



APFCB News

The Newsletter of the Asia-Pacific Federation for Clinical Biochemistry
and Laboratory Medicine for circulation among APFCB and IFCC members

2017
Issue 1

一九九七年
十二月
二日

Publication Team, 2017 Issue 1

Chief Editor	Praveen Sharma Jodhpur, India praveensharma55@gmail.com
Immediate past Chief Editor	Joseph Lopez Kuala lumpur, Malaysia jblopez2611@gmail.com
General and Case Studies Editors	Leslie Lai Kuala lumpur, Malaysia lesliecharleslai@gmail.com
	Tester Ashavaid Mumbai, India tashavaid@gmail.com
	Aysha Habib Karachi, Pakistan aysha.habib@aku.edu

APFCB Membership

Members

Australasian Association of Clinical Biochemists (AACB)
Association of Clinical Biochemists of India (ACBI)
Association for Clinical Biochemistry, Sri Lanka (ACBSL)
Chinese Society of Laboratory Medicine (CSLM)
Chinese Association for Clinical Biochemistry, Taiwan (CACB)
Hong Kong Society of Clinical Chemistry (HKSCC)
Indonesian Association for Clinical Chemistry (IACC)
Iranian Association of Clinical Laboratory Doctors (IACLD)
Japan Society of Clinical Chemistry (JSCC)
Korean Society of Clinical Chemistry (KSCC)
Malaysian Association of Clinical Biochemistry (MACB)
Mongolian Association of Health Laboratories (MAHL)
Nepal Association for Medical Laboratory Sciences (NAMLS)
Pakistan Society of Chemical Pathologists (PSCP)
Philippine Association of Medical Technologists (PAMET)
Singapore Association of Clinical Biochemistry (SACB)
Thailand Association of Clinical Biochemists (TACB)
Vietnamese Association of Clinical Biochemistry (VACB)

Affiliate Members

Association of Medical Biochemists of India (AMBI)
College of Community Physicians of Sri Lanka (CCPSL)
Chinese Association of Clinical Laboratory Management CACLM)
Macao Laboratory Medicine Association (MLMA)
Nepalese association of Clinical Chemistry (NACC)
Philippine Council for Quality Assurance in Clinical Laboratories (PCQACL)

Corporate Members

Abbott Diagnostics
Beckman Coulter
Becton Dickinson
Bio-Rad
Diasorin Ltd
Diasys Diagnostic Systems, GmbH
Kopran Laboratories Ltd
Mindray
Ortho-Clinical Diagnostics
Randox Laboratories
Roche Diagnostics
Sekisui Medical Co Ltd.
Siemens Healthcare Diagnostics
Sukraa Software Solution Pvt. Ltd.
SYSMEX
Technidata Medical Software
Wondfo Guangzhou
Snibe

APFCB Executive Board and Chairmen
Of Committees, Elected November, 2016

Executive Board

President	Sunil K Sethi Department of laboratory medicine National University Hospital, Singapore sunil_sethi@nuhs.edu.sg
Immediate Past President	Leslie Lai Gleneagles , Kuala Lumpur, Malaysia lesliecharleslai@gmail.com
Vice-President	Endang W. Hoyaranda Prodia Group, Jakarta, Indonesia endang.hoyarnda@prodia.co.id
Secretary	Helen Martin Unit Head Toxicology, Chemical Pathology, SA Pathology Helen.Martin2@sa.gov.au
Treasurer	Leila Florento leilaflorento@gmail.com
Corporate Representative	Alexender Wong Siemens Healthcare Diagnostics Holding GmbH, Germany alexander.wong@siemens.com

Chairman of Committees

Communications	Praveen Sharma India praveensharma55@gmail.com
Education & Laboratory Management	Tony Badrick Australia Tony_Badrick@snp.com.au
Scientific	Kiyoshi Ichihara Japan ichihara@yamaguchi-u.ac.jp
Congress and Conference	Elizabeth Frank India anet21frank@gmail.com

Submissions

The APFCB News welcomes suitable contributions for publication. These should be sent electronically to the Chief Editor. Statements of opinions are those of the contributors and are not to be construed as official statements, evaluations or endorsements by the APFCB or its official bodies.

Cover page: "Beautiful Terraced Ricefields in China".
Contributed by Tan It Koon
Founding and Past President APFCB

Address

The registered address of APFCB is as follows:
APFCB, c/o Solid Track Management Pte Ltd.
150 Cecil Street, #10-06, Singapore 069543
Tel: 6223 9118 Fax: 6223 9131

Contents

From the desk of Chief Editor – Praveen Sharma	01
Message from APFCB President – Sunil Sethi	02
Member Societies – Annual activities reports 2017	
Australasian Association of Clinical Biochemists(AACB)	04
Chinese Society of Laboratory Medicine (CSLM)	10
Hong Kong Society of Clinical Chemistry (HKSCC)	12
Indonesian Association for Clinical Chemistry (IACC)	15
Singapore Association of Clinical Biochemistry (SACB)	17
Features	
Scientific article: Molecular Diagnosis and Cancer	20
Beautiful Terraced Ricefields in China – Tan It Koon	31



From the desk of Chief Editor

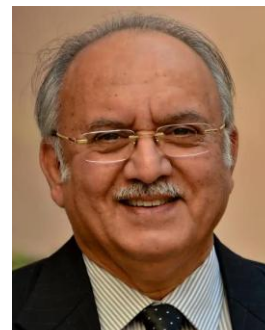
Dear Colleagues,

Greetings!

It is my pleasure to take you through the first issue of APFCB News 2017 which highlights the major activities occurring in the various member societies during the first half of the year. The idea of coming up with two issues is to cover maximum events occurring in each member societies. There are many activities occurring right through the year and not all could find space in an annual issue. The first issue although a small one, has proven to be important one with many member societies actively sending their half yearly reports. I take this opportunity to thank all member societies and national representatives who have sent their contributions. I would also like other member societies and corporate members to contribute and make optimal use of the biannual publishing issues.

The cover page of the APFCB news 2017 issue 1 is a painting by the founding President Prof Tan It Koon. It shows "Beautiful Terraced Rice-Fields in China". There is a write up describing the painting by Prof Tan It Koon. We have been extremely fortunate to have consistently got his support and he has been an active contributor to the progress and development of APFCB. I'm thankful to him for providing beautiful paintings from his art treasure since APFCB News 2010.

Praveen Sharma
Chief Editor



Message from APFCB President...



Dear friends and colleagues,

I am delighted to be able to share this first 2017 APFCB e-Newsletter with all of you. I would like to thank Professor Praveen Sharma and the editorial team for putting together, yet another well-constructed update from the various national societies of the APFCB.

2017 has signaled a change in APFCB administrative management. Following the elections of November 2016 in Taipei, Taiwan, the new Executive Board took office on 1 January 2017. There were immediate housekeeping issues like change in banking signatories and corporate secretariat functions. We also recently managed to activate electronic banking to facilitate efficient banking transactions.

The APFCB EB and available appointed Committee Chairs met in Singapore in February 2017 to map out the strategy and proposed activities for the year. Each committee was tasked with continuing the good work of the past administration as well as to kick off new initiatives.

I am proud to announce the second APFCB-MACB Chemical Pathology course to be held over two days in Kuala Lumpur, Malaysia. The programme is wide ranging and will cover topics on statistics, core clinical biochemistry and laboratory automation, point of care testing and clinical case studies. This is an excellent learning opportunity and refresher course for all of us working in this field of healthcare. I have no doubt that this event will be a resounding success.

Another upcoming scheduled activity is the 2nd APFCB-SACB-Siemens Specialty Meeting on Laboratory Excellence. This half day meeting in Singapore is in late September and will capitalize on the expertise of the College of American Pathologists (CAP) faculty who would be travelling to the region. I would like to thank Siemens Healthiness for their support in the organization and execution of the event.

My heartiest congratulations to Anil Gautam, from the Department of Medical Laboratory Science.

Faculty of Health Science, Pokhara University, Kaski, Nepal. Anil is the proud recipient of the APFCB-AACB Travel Scholarship. He will be supported to attend the 55THAACB Annual Conference in Melbourne, Australia in September 2017.

The APFCB is also collaborating with other global federations and societies and we have very strong links the IFCC, AACC and WASPaLM.

