjacent building next to the Endoscopy Suite to further process and store them prior to analysis.



Photo with the Master, Prof KL Goh

Following this I returned to Sydney to analyse my samples. I am currently in the process of finalising my thesis, and am grateful to all my supervisors for giving me the opportunity to train under them as well as being able to learn from their wealth of knowledge. To a certain degree there have been periods that parallel the famous opening line to A Tale of Two Cities: "It was the best of times, it was the worst of times". Nevertheless, I can proudly say that I have gone through all this, making me a better person in preparation for a lifetime career in Gastroenterology.

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#### Application of Next Generation Sequencing in Gastrointestinal Diseases

Norfilza M Mokhtar, MD PhD<sup>1,3</sup> & Raja Affendi Raja Ali, MD FRCP (Edin)<sup>2,3</sup>

#### <sup>1</sup>Department of Physiology <sup>2</sup>Gastroenterology Unit, Faculty of Medicine <sup>3</sup>Medical Molecular Biology Institute, UKM Medical Centre, Kuala Lumpur

Recent approaches towards understanding gastrointestinal diseases have transformed enormously for many years. It began with a comprehensive study of a single gene to an array of thousands of genes in association with the completion of the first era of the Human Genome Project in 2003. The application of next generation sequencing in human diseases can be translated into clinical practice with the aim to dissect the molecular details of the diseases and relate with the prognosis of the disease and therapeutic response.

The application of next generation sequencing has provided the real picture of human genome in order to understand the molecular networks in the normal cells as well as in the diseases. The technology has led to the so called 'personalised medicine', whereby the clinicians are trying to match the treatment with the disease characteristics using the information from the DNA sequencing.<sup>1</sup> The newer version of sequencing has massive improvements in term of the total cost, timing and sample preparation as compared to the conventional sequencing. The recent focus in research is to analyze the massive sequencing data and trying to answer multiple research questions. However until today, there are still major hurdles in translating the findings obtained from the laboratory to the clinical settings.

The application of the new technology has discovered novel mutations in the commonest gastrointestinal disease, which is colorectal cancer. The accepted fact on the formation of this cancer is that it is a result of an accumulation of several genetic and epigenetic alterations.<sup>2</sup> Our group has recently characterised colorectal cancer using two types of microarray i.e. gene expression and copy number variation profling and revealed 56 overlapping genes that reside within chromosome 8, 20 and 22.<sup>3</sup> The accumulation of genomic alterations, which are hypothesised to be induced by genomic instability.<sup>4</sup> Genomic instability will increase the tendency of the genome to acquire mutations, which will affect several important processes in maintaining and replicating the

#### References

- 1. Shendure J, Ji H. Next-generation DNA sequencing. Nat Biotechnol. 2008 Oct;26(10):1135-45.
- 2. Fearon ER. Molecular genetics of colorectal cancer. Annu Rev Pathol. 2011;6:479-507.
- 3. Ali Hassan NZ, Mokhtar NM, Kok Sin T, Mohamed Rose I, Sagap I, Harun R, et al. Integrated analysis of copy number variation and genome-wide expression profiling in colorectal cancer tissues. PLoS One. 2014;9(4):e92553.
- 4. Al-Sohaily S, Biankin A, Leong R, Kohonen-Corish M, Warusavitarne J. Molecular pathways in colorectal cancer. J Gastroenterol Hepatol. 2012 Sep;27(9):1423-31.
- Xu Z, Huo X, Tang C, Ye H, Nandakumar V, Lou F, et al. Frequent KIT mutations in human gastrointestinal stromal tumors. Sci Rep. 2014;4:5907.

genome. Using this knowledge, DNA sequencing using Ion Torrent next generation sequencing platform focusing on 45 cancer-related genes was performed on gastrointestinal stromal tumours (GIST).<sup>5</sup> KIT was found to be the most frequently mutated gene among these patients. Patients with GIST harbor KIT mutation at exon 11 responded better to the tyrosine kinase inhibitor such as Gleevec.<sup>6</sup>

A few years back, genome wide association study (GWAS) was considered as the most powerful tool to study the association between phenotypes and genotypes and also to identify common, low-penetrance susceptibility loci in a particular disease. Several loci were identified to be associated with colorectal cancer for example long arm of chromosome 8 (8q24 (128.1-128.7 Mb, rs6983267).<sup>7</sup> This finding was made known to the clinicians in order to detect the disease at an early stage and can be treated with full recovery. With the Next Generation Sequencing platforms, the diseases can be classified based on their molecular subtypes, resequencing of whole genome or targeted for discovery of mutation or polymorphism.<sup>8</sup>

For a better understanding in terms of the strengths and limitations of next generation sequencing, we need to understand biological and informatics challenges and caveats. Sampling issues such as biopsy method and contamination from neighbouring tissues may seriously affect in the sequencing data. It is important to select biologically homogenous sample populations, balancing a design with respect to all factors that can confound results among the comparison groups, and handling samples uniformly through the course of the entire experiment when designing a sequencing experiment. The second challenge is the bioinformatics analysis of the data. There is still a problem in the clinical decision-making especially for the mutations that are novel and no actionable strategies. However, additonal information based on the previous literatures may help to link the mutations with druggable pathway. It is necessary for the clinicians or scientists to put aside money to be spent for downstream experiments to ensure that the mutations are pathological.

- Heinrich MC, Corless CL, Duensing A, McGreevey L, Chen CJ, Joseph N, et al. PDGFRA activating mutations in gastrointestinal stromal tumors. Science. 2003 Jan 31;299(5607):708-10.
- 7. Gerber MM, Hampel H, Schulz NP, Fernandez S, Wei L, Zhou XP, et al. Evaluation of allele-specific somatic changes of genome-wide association study susceptibility alleles in human colorectal cancers. PLoS One. 2012;7(5):e37672.
- Voelkerding KV, Dames S, Durtschi JD. Next generation sequencing for clinical diagnostics-principles and application to targeted resequencing for hypertrophic cardiomyopathy: a paper from the 2009 William Beaumont Hospital Symposium on Molecular Pathology. J Mol Diagn. 2010 Sep;12(5):539-51.

# **CALENDAR OF EVENTS**

MSGH BULLETIN

## **NATIONAL EVENTS**

The GUT Meeting Date: 21<sup>st</sup> - 23<sup>rd</sup> August 2015 Venue: Persada Johor International Convention Centre

## **INTERNATIONAL EVENTS**

United European Gastroenterology Week (UEGW) Date: 24<sup>th</sup> - 28<sup>th</sup> October 2015 Venue: Barcelona

# The American Association Study of Liver Diseases (AASLD)

Date: 13<sup>th</sup> - 17<sup>th</sup> November 2015 Venue: Moscone West Convention Center San Francisco, California

The Gastro 2015: The World Gastroenterology Organisation (WGO) and the Gastroenterological Society of Australia (GESA)

Date: 28<sup>th</sup> September - 2<sup>nd</sup> October 2015 Venue: Brisbane Convention and Exhibition Centre, Australia

> Asia Pacific Digestive Week (APDW) Date: 3<sup>rd</sup> - 6<sup>th</sup> December 2015 Venue: Taiwan