The APFCB will be supporting a symposium entitled 'Informatics and Laboratory Results' at the 29THWASPaLM World Congress in Kyoto, Japan in November 2017. There are a number of ongoing projects under discussion with our global partners and many APFCB member societies will benefit from scientific and technical workshops planned for 2018 and 2019.



The APFCB EB recognizes the value of collaboration and look forward to working with every member society to bring scientific and academic events to local participants. I urge everyone within the APFCB region to actively participate in your national and regional events.

I wish everyone a happy and successful year ahead!

Best regards

Sunil Sethi
President APFCB





Australasian Association of Clinical Biochemists (AACB)

Activity report for January – June 2017 by Helen Martin, President AACB

Current Council members

President: Ms Helen Martin

Vice President – Finance, Planning and Branches: Mr Bruno Sonza

Vice President – Education and Training: A/Prof Ken Sikaris

Vice President – Scientific and Regulatory Affairs: Ms Maxine Reed

Vice President – Media and Communications: Dr Peter Vervaart

Chair, Board of Examiners: Mr. Greg Ward

Branch Representatives to Council

New South Wales & Australian Capital Territory (NSW & ACT): Mr. Peter Ward

New Zealand (NZ): Dr. Samarina Musaad

Queensland (QLD): Ms. Kate Waller

South Australia and Northern Territory (SA & NT): MS Aida Mulabecirovic

Tasmania (TAS): Mr. Robert White

Victoria (VIC): Ms. Intissar Bittar

Western Australia (WA): Mr. William McConnell

Council meeting

Council met at the national office in Sydney on the weekend of 1st and 2nd April with strategic objectives being reviewed on the Saturday and general business conducted on the Sunday. At the strategic planning meeting there was a great deal of discussion about the “Value of Pathology” and how we can more effectively demonstrate this to those paying for the knowledge we provide.

Branch Activities

Roman Lecture

The feature event for State and Territory Branches during the first half of this year has been the Roman Lectureship. This lecture has been awarded annually by the AACB since 1973 and is named in honour of Dr Wadim Roman, a founding father of the AACB. Dr Roman was a gifted scientist with deep knowledge in many areas of Clinical Biochemistry but more important, he was a dedicated promoter of education for young scientists and it is this passion that is most honored by this travelling lectureship.

This year's recipient is Jill Tate, a Senior Scientist at the Pathology Queensland Department of Chemical Pathology at the Royal Brisbane and Women's Hospital in Brisbane, Australia. Jill is well known internationally for her work with IFCC committees and working groups, most recently as the Chair of the working group for the Standardization of Cardiac Troponin I (IFCC WG-TNI). Nationally she is known for her significant contributions to AACB particularly as the Chair of the Harmonisation Committee which is working on a range of harmonization activities including common reference intervals, standardised units, terminology and reporting in pathology, and critical laboratory results. Jill's 2017 Roman Lecture was entitled “The Paraprotein, an enduring biomarker, a thoughtful, entertaining and comprehensive



look at the contribution of paraprotein measurement and typing in the diagnosis and management of myelodyscrasias from the 1960's to today. She also brought us up to date with laboratory requirements in meeting the latest Multiple Myeloma clinical guidelines.

NSW & ACT

February: Clinical review & BBQ.

Complement and its clinical relevance "Dr. Ari Murad"

Autoimmune presentations in children "Dr Melanie Wong"

Graves Disease and Mab. "Prof Huy Tran"

March: Laboratory Interferences: Handling the seen and the unseen "Prof Graham Jones"

April: Industry update with presentations from Beckman-Coulter, Bio-Rad, Roche and Siemens

May: Roman lecture. Jill Tate

June: NSW Posters from 2016 AACB Annual Scientific Meeting. Various presenters.

NZ

June 1st: scientific education seminar "The Eclectic World of Clinical Chemistry was held in Auckland"

Full day meeting with sessions on Troponin, mass spectrometry, point of care testing, and cases presented by young scientists.

QLD

March: Posters and presentations from 2016 AACB Annual scientific meeting

July: 15-16th Weekend meeting Saturday 15th

One Note - uses and applications

Reproductive Hormones

Thyroid function and testing

Calcium Phosphate regulation Sunday 16th

SA & NT

February: Clinical cases - Dr Devika Thomas

March: Clinical cases from the Northern Territory. Dr Geetha Rathnayake

April: Adolescent PCOS - Dr Alexia Pena

May: Roman Lecture. Jill Tate

June: Young scientist's presentations. *Shayne Wallis (winner)*, Narelle Burke, Yuze Goa, Khoa Lam

July: OGM and quiz night. Teams compete for "The Golden Pipette"

TAS

Weekend meeting was held 15-16th July at the White Sands Estate in Iron house Point.

VIC

February: Cases in clinical biochemistry. Various presenters

March: Fluids survey. John Calleja

April: Dr Ann Read - Career celebration and dinner

May: QC for the 21st Century. Dr Tony Badrick

June: AGM and Laboratory visit to the new Peter MacCallum and Victorian



Comprehensive Cancer Centre
July: Roman lecture – Jill Tate

WA

March: Physiology of Pregnancy – new insights into hCG and relaxin
“Dr Narelle Hadlow”
April: Back to Basics – pre-analytical factors. Brian Smith and Conchita Boyder
May: Roman Lecture. Jill Tate
June: Alzheimers research update “Dr John Mamo”
July: OGM

National Meetings

Chemical Pathology Course – 6th–10th February 2017

The AACB–RCPA Chemical Pathology Course is the national educational highlight of the first half of our calendar year. The organizing committee, chaired by Robert White, provided a comprehensive program covering a wide range of exam curriculum topics as well as a number of interactive sessions. The interactive quiz (which was a popular addition to the 2016 course) was provided for the Hobart meeting, and ran at the end of each day. This proved very popular and a great way to review the day’s talks. This year, 123 delegates from 7 countries attended the course held in Hobart at the Wrest Point Convention Centre on the picturesque shores of Sandy Bay. Scholarships to support attendance were awarded to:

Program

Monday 6th Morning sessions

Options for professional qualifications “Mr. Greg Ward”
Photometry “Mr. Dale Kunde”
HPLC. Mr. Steven Weier
Thyroid disease in pregnancy “Dr Thomas Cade”
Markers of Pre-eclampsia “Prof Shaun Brennecke”
Neonatal hypoglycaemia “D Tina Yen”

Monday 6th Afternoon sessions

Standardisation Harmonisation and Traceability “Mr. David Hughes”
Method comparison and reference intervals “Ms Kate Waller”
External QA Mr. Peter Graham
Quiz day1
Meet the Examiners “Mr. Greg Ward”
Window on a viva voce exam “Mr. Greg Ward and Ms Helen Martin”

Tuesday 7th Morning sessions

Calcium, magnesium and Phosphate “Prof John Burgess”
Vitamin D and PTH and Prof Howard Morris
Bone markers “Dr. Penny Coates”
Cystic fibrosis Daignosis and management “Prof Francis Bowling”
A devil of a disease “Dr Bruce Lyons”
Bile acid metabolism in health and disease “Prof Fancis Bowling”



Tuesday 7th afternoon sessions

Markers of acute kidney damage "Dr. Richard Yu"

Water and sodium/potassium "Mr. Dale Kunde"

Acid-base regulation "Dr Sam Hitchins"

Quiz day2

Breakout sessions: Cases

Session 1 "Mr. Rob White and Dr udayan Ray"

Session 2 "Ms. Helen Martin"

Session 3 "Dr Tina Yen"

Wednesday 8th morning sessions

Lead poisoning and heavy metals "Dr Wayne Rankin"

The unconscious/ poisoned patient "Dr Doug Chesher"

Digoxin Ms Joanne Webb

Troponins "Dr Brian Doyle"

Natriuretic peptides "Mr Steven Weier"

Quiz day3

Wednesday 8th afternoon – free time**Thursday 9th morning sessions**

Acute hepatitis and vial serology "Ms Belinda Chamley"

NAFLD/NASH "Dr Ros Malley"

The metabolic syndrome. Dr Udayan Ray

Diabetes mellitus and Ms Elizabeth Byrnes

HbA1c and the diagnosis and monitoring of Diabetes Mellitus "Ms Kate Waller"

Folate "Me Rob White"

Thursday 9th afternoon sessions

Biochemical investigation of hypertension "Dr Wayne Rankin"

Bioenic amines/carcinoid Dr Louise Prentice Quiz day 4

Friday 10th morning sessions

Emerging technologies "Dr Peter Vervaart"

Anit – mullerian hormone "Prof Venkat Parameswaran"

Sweat testing "Dr Susan Matthews & Ms Angela Chiriano"

RCPAQAP survey report interpretation "Ms Samantha Shepherd"

RCPAQAP End of cycle report interpretation "Mr Wilson Punyalack"

Quiz day 5

Harmonization Workshop 17–18th May**Holiday Inn Sydney Airport**

AACB has been actively working to promote harmonized laboratory practice since 2011. Annual workshops have been held since 2012 to facilitate achieving harmonized reference intervals and promote harmonized laboratory practice throughout Australia. Previous workshops have achieved proposed harmonized RI for many routine chemistry analytes and uptake is ~80% across Australian labs.

Areas for discussion at this particular workshop were:

- Australian TFT reference intervals in pregnancy
- Recalibration changes for TFT assays
- Chemistry reference intervals in pregnancy and adults; Lipid reference intervals



Recommendations for Critical Values

Calculated parameters and outlier removal in reference interval determination
Endocrine dynamic function test protocol harmonisation

Webinars

Webinars for 2017 have been:

February: Common interferences in Laboratory Tests. Maxine Reed

April: Body Fluids survey John Calleja

June: Method validation. Steven Weier

Publications

Clinical Biochemist Newsletter is published quarterly and as the name implies, is principally intended to keep the membership informed about AACB activities; issues this year were released in March and June.

The Clinical Biochemist Reviews is a peer reviewed journal of review style articles also published quarterly; two editions have been produced so far this year.

Volume 38 (i) containing the following articles:

1. Reducing the Environmental Impact of Clinical Laboratories Joseph Lopez et al
2. Working Up a Good Sweat – The Challenges of Standardising Sweat Collection for Metabolomics Analysis. Joy N Hussain et al
3. Molecular Aspects of Wound Healing and the Rise of Venous Leg Ulceration: Omics Approaches to Enhance Knowledge and Aid Diagnostic Discovery. Daniel A Broszczak et al.

1. Volume 38 (ii) containing the following articles:

1. Clinical Utility and Measurement of Procalcitonin. InatanSamsudin, Samuel Vasikaran
2. Metabologenomics of Pheochromocytoma and Paraganglioma: An Integrated Approach for Personalised Biochemical and Genetic Testing Graeme Eisenhofer et al.
3. The Management of Post Analytical Correction Factors Roger Barton et al.





AACB Hosts National Workshop on the “Value of Pathology”

Healthcare organizations throughout the world are discussing the sustainability of healthcare given the present trend of ever increasing costs and increasing awareness of the potential harm for patients.

The prime goals of these discussions were firstly to identify and focus on value of healthcare as opposed to activity and secondly to consider funding models which would support a value-based approach. The AACB hosted a national Workshop to provide a forum for discussion of these issues in relation to pathology. Thirty delegates included pathology professionals together with a strong delegation from the Australian Government Department of Health, representatives from epidemiology, health economics, radiology, pharmacy, the National Prescribing Service, IVD industry and research academics. Speakers included Dr Megan Kearney, Department of Health, discussing concerns for the current model for clinical laboratory reimbursement and Dr Tony Badrick, National Pathology Accreditation Advisory Council, addressed the view that clinical laboratory needed to transition from a compliance model to a greater focus on risk.

Representatives of international groups working on these issues included Dr Paul Epner, Society to Improve Diagnosis in Medicine; Professor Howard Morris, IFCC–WASPaLM Joint Committee on Value of Laboratory Medicine and Professor Rita Horvath, EFLM Committee on Test Evaluation presented on their activities. Professor Libby Rough head, Research Centre for Quality Use of Medicines, University of South Australia described the parallels between the pressures on pharmacy and laboratory medicine and provided a description of how a value-based model of laboratory medicine might be researched and developed. The delegates workshopped the major issues raised by the presentations and discussion arriving at the conclusion that the two major topics to be addressed are “(1) To develop a centre of excellence for value in pathology research based in a university and” (2) To investigate the extended use of decision support for clinical laboratory test requesting by clinicians. Individuals were assigned to lead these undertakings and it was resolved that the group would maintain this activity under the auspices of the AACB but maintain close collaboration with international work particularly through the international professional organizations IFCC and WASPaLM and regional federations APFCB, EFLM and NAFCC.





Chinese Society of Laboratory Medicine (CSLM)

2016 National Conference

2016 National Conference of CSLM was held on Sep 21–24, 2016 in Chongqing. The conference was highlighted by various forms of academic exchange, including plenary lectures, keynote lectures, satellite meetings, oral presentation and post presentation. The academic committee of the conference received 2,821 abstract submissions. Ninety-three abstracts were selected for oral presentation, among which, thirteen submissions were delivered in forms of English speech contest. Meanwhile, 429 abstracts were presented in the form of posters. After a strict peer review process, the academic committee awarded 31 outstanding posters and 46 excellent research papers and gave three grades of prizes to the competitors in the English speech.

Education

1. The distance training project was co-hosted by Hunan Society of Laboratory Medicine and Jiangxi Society of Laboratory Medicine on April 6, 2016. It is estimated that more than 3000 people participated in the on-line training program.
2. Laboratory Medicine Branch of Provincial (Autonomous regional) Medical Association in western and northeast region co-hosted the remote training project in Yinchuan, Sep 2, 2016. It is estimated that more than 3000 people participated in the on-line training program.
3. On November 18, 2016, Laboratory Medicine Branch of Provincial Medical Association of Yunnan, Guizhou and Sichuan provinces co-hosted the remote training project in Kunming, Guiyang and Chengdu. It is estimated that more than 3000 people participated in the on-line training program.
4. Lab Tests Online CN offers education and information on laboratory tests to help patients better understand their health care. In 2016, CLSM have launched 4 tests and modified 2 conditions.

International relations

On Sep 23, 2016, at the 2016 National Conference of CSLM, AACC task force in Asia-Pacific region have given special reports on Sino-American clinical laboratory education/ training exchanges and quality management in medical laboratory, which offered opportunities for us to learn about the education, qualification certification, responsibilities and management of laboratorians in America, as well as their report model of clinical results and laboratory risk management.



'The Best of AACC China' – the first joint forum of Chinese Society of Laboratory Medicine (CSLM) and American Association of clinical chemistry (AACC) was held on Oct 21–22 in Shanghai, China. The forum is sponsored by the China Medicine Education Association (CMEA), with the vision to augment the academic level of laboratory medicine in China and to promote the international communication between the specialists and scholars. Given the theme of "Rigorous Testing for Precision Medicine", the forum selected the best topics from the 68th AACC annual meeting (2016), featured with clinical molecular diagnostics and mass spectrometry technologies, clinical laboratory management, and trends in laboratory medicine. The conference will provide the experts from both China and United States with a great chance to cooperate and explore the latest research progress in the field of laboratory medicine.

2017 National Conference

By the Chinese Medical Association, Chinese Society of Laboratory Medicine, the thirteenth National Laboratory Medicine Conference (2017 National Laboratory Medicine Conference) will be held Sep 20–23, 2017 in Hangzhou, Zhejiang Province. This large-scale laboratory academic conference will also be China annual inspection of clinical laboratory science.

The Conference will also hold continuing education, photography photo exhibition, and clinical laboratory equipment exhibitions.

Welcome clinicians, researchers and laboratorians to actively participate this event.





Hongkong society of clinical chemistry (HKSCC)

HALF-YEAR REPORT OF 2017

This year started with the Annual Scientific Meeting (ASM) and Annual General Meeting (AGM) of the Hong Kong Society of Clinical Chemistry held on 14 January 2017. The theme of our scientific meeting was "Toxicology and Poisoning in Hong Kong".

There were three presentations by invited local speakers: "Superwarfarin poisoning in Hong Kong" by Dr Doris Ching; "Heavy metal poisoning in Hong Kong I: arsenic toxicity and speciation" by Dr Jeffrey Kwok; and "Heavy metal poisoning in Hong Kong II: sporadic, periodic and catastrophic" by Dr Sammy Chen. These were followed with four presentations from the industries (Roche, Thermo-Fisher, Bio-Rad and Sciex).

Education activities for the year carried on with presentations by distinguished academia and scientists. One scientific meeting was organized in the first half year of 2017. Professor Daniel W. Chan, External Examiner for Chemical Pathology, Chinese University of Hong Kong delivered a dinner lecture at the Cordis Hong Kong Hotel on 9th May 2017. The title of his talk was 'Tumor Marker Case Studies: A Practical Guide for 2017 and Beyond'. The event was well attended by 154 members and guests.

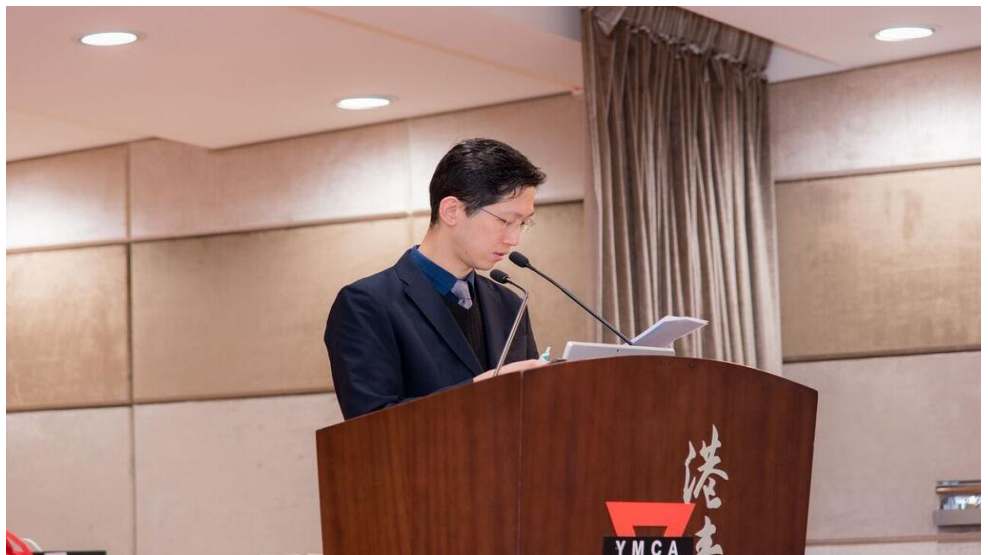
Council 2017 – 2018

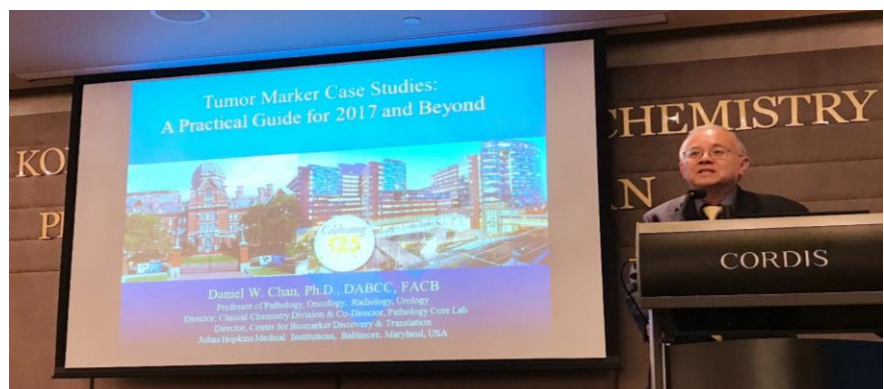


ASM 2017 (14 Jan 2017): Dr Doris Ching, Dr Jeffrey Kwok, Dr Sammy Chen and Industrial Exhibition



Dinner lecture (09 May 2017): Professor Daniel W. Chan







HIMPUNAN KIMIA KLINIK INDONESIA
INDONESIAN ASSOCIATION FOR CLINICAL CHEMISTRY

IACC Activities 2017 for APFCB News Semester 1

1. Seminar

IACC held Seminar on Molecular Diagnostic. The topic is Essential Practical Molecular Diagnostics. We invited some speakers who expert in this field from some Research Centers and Teaching Hospitals in Indonesia. Agenda:

PLENNARY SESSION

Growing Needs for Practical Molecular Diagnostics: Indonesia's Preparedness for Current Trend	Dr. Francisca Sriwetami Tanoerahardjo, SpPK, MSi
How to start Molecular Diagnostic Laboratory	Dr. Dewi Lokida, SpPK
MORNING SESSION:	Moderator:
Molecular Diagnostics in Infectious Disease	Dr. Alida R. Harahap, pPK(K), PhD
Tuberculosis – Simple Molecular Diagnostics in Primary Health Care	Prof. Dr. Ida Parwati, SpPK(K), PhD
Malaria – Battle Against Ongoing Drug Resistance	Prof. Syafruddin, PhD
Hepatitis Virus Genotyping – The Clinical Implications	Prof Dr. David Handojo Muljono, SpPD, FINASIM, PhD
International Guidelines on HIV – A Demand for Molecular Diagnostics	Dr. July Kumalawati, DMM, SpPK(K)
AFTERNOON SESSION:	Moderator:
Molecular Diagnostics in Malignancy	Prof. Siti Boedina Kresno, pPK(K)
Early Detection Saves Lives – Human Papillomavirus (HPV) and Molecular Diagnostics for Cervical Cancer	Dr. Sri Hartini, SpPK(K), MARS
Molecular Diagnosis in Leukemia – Benchmarking Dharmas National Cancer Hospital	Dr. Agus Kosasih, SpPK, MARS
Sneak peek into the future: Immunotherapy -- Nasopharynx Carcinoma as a model	Dr. Demak L. Tobing, SpPK





Prof Dr. dr. David Handojo Muljono, SpPD, FINASIM, PhD from Eijkman Institute for Molecular Biology kindly shared his experience on Hepatitis Virus Genotyping in Indonesia.

2. Young Scientist IFCC

IACC encourage and support Indonesian young scientist to join Young Scientist program initiated by IFCC.



Trilis Yulianti—one of Indonesian Young Scientist granted IFCC–ROCHE Travel Scholarship to attend Euromedlab 2017



Singapore Association of Clinical Biochemistry (SACB)

SACB Education Programme 2016

The annual education programme, consisting of 10 lectures held on Wednesday evenings, was conducted from August to October 2016 at the National University Hospital. In total, there were 69 participants in last year's programme. Lectures on clinical biochemistry topics included:

- pre-analytical variables
- calcium, magnesium and phosphate
- trace metals
- organic acids
- clinical case studies

Management and professional topics such as key performance indices, career progression in the clinical laboratory, laboratory safety and chemicals management were very well received by the participants. Last but not least, the topical issue of Zika virus-related laboratory testing was introduced by our local experts.

Annual Scientific Meeting and Annual General Meeting 2017

On 4th March 2017, our Annual Scientific Meeting (ASM) and Annual General Meeting (AGM) were held at the Carlton Hotel, Singapore. Once again, the scientific programme consisted of topical discussions delivered by both local and external experts:

Topic	Speaker
Ordering A Lipid Profile – Does My Patient Need To Fast?	Prof. Tavintharan Subramaniam
Serum vs. Plasma: Which Specimen Should You Use?	A/Prof Robert Hawkins
Critical Success Factors of a POCT Programme	Prof Aw Tar Choon
Point of Care Testing Management with Open Connectivity	Mr Roman Rosenkranz
Exploring the Use of Tumour Markers in Lung Cancer Patient Management	Dr Mikki Koo
The Challenge of Acute Kidney Injury	Dr Rafael Rivero
The Role of Clinical Laboratory Informatics in Improving Patient Care	Dr Vishwesh Vishnumurthy

There were three local speakers at this year's ASM. A/Prof Subramaniam explained the latest lipid guidelines and the biochemistry of lipoproteins. He also shared with the audience some data from a local study, shedding light on the pros and cons of fasting lipid profiles.

In his informative talk, A/Prof Hawkins compared the different types of anti-coagulants in clinical laboratories and explained in detail their pros and cons. The audience learned the benefits of using plasma specimens but were also reminded of the limitations of using plasma for routine analysis.



Prof Aw spoke on the latest issues and challenges in point-of-care testing, including user identification, patient identification, transcription errors, inventory management and other pre- and post-analytical issues.

Other speakers covered a variety of topics ranging from information technology, quality controls, acute kidney injury to tumour markers. All in all, the scientific meeting was very well received. Of course, participants enjoyed the annual opportunity to network with colleagues from various laboratories, and catch up with old friends, in addition to learning about the latest developments in the profession.



SACB Council members and speakers at the Annual Scientific Meeting.

APFCB Congress 2016, Taipei

SACB organised a symposium dedicated to the topic of point-of-care testing (POCT) on 28 November 2016 as part of the scientific programme at the APFCB Congress. Three speakers from different hospitals in Singapore spoke on topical issues about POCT. The titles of the presentations were: (1) Point-of-care testing – governance, guidelines, accreditation (by Dr Wong Moh Sim); (2) Secrets of managing a successful POCT programmes (by Dr Leslie Lam), and (3) Point of care connectivity and more (by Dr Sharon Saw). In addition, SACB sponsored three young scientists to attend and present posters at the APFCB Congress in Taipei:

Scholarship recipient	Institution	Title of poster
Heng Ping Ying	Khoo Teck Puat Hospital	Validation of reference intervals for endocrine, cardiac and inflammatory biomarkers in a multi-ethnic population
Neo Siew Fong	National University Hospital	Effects on lipid profiles from diet interventions in normal population
Teo Wee Meng Henry	Ng Teng Fong General Hospital	Comparison of critical results notification at two regional hospitals in Singapore



Figure1. Dr. Leslie Lam and Henry Teao at the poster exhibition area

All in all, the last twelve months have been rather busy for SACB in terms of educational and scientific activities!

Molecular Diagnosis and Cancer – an update

Shailendra Dwivedi, Purvi Purohit, Radhieka Misra, Puneet Pareek, Apul Goel,*

Sanjay Khattri, Kamlesh Kumar Pant, Sanjeev Misra, Praveen Sharma

The last decade has seen a tremendous advancement in the field of clinical and translational research in cancer owing to the increased knowledge about the pathogenesis of cancer. Our healthcare system is critically and crucially dependent upon diagnostics. Today's medical decision making is strongly based upon the diagnostics results. The paradox of carcinogenesis today has certain significant hallmarks like sustaining proliferative signalling, evading growth suppressors, resisting cell death, enabling replicative immortality, inducing angiogenesis and activating invasion and metastasis. The genetic diversity and genome instability together are the underlying causes that expedite the acquisition of these hallmarks. A rapid and steadfast progress in molecular research has quite simplified the carcinogenesis paradox. Cancerous cells sometimes have mutations in oncogenes, such as KRAS and CTNNB1 (b-catenin) [1] and analysis of the molecular signature of cancerous cells, helps physicians in characterization of cancer and choice of appropriate therapy. By 2010, there had been an increase in the number of assays that incorporate an array of antibodies against specific protein marker molecules and as an emerging technology, there are hopes for multiplexing that could measure many markers at once [2]. The advances in molecular diagnosis has seen an increase in the precision of diagnosis as well as prognosis of cancer. With the advent of era of personalized medicine, using precise targets for diagnosis of cancers is important since specific drug therapies will be targeted against these molecules. [3]. In the current review we focus on the updates in the genomics, Transcriptomics, and proteomics of cancer diagnosis and prognosis, along with the latest diagnostic tests being used in different carcinomas.

Prostate Cancer

Genomics/Epigenetic and SNPs based markers

Over the past thirty years epigenetic has broadened its field and played an important role in the study of cancer genetics. Epigenetics involves the non-coded heritable changes in gene expression which includes DNA methylation, histone modifications and noncoding RNA induced transcriptional changes. Several epigenetic markers have proven useful in cancer diagnosis. The HAT p300 and HDM EZH2 (histone modifiers) have shown to be over expressed in PCa and their expression levels precisely linked with different disease stages, making them promising markers for PCa and possibly be used as a standard dual biomarker. Hypermethylation and gene silencing is yet another important modification, which has been documented for cell cycle regulation such as anaphase promoting complex (APC) and Ras association domain containing protein 1 (RASSF1a), detoxification enzymes e.g., glutathione S-transferase Pi 1 (GSTP1). Furthermore, combined assays for GSTP1 and APC hyper methylation have unlimited potential for detecting PC a in clinical samples up to 100% sensitivity.



The risk of PCa can also be evaluated from single nucleotide polymorphisms (SNPs) of alleles in different region of chromosome (EHBP1, THADA, ITGA6, EEFSEC, PDLIM5, FU20032, SLC22A3, JAF1, LMTK2, NKX3, CMYC, MSMB, CTBP2, HNF1B, KLK2-3, TNRC6B, BIK, IL-10, IL-18 [4], NUDT10-11) which influence the behavior of the disease and its progression by changing expressions of mRNA and protein [5]. This has been explored and documented in more than 9000 patients (9893-61, 388 patients) [6].

Transcriptomics based markers

Transcriptomics is the study of all the RNAs including mRNA, tRNA, rRNA and novel non coding RNAs. The noncoding RNA (ncRNA) is a relatively novel field in Cancer research. The term ncRNA encompasses the well-studied functional RNAs like rRNA and tRNA, as well as microRNA (miRNA; previously known as small ncRNA) including long ncRNA (lncRNA) and small interfering RNA (siRNA). Three known lncRNAs which have been validated for significance in detecting, screening and monitoring PCa [80], because of their high specificity and sensitivity. These include PCa non coding RNA-1 (PRNCR1), prostate-specific gene 1 (PSGEM1), and PCa antigen 3 (PCA3); also referred to as differential display 3 (DD3). Recently it has also been proposed that PCGEM1 gene, which encodes lncRNA is highly prostate-specific. Moreover, the screening of TMPRSS2-ERG fusion (TEF) techniques as examined by Immunohistochemistry, FISH and RT PCR found to have significance in the diagnosis PCa. However the TE fusion in combination with PCA3 mRNA may prove more beneficial in diagnosis [7]. Circulating microRNAs (miRNA) have newly been supposed to be biomarkers for non-invasive diagnosis in various tumors [8]. Several gene expression studies also reported altered interleukins expression in PCa patients [9]. These differentially regulated miRNAs lead to changes in the expression and activity of their targets in PCa. The miRNA expression changes with the development and progression of PCa as some of the cancer-related genes are regulated by them and thus its dysregulation has significance in PCa. Using a mouse xenograft model, Mitchell et al. [10] have demonstrated that miRNAs originated from the human PCa xenografts enter the circulation and thus reported that miR-141 is up regulated in sera of metastatic PCa patients which can distinguish PCa patients from healthy controls with high sensitivity and more accuracy.

Proteomics based markers

Proteomics also play a dynamic role in the field of biomarker, specially in non-invasively collected bio fluids as for prognosis [CGRP, VEGF, endoglin (CD105), chromogranin-A, neuron-specific enolase, interleukin-6 transforming growth factor- β , other methylated genes including RASSF1a, APC, RARB2 and CDH1, prostate-specific cell antigen, testosterone, estrogen, sex hormone binding globulin, caveolin-1, E-cadherin, β -catenin, MMP-9, tissue inhibitor of MMPs (TIMP 1, 2) progastrin-releasing peptide (ProGRP 31-98)] and diagnosis (PSP94, ZAG, prostasome (autoantibodies), huntingtin interacting protein 1 (auto-antibodies), TSP-1, leptin, ILGF-1, -2, human kallikrein 2, α -methylacyl-CoA racemase (auto-antibodies), early prostate cell antigen-1, -2, GSTP1 hypermethylation, cytokine macrophage MIF, hK11, apolipoprotein A-II). Some like urokinase-type plasminogen activator system, prostate membrane-specific antigen, hepatocyte growth factor, MIC-1, EGFR family (c-erbB-1 (EGFR),



c-erbB-2 (HER2/neu), c-erbB-3 (HER3) and c-erbB-4 (HER4) [11], have shown their unique potency in diagnosis as well as prognosis [9]. More recently Dwivedi et al. [12–17] have proposed circulating serum interleukin-18 as a diagnostic biomarker and interleukin-10 for prognosis. The significance of WNT5A, EZH2, MAPK pathway members, AR, various androgen metabolism genes are also over expressed in metastatic PCa and c-FOS jun B down-regulated thus also have significance as biomarker. Several other promising molecular markers for this cancer which are reportedly over expressed are human kallikrein-related peptidase 2 (hK2), early PCa antigen (EPCA), α-methylacyl-coA racemase (AMACR), insulinlike growth factors and binding proteins (IGFBP-2 and IGFBP-3), TGF-β1, elevated circulating levels of the interleukin-6 (IL-6), and its receptors, urokinase plasminogen activator (uPA) and receptor (uPAR), enhancer of zeste homolog 2 (EZH2), and prostate-specific membrane antigen (PSMA) [18].

Breast Cancer

Breast cancer is a leading public health issue globally. The number of new cases of female breast cancer was 124.9 per 100,000 women per year and the number of deaths was 21.2 per 100,000 women per year, age adjusted and based on 2010–2014 cases and deaths. (National Cancer Institute stats report <https://seer.cancer.gov/statfacts/html/breast.html>).

Immunohistochemistry based markers

The more typical approach to breast cancer diagnostics via hormone receptor analysis is IHC. IHC involves the use of antibodies and enzymes, such as horseradish peroxidase, to stain tissue sections for the tumor antigens of interest. This analysis method can be performed on either frozen or formalin-fixed paraffin-embedded (FFPE) tissue, as well as on small amounts of tissue acquired in procedures such as core biopsies.

IHC also has the advantage of not only determining the percentage of positive nuclei but also the intensity of staining in individual nuclei. Unfortunately, in addition to a lack of inter laboratory standardization of the IHC technique, the process for characterizing the positivity of either ER or PR staining is performed subjectively by a pathologist, thereby introducing variability in interpretation. Regardless of this subjectivity in staining intensity, IHC is by far the most common approach to evaluating hormone status in breast cancer today. Another major prognostic marker that is currently recommended for the evaluation of primary invasive breast cancer is the human epidermal growth factor receptor 2, also known as HER2.

HER2 is an oncogene belonging to the EGF receptor (EGFR) family. Approximately 10 – 40% of the primary tumours show gene amplification of HER2 and HER2 protein over expression is found in almost 25% of breast cancers [19].

HERmark™ Assay: In an effort to expand the available methods of HER2/neu analysis, Monogram Biosciences has recently released the HERmark™ breast cancer assay, which measures total ER2 protein (H2T) and functional HER2 homodimer (H2D) levels on the cell surface of FFPE breast cancer tissue. It practices a dual antibody system in which a fluorescent tag on one antibody is cleaved by a second antibody containing a photo-activated molecule.



The fluorescent tags are then quantified using capillary electrophoresis (CE). HERmark™ reports whether a patient is HER2-negative, -positive or -equivocal based on quantified HER2 protein levels expressed as numeric values (HERmark, Monogram Biosciences, Inc. www.hermarkassay.com).

Transcriptomics Based Bio markers: Theros H/ISM and MGISM Theros H/ISM is a molecular diagnostic test that assesses the ratio of HOXB13:IL17BR gene expression as a predictor of clinical outcome for breast cancer patients treated with tamoxifen. A high level of expression of the two-gene ratio has been associated with tumour aggressiveness and failure to respond to tamoxifen [20]. Theros MGISM is an additional test that uses a five-gene expression index to stratify breast cancer patients into high or low risk of recurrence by reclassifying grade 2 (intermediate proliferative) tumors into grade 1-like or grade 3-like outcomes [21].

Another important diagnostic test is Mamma Print™. The Mamma Print test is a molecular diagnostic tool that evaluates a breast cancer patient's chance for tumour recurrence. It uses a 70-gene signature that has been reported to have independent prognostic value over clinic-pathologic risk assessment in patients with node-negative breast cancer.

The test needs a fresh sample (at least 3 mm in diameter) obtained during a surgical biopsy to be sent to the Agendia laboratory in Amsterdam in an RNA-stabilizing solution for analysis. RNA is isolated from the sample, amplified and hybridized with a standard reference to the Mamma Print microarray to obtain the 70-gene expression profile [22]. This method has been shown to have an extremely high correlation of prognostic prediction to tumour recurrence ($p < 0.0001$). In 2007, the US FDA approved the Mamma Print test for use on freshly frozen tissue. Although the Mamma Print gene expression profile has the potential to be a useful diagnostic tool, there are many limitations that need to be taken into consideration.

Yet another Transcriptomics based marker is Oncotype DX assay. It is a 21-gene expression assay that uses qRT-PCR and microarray technologies to characterize patients who may be positively treated with chemotherapy and estimate the likelihood that invasive breast cancer will recur after treatment. The Oncotype DX assay uses FFPE tissue blocks that can be shipped from anywhere in the USA and internationally. Currently, Oncotype DX is the standard breast cancer screening test for women with early stage (Stage I or II), node-negative, invasive breast cancer. The assay reports a recurrence score that ranges from 0 to 100, indicating the probability of cancer recurring within 10 years of the original diagnosis. The recurrence score is then categorized into one of three groups: low, intermediate or high risk. There is a particular urgency for such information in women with early-stage breast cancer, where the great variety of treatment options can be narrowed down and tailored to each patient. Both ASCO and the National Comprehensive Cancer Network (NCCN) have incorporated the Oncotype DX assay into their guidelines [23]. MicroRNA deregulation in breast cancer was primarily described by Iorio and colleagues in 2005. miR-10b was one of the three microRNAs in the Iorio et al. study that demonstrated significant down regulation in breast cancer cells compared with primary human mammary epithelial cells (HMECs). However, in a successive study, miR-10b appeared to be highly expressed in metastatic cancer cells.



Functional studies have described that miR-10b over expression promotes cell migration and invasion in vitro, and initiates tumor invasion and metastasis in vivo. Since this first study, there has been a surge of data added on the expression of various microRNAs and their roles in breast cancer. miR-21 has surfaced in multiple studies as having consistent and significant increased expression in breast cancer cell lines and human tissue when compared with normal cells and tissues. Additionally Multiple studies have also demonstrated a significant association between expression of miR-206 and the expression of estrogen receptors (ER) in breast cancer. Iorio et al.[24] were the first to show that miR-206 expression was raised in those tumors that were ER positive. miR-125a and miR-125b were first reported in a microRNA profile study to be significantly down regulated in HER2-positive breast cancers. Computation analysis then confirmed target sites at the 3'UTR regions of HER2 and HER3 for these microRNAs. (Mattie et al. 2006) A tissue culture analysis showed that overexpression of miR-125a or miR-125b in an ErbB2- dependent cancer cell line (SKBR3) suppressed HER2 and HER3 transcript and protein levels, which decreased cell motility and invasiveness [25]. Recent advancements and investigations in the field of liquid biopsy-based biomarkers, especially DTCs and CTCs bearing molecular signature have the capability to behave as potential biomarkers and can discriminate breast cancer between localized to metastasizing one. Further our current project SERBNPDF 2015/000322 DST, New Delhi also showing unique trends of various miRNA with cancer stem cells in breast cancer patients.

Lung Cancer

Lung cancer is the major cause of cancer-related death in the world, with Non-small cell lung carcinoma (NSCLC) responsible for 80-85% of all lung cancers, and lung adenocarcinoma being the most typical histologic type in the United States. Enhancements in our knowledge of molecular alterations at multiple levels (genetic, epigenetic, protein expression) and their functional importance have the potential to impact lung cancer diagnosis, prognostication and treatment. In lung cancer as in other malignancies, tumorigenesis narrates to activation of growth promoting proteins [e.g., v-Kiras2 Kirsten rat sarcoma viral oncogene homolog (KRAS), epidermal growth factor receptor (EGFR), BRAF, MEK-1, HER2, MET, ALK and rearranged during transfection (RET)] as well as inactivation of tumour suppressor genes [e.g., P53, phosphatase with tensin homology (PTEN), LKB-1 [26]. Lung cancers have extremely complex genomes with a recent large scale exome sequencing study of 31 non-small cell lung cancer (NSCLC) identifying 727 previously undescribed mutated genes or undescribed in the COSMIC database.

Genomic studies have established previously well-known alterations in lung cancer such as KRAS, EGFR and BRAF and also identified low frequency but recurrent mutations that are novel in lung cancer including potentially targetable alterations in JAK2, ERBB4, RET, fibroblast growth factor receptor 1 (FGFR1), and discoidin domain receptor 2 (DDR2) [27]. Amplification is another mechanism of activation of oncogenes such as MET in adenocarcinoma, fibroblast growth factor receptor 1 (FGFR1) and discoidin domain receptor 2 (DDR2) in SCC. The role of tumour suppressor genes is increasingly recognized with aberrations reported in TP53, PTEN, RB1, LKB1 and p16/CDKN2A. The occurrence of these molecular targets as labelled above now defines the characteristics of NSCLC,



with EGFR mutation and ALK rearrangements being the most clinically relevant at present. The prevalence of these mutations varies in lung cancer arising from patient in different regions. Activating EGFR mutations were found in up to 20% of Caucasians while in the Asian populations these EGFR mutations can be present in up to 40% of patients with NSCLC. These ethnic difference in NSCLC properties seems to be not limited to the presence of activating EGFR mutations but is also evident in other driver oncogenic mutation profiles (including ALK, KRAS, MET etc.), histology. The presence of these driver mutations is normally found to be mutually exclusive to others in the same tumour [28]. In lung ADC among Asians, ALK rearrangement is seen in up to 7% of patients with lung ADC. Based on current reports of therapeutic molecular targets of EGFR mutation and ALK gene rearrangement in NSCLC and the availability of corresponding targeted agents, an algorithm of testing for molecular targets in NSCLC is proposed, which signifies a stepwise approach to testing for individual targets, beginning with EGFR then, if negative, ALK fusion gene or other potential targets if appropriate. Among NSCLC, adenocarcinoma accounts for up to 80% of histological subtypes. There are previous reports of correlations between histological subtypes of ADC demonstrating micropapillary features with presence of activating EGFR mutations, leading to the suggestions that the presence of specific mutations in NSCLC in fact represent heterogeneity in cancer biology and also response to therapy [29]. Given the heterogeneity of lung cancer histology, however, histological subtypes are hard to be used as the sole reliable marker for guidance to molecular phenotyping and selection of targeted therapy. Targeting therapeutic oncogenic mutations like EGFR and ALK can give dramatic initial treatment response or at least an initial stable clinical disease.

Oral Cancer

Oral cancer is among the 10 most common cancers worldwide, and is particularly seen in disadvantaged elderly males. Early detection and quick treatment provide the best chance for cure. The most predictive of the molecular markers thus far available and assessed in OSCC development include the TSG p53 protein expression, chromosomal polysomy (DNA ploidy), and changes (termed loss of heterozygosity; LOH) in chromosomes 3p or 9p (probably due to changes in the TSG p16). The practise of such biomarkers as adjuncts to routine histopathological assessment can possibly help better prognosis and effective management of PMLs but their routine use is still hindered by the cost and complexity of the tests, the lack of facilities in some laboratories, and limited outcome studies to date. More readily available markers, such as those of cell proliferation (Ki-67 antigen) and apoptosis (Bax, Bcl-2), may also play a diagnostic role: apoptotic Bcl-2 expression decreases significantly in dysplastic and early invasive lesions and then increases almost to normal tissue level in consequent stages while Ki-67 expression increases sharply in initial stages of OSCC, but significantly decreases in later stages [30].

An important non-invasive strategy to collect oral cancer cells is via the brush biopsy, which utilizes a small nylon brush to gather cytology samples. The samples are then sent for computer scanning and analysis (Oral CDx) to identify and display individual cells. If suspect cells are identified, a pathologist then examines them to determine the final diagnosis and, in samples judged to be cancerous, a printout of the abnormal cells from the computer display and a written pathologist's report are returned to the clinician with the recommendation



that a positive result be followed with a conventional incisional biopsy. The technique has proved rather controversial, with concern largely related to the question of false negative results. Promoter hyper-methylation patterns of TSG p16, O6-methylguanine-DNA-methyltransferase, and death-associated protein kinase have been characterized in the saliva of head and neck cancer patients [31]. Forensic science has since shown that saliva can contain a number of messenger ribonucleic acid (mRNA) fragments including salivary specific statherin, histatin 3, and the proline-rich proteins PRB1, PRB2 and PRB3, as well as the ubiquitously expressed spermidine N1 acetyl transferase (SAT), b-actin, and glyceraldehyde-3-phosphate dehydrogenase (GAPDH). The mRNAs in saliva such as b-actin, SAT and interleukin-8 are relatively stable despite the presence of salivary ribonucleases. mRNAs in saliva have been tested in over 300 saliva samples from OSCC patients and healthy people, and the signature was always present in higher levels in the saliva of OSCC patients than in saliva from healthy people, with an overall accuracy rate of about 85%. Four salivary mRNAs (OLF/EBF associated zinc finger protein [OAZ], SAT, IL8, and IL1b) collectively have a discriminatory power of 91% sensitivity and specificity for OSCC detection [32]. Seven mRNA molecules: transcripts of:

1. IL8 (interleukin 8) playing a role in angiogenesis; replication; calcium-mediated signaling pathway; cell adhesion; chemotaxis; cell cycle arrest; immune response,
2. IL1B (interleukin 1B) which takes part in signal transduction; proliferation, inflammation and apoptosis
3. DUSP1 (dual specificity phosphatase 1) with a role in protein modification; signal transduction and oxidative stress,
4. H3F3A (H3 histone, family 3A) having a DNA binding activity,
5. OAZ1 (ornithine decarboxylase antizyme 1) taking part in polyamine biosynthesis
6. S100P (S100 calcium binding protein P) with a role in protein binding and calcium ion binding, and
7. SAT (spermidine/ spermine N1-acetyltransferase) which takes part in enzyme and transferase activity were found significantly elevated in OSCC patients rather than in healthy controls [33].

Conclusion

Now, genetics has become the driving force in medical research and is now ready for integration into medical practice. Human genome draft (bio-informatics) with advancement in current techniques now opens new vistas in the fields of novel therapeutics such as Pharmacogenomics, Nutrigenomics that may transform the management of untreated disease and disorders [34–36]. In the upcoming years, molecular diagnostics will continue to be of critical importance to public health worldwide. Molecular diagnostic offers physicians with critical information based on the early exploration of pathogens and subtle changes in patients' genes and chromosomes, allowing for earlier diagnosis, selection of appropriate therapies and monitoring of disease progression.



References

1. Aftimos PG, Barthelemy P, Awada A. Molecular biology in medical oncology: diagnosis, prognosis, and precision medicine. *Discov Med*. 2014;17(92):81–91.
2. Harvey P, Basuita A, Endersby D, Curtis B, Iacovidou A, Walker M. A systematic review of the diagnostic accuracy of prostate specific antigen. *BMC Urol*. 2009;10(9):14.
3. Sethi S, Ali S, Philip PA, Sarkar FH. Clinical Advances in Molecular Biomarkers for Cancer Diagnosis and Therapy. *Int. J. Mol. Sci*. 2013, 14, 14771–14784; doi: 10. 3390/ijms140714771
4. Dwivedi S, Goel A, Khattri S, Mandhani A, Sharma P, Misra S, et al. Genetic variability at promoters of IL-18 (pro-) and IL-10 (anti-) inflammatory gene affects susceptibility and their circulating serum levels: an explorative study of prostate cancer patients in North Indian populations. *Cytokine*. 2015;74(1):117–22.
5. Ma Y, Li Y, Cui H, Liang X, Tang Z, Li X, et al. Re-evaluation of interval debulking surgery in advanced epithelial ovarian cancer. *Zhonghua Fu Chan Ke Za Zhi*. 2012;47(5):355–60.
6. Willard SS, Koochekpour S. Regulators of gene expression as biomarkers for prostate cancer. *Am J Cancer Res*. 2012;2(6):620–57.
7. Tomlins SA, Aubin SMJ, Siddiqui J, Lonigro RJ, Sefton–Miller L, Miick S, et al. Urine TMPRSS2: ERG fusion transcript stratifies prostate cancer risk in men with elevated serum PSA. *Sci Transl Med*. 2011;3(94):94ra72.
8. Srivastava A, Goldberger H, Afzal Z, Suy S, Collins SP, KumarD. Detection of circulatory microRNAs in prostate cancer. *Methods Mol Biol Clifton NJ*. 2015;1238:523–38.
9. Dwivedi S, Goel A, Mandhani A, Khattri S, Sharma P, Misra S, et al. Functional genetic variability at promoters of pro-(IL-18) and anti-(IL-10) inflammatory affects their mRNA expression and survival in prostate carcinoma patients: five year follow-up study. *Prostate*. 2015;75(15):1737–46.
10. Mitchell PS, Parkin RK, Kroh EM, Fritz BR, Wyman SK, Pogosova–Agadjanyan EL, et al. Circulating microRNAs as stable blood-based markers for cancer detection. *Proc Natl Acad Sci USA*. 2008;105(30):10513–8.
11. Drake RR, Kislinger T. The proteomics of prostate cancer exosomes. *Expert Rev Proteomics*. 2014;11(2):167–77.
12. Dwivedi S, Goel A, Natu SM, Mandhani A, Khattri S, Pant KK. Diagnostic and prognostic significance of prostate specific antigen and serum interleukin 18 and 10 in patients with locally advanced prostate cancer: a prospective study. *Asian Pac J Cancer Prev APJCP*. 2011;12(7):1843–8.



13. Dwivedi S, Shukla KK, Gupta G, Sharma P. Non-invasive biomarker in prostate carcinoma: a novel approach. *Indian J Clin Biochem IJCB*. 2013;28(2):107-9.
14. Dwivedi S, Goel A, Khattri S, Mandhani A, Sharma P, Pant KK. Tobacco exposure by various modes may alter proinflammatory (IL-12) and anti-inflammatory (IL-10) levels and affects the survival of prostate carcinoma patients: an explorative study in North Indian population. *Biomed Res Int*. 2014;2014:158530.
15. Dwivedi S, Singh S, Goel A, Khattri S, Mandhani A, Sharma P, et al. Pro-(IL-18) and anti-(IL-10) inflammatory promoter genetic variants (intrinsic factors) with tobacco exposure (extrinsic factors) may influence susceptibility and severity of prostate carcinoma: a prospective study. *Asian Pac J Cancer Prev APJCP*. 2015;16(8):3173-81.
16. Dwivedi S, Goel A, Mandhani A, Khattri S, Pant KK. Tobacco exposure may enhance inflammation in prostate carcinoma patients: an explorative study in north Indian population. *Toxicol Int*. 2012;19(3):310-8.
17. Dwivedi S, Goel A, Khattri S, Sharma P, Pant KK. Aggravation of inflammation by smokeless tobacco in comparison of smoked tobacco. *Indian J Clin Biochem IJCB*. 2015;30(1):117-9.
18. Kattan MW, Eastham J. Algorithms for prostate-specific antigen recurrence after treatment of localized prostate cancer. *Clin Prostate Cancer*. 2003;1(4):221-6.
19. Krishnamurti U, Silverman JF. HER2 in breast cancer: a review and update. *Adv Anat Pathol*. 2014;21(2):100-7.
20. Zhao L, Zhu S, Gao Y, Wang Y. Two-gene expression ratio as predictor for breast cancer treated with tamoxifen: evidence from meta-analysis. *Tumour Biol*. 2014;35(4):3113-7.
21. Rajput AB, Hu N, Varma S, Chen C-H, Ding K, Park PC, et al. Immunohistochemical assessment of expression of centromere protein-A (CENPA) in human invasive breast cancer. *Cancers*. 2011;3(4):4212-27.
22. Buyse M, Loi S, van't Veer L, Viale G, Delorenzi M, Glas AM, et al. Validation and clinical utility of a 70-gene prognostic signature for women with node-negative breast cancer. *J Natl Cancer Inst*. 2006;98(17):1183-92.
23. Kip M, Monteban H, Steuten L. Long-term cost-effectiveness of Oncotype DX versus current clinical practice from a Dutch cost perspective. *J Comp Eff Res*. 2015;4(5):433-45.
24. Iorio MV, Ferracin M, Liu C-G, Veronese A, Spizzo R, Sabbioni S, et al. MicroRNA gene expression deregulation in human breast cancer. *Cancer Res*. 2005;65(16):7065-70.



26. Wang W, Luo Y. MicroRNAs in breast cancer: oncogene and tumor suppressors with clinical potential. *J Zhejiang Univ Sci B*. 2015;16(1):18–31.
27. Hensing T, Chawla A, Batra R, Salgia R. A personalized treatment for lung cancer: molecular pathways, targeted therapies, and genomic characterization. *Adv Exp Med Biol*. 014;799:85–117.
28. Cancer Genome Atlas Research Network. Integrated genomic analyses of ovarian carcinoma. *Nature*. 2011;474(7353): 609–15.
29. Clamon GH, Bossler AD, Abu Hejleh T, Furqan M. Germline mutations predisposing to non-small cell lung cancer. *Fam Cancer*. 2015;14(3):463–9.
30. Black RC, Khurshid H. NSCLC: an update of driver mutations, their role in pathogenesis and clinical significance. *RI Med J*. 2015;98(10):25–8.
31. Gomes CC, Fonseca-Silva T, Galvão CF, Friedman E, De Marco L, Gomez RS. Inter- and intra-lesional molecular heterogeneity of oral leukoplakia. *Oral Oncol*. 2015;51(2):178–81.
32. Rosas SL, Koch W, da Costa Carvalho MG, Wu L, Califano J, Westra W, et al. Promoter hypermethylation patterns of p16, O6-methylguanine-DNA-methyltransferase, and death-associated protein kinase in tumors and saliva of head and neck cancer patients. *Cancer Res*. 2001;61(3):939–42.
33. Rosin MP, Lam WL, Poh C, Le ND, Li RJ, Zeng T, et al. 3p14 and 9p21 Loss is a simple tool for predicting second oral malignancy at previously treated oral cancer sites. *Cancer Res*. 2002;62:6447–50.
34. Zimmermann BG, Wong DT. Salivary mRNA targets for cancer diagnostics. *Oral Oncol*. 2008;44(5):425–9.
35. Ahmed MU, Saaem I, Wu PC, Brown AS. Personalized diagnostics and biosensors: a review of the biology and technology needed for personalized medicine. *Crit Rev Biotechnol*. 2014;34(2):180–96.
36. Regierer B, Zazzu V, Sudbrak R, Kühn A, Lehrach H. Future of medicine: models in predictive diagnostics and personalized medicine. *Adv Biochem Eng Biotechnol*. 2013;133:15–33.
37. Dwivedi S, Yadav SS, Singh MK, Shukla S, Khattri S, Pant KK. Pharmacogenomics of Viral Diseases. In: Barh D, Dhawan D, Ganguly N, editors. *Omics for personalized medicine*. New Delhi: Springer; 2013. p. 637–76.



Beautiful Terraced Rice-Fields in China

Dr Tan It Koon



Rice is the staple food of Asia and part of the Pacific. Over 90 percent of the world's rice is produced and consumed in the Asia-Pacific Region. Ideally, land used for rice plantation is flat with good irrigation. However, in many rice-growing countries, large areas are hilly or mountainous.

Ingenious and resourceful local farming community turned the sloping areas into productive terraced farming fields' by cutting flat areas along the slope of hills and mountains in the form of graduated terraces to grow crops on all sides of hills and mountains.

Though labour-intensive, the method has been employed effectively to maximize arable land area in variable terrains and to reduce soil erosion and water loss.

Besides rice, other crops with varying time for maturity and harvest are also cultivated at the same time, or at other times. Algae with bright colour grow on the surface of the still and shallow water in some of the terraces. These contribute to the fascinating and changing view of multi-coloured patches in the fields that appear like a modern abstract painting consisting of lines, geometrical shapes and colours.

In addition to their important primary role of rice and other crop production, the terraced fields are beginning to help generate additional income because of the unusual views they offer to city dwellers. The spectacular scenic beauty of some of these areas in the more remote parts of the Philippines, China and Vietnam are attracting the attention of avid travellers in more recent times.

Photographs and video recordings captured on hand-phones and posted on the internet have helped publicize the scenic beauty of the terraced rice-fields which are located at relatively undeveloped and inaccessible areas.

With increasing demand for eager's visitors, they are becoming well-known and popular scenic spots and unique attractions for nature-loving tourists, artists and photographers. Roads and other relevant facilities for tourists are being developed to facilitate access to such places.

Most spectacular. The fields are mainly divided into 3 scenic spots including Bada, Laohuzui (the Mouth of Tiger) and Duoyi Tree areas. All the terraced fields are situated on the hills with slope gradient varying from 15 to 75 degree. The highest mountain has about 3000 terraced fields from the bottom to the top.

This painting is inspired by my visits to the terraced rice-fields in China and captures my impression of the beauty and magnificence of the hilly areas which consist of numerous long irregular strips of land carved closely in parallel on slopes. Colour of the crops, algae, and the reflection of changing colour of the sky from the shallow water in each enclosed elongated strips of land give rise to an interesting jigsaw puzzle landscape painting with ever-changing variation in the shades and colours of its constituent pieces.

