NEWSLETTER OF THE HONG KONG COLLEGE OF PATHOLOGISTS

PATHOLOGUE

The Hong Kong College of Pathologists, Incorporated in Hong Kong with Limited Liability

THE HONG KONG COLLEGE OF PATHOLOGISTS
SCIENTIA ILLUMINAT MEDICINAM
香港病理學專科學院

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FROM THE CHIEF EDITOR

Dear Fellows and Members,

Laboratory Accreditation has become an important issue in the practice of Pathology. In the Featured Article: Laboratory Accreditation : Relevance to the Pathologist in Hong Kong, the Editorial Board aimed to explore this topic, with the valuable input from Dr. Michael Chan, Dr. Chan Keeng Wai, Dr. Robert Collins, Prof. Christopher Lam, Dr. Wilina Lim, and Dr. Wong Kit Fai. We would like to take this opportunity to thank the contributors once again.

In the Topical Update: Immunogenetics: MHC and non-MHC, Dr. Janette Kwok shared with us her knowledge in a field which is unfamiliar to most fellows. In Out of the Whitecoat section, Dr. Andrew Choi provided us with a glimpse of his fulfilling post-early retirement life. In Fellows' Laurels section, we are proud to announce the achievements of Prof. Irene Ng and Prof. Alfred Lam. Please continue to keep us informed on similar good news so that we can share them with other fellows and members.

The Annual General Meeting (AGM) this year will take place on 22nd November, 2008 (Sat.), together with the 4th Trainee Presentation Session and the T.B. Teoh Foundation lecture (which will be delivered by Prof. Kan Yuet-Wai). Please come and support our College and our trainees.

See you all at the AGM on 22nd November, 2008 (Sat.)!

Dr. Alexander C.L. Chan
Chief Editor

(Please send comments to:
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Message from the President

This is the second newsletter this year. I must admit that I keep forgetting how short a year is. Although I have done some of the things I hoped to do this year, there are many things I wanted to do, but did not succeed in completing.

This year, I continued to attend the International Liaison Committee of Presidents in Johannesburg in South Africa from September 18 – 20, 2008. The host was Dr. Simon Naylor, the President of the College of Pathologists of South Africa. Also present were the Presidents of the Royal College of Pathologists, the Association of Clinical Pathologists, the Royal College of Pathologists of Australasia, the American Society of Clinical Pathologists, the College of American Pathologists and the Faculty of Pathology of the Royal College of Physicians of Ireland. The subjects covered touched upon the future of Pathology practice, point of care testing, Pathology training in the developing world, national reviews of Pathology services and cross country contract out Pathology services.

There is a new CME/CPD cycle starting this year. Though the changes seem to be minor, it may affect our way of learning and continuing education. Please take a good look at the new scheme and make yourself adapted to it.

The training regulation is also amended this year. The addition of written examination into the Clinical Microbiology and Infection is to reflect the need in ensuring the standard of the specialist.

This year's annual general meeting will be on 22 November 2008 and I invite you all to attend. In particular, this year's T.B. Teoh lecturer, Prof. Y. W. Kan, who is our Honorary Fellow, will deliver the lecture titled "Haemoglobin genetics: from diagnosis to treatment". Please come and give your support.

Dr. NG Wing Fung,
the President

THE HONG KONG COLLEGE OF PATHOLOGISTS

17th T.B. Teoh Foundation Lecture:

"HAEMOGLOBIN GENETICS, FROM DIAGNOSIS TO TREATMENT"

Professor KAN Yuet Wai,

Louis K. Diamond Professor in Hematology,
University of California, San Francisco,
California, U.S.A.

22nd November, 2008 (Sat.)
7:00 p.m. – 8:00 p.m.

The Pao Yue Kong Auditorium,
The HKAM Jockey Club Building,
99 Wong Chuk Hang Road,
Aberdeen, Hong Kong.

1CME/CPD point for the Hong Kong College of Pathologists
1 CME/CPD point for attendance applied for other Colleges

All are welcome. Registration is not required.
For enquiries, please contact HKCPath at 2871 8756, or visit www.hkcpath.org

Featured Article -

Laboratory Accreditation: Relevance to the Pathologist in Hong Kong

BACKGROUND

The relationship between the pathologist and laboratory accreditation is a complex one, and this featured article attempts to look into this issue. We are grateful to Dr. Michael Chan, Chairman of the College's Laboratory Accreditation Committee, to pen the introduction, and to five Fellows from different Pathology subspecialties and from laboratories accredited by different bodies for accepting our invitation to share their views on the subject. The fellows contributing to this article are:

- ***Dr. CHAN Keeng Wai (Specialty: Anatomical Pathology), Diagnostix Pathology Laboratories (accredited both by NATA – the National Association of Testing Authorities, Australia and HOKLAS – the Hong Kong Laboratory Accreditation Scheme)***
- ***Dr. Robert COLLINS (Specialty: Anatomical Pathology), Department of Pathology, Queen Mary Hospital (accredited by CAP – the College of American Pathologists); Dr. Collins was also the first Chairman of the Working Party in Medical Testing, Accreditation Advisory Board, Hong Kong Accreditation Service (HKAS)***
- ***Professor Christopher LAM (Specialty: Chemical Pathology), Department of Chemical Pathology, the Chinese University of Hong Kong (CUHK) (accredited by NATA)***
- ***Dr. Wilina LIM (Specialty: Clinical Microbiology and Infection), Public Health Laboratory Services Branch (PHLSB), Centre for Health Protection, Department of Health (accredited by HOKLAS)***
- ***Dr. WONG Kit Fai (Specialty: Haematology), Department of Pathology, Queen Elizabeth Hospital (accredited by NATA); Dr. Wong is also the present Chairman of the Working Party in Medical Testing, Accreditation Advisory Board, HKAS.***

Introduction by Dr. Michael Chan (Chairman of our Laboratory Accreditation Committee)

In the early 1990's, HKAS had been planning to extend the accreditation service to medical testing. A recorded early meeting was held between HOKLAS and the College in October 1993 – exactly two years after the inauguration of the College. However, due to lack of resources, there was not much progress. In the late 1990's, some laboratories in Hong Kong started to seek accreditation status with the NATA and the Royal College of Pathologists of Australasia (RCPA) with success in 1999. Then, this direction has been followed by more major public and private laboratories seeking their accreditation status with either NATA or CAP. After a decade of discussion, the policy decision on laboratory accreditation was finally made by the Hong Kong Government which was welcomed by HKAS and the medical sector. The Secretary for Health and Welfare announced in October 2001 that HKAS would extend to cover the clinical pathology laboratories in 2003; the preparation of the accreditation programme for medical laboratories went into full speed.

In January 2002, Dr. Robert J. Collins, our former President was appointed to the Accreditation Advisory Board (AAB) to advise the board on matters related to laboratory accreditation for medical testing. In April, a Working Party (WP) on Medical Testing was formed under the AAB to start the preparatory work for this long awaited programme. The WP comprised a balanced representation of pathologists, biomedical scientists, and medical technologists from various pathology sub-specialties including Histopathology, Cytopathology, Clinical Microbiology & Infection, Chemical Pathology, Haematology, and Immunology. There were also representatives from both the public and private medical sector. In December 2002, a Memorandum of Understanding (MOU) was signed between our College and HKAS for co-operation in the laboratory accreditation programme for medical testing. The role of our College is to provide professional input to the laboratory accreditation process; to advise on the technical criteria for accreditation; and to update HKAS on relevant technical advances in medical laboratory practice.

In order to let our stakeholders have wider information and knowledge about accreditation, HKAS invited an accreditation expert, Mr. Phil Barnes, from the International Accreditation New Zealand (IANZ) to hold an open seminar on "*Building Confidence in Medical Testing*" to all stakeholders. A total of 280 representatives of clinical laboratories attended this seminar, showing wide interest in the accreditation programme and eagerness to gain knowledge of the accreditation criteria.

During the preparatory work and drafting of the supplementary criteria, Dr. Wong Kit Fai succeeded Dr. Collins to be the Chairman of the WP of the AAB, and successfully narrowed the gaps and discrepancies between various stakeholders after some rounds of consultation. In February 2004, a local laboratory accreditation programme acceptable by all interested parties was launched.

The local medical programme has now been running in its fifth year, and 21 accreditations had been granted to a total of 55 laboratories. The first accreditation was granted in March 2005 to four laboratories under the Virology Division of Public Health Laboratory Services Branch, Centre for Health Protection, Department of Health. All the laboratories under the Department of Health became accredited in April 2007. The applications came in slowly in the first two years, but rocketed in the third year when most laboratories had their quality system established and documentations completed. Accreditation of the first hospital laboratory under Hospital Authority took place in September 2006. Up till now, nearly all pathology departments of most public hospitals have been accredited either by HKAS or by other overseas accreditation bodies (NATA or CAP). The ball has also been rolling in the private sector. Accreditation in the private sector occurs much quicker than expected. Nine accreditations had already been granted in the private sector and two more are expected in the very near future. The list of accredited laboratories by HKAS can be found at http://www.itc.gov.hk/en/quality/hkas/hoklas/directory/medical.htm.

The success of the medical accreditation programme is deeply in debt to our dedicated medical professionals in Hong Kong. Inevitably associated with the increasing applications, the number of assessments increased greatly in the last year. There was great demand in the number of assessors helping out in these assessments. HKAS trained over 120 potential assessors and appointed about two-thirds. Many assessors are our Fellows. Without the sacrifice of their time and effort, these assessments would not be successfully conducted. As a laboratory professional, we all have a vision to uplift the quality of the clinical pathology service in Hong Kong. Finally, I would like to thank Ms. Bella Ho of HKAS to provide updated information.

The role of our College is to provide professional input to the laboratory accreditation process; to advise on the technical criteria for accreditation; and to update HKAS [Hong Kong Accreditation Service] on relevant technical advances in medical laboratory practice.

Interview with Fellows

Question 1.
When and why did you decide to obtain laboratory accreditation for your laboratory?

Dr. Lim started to be involved with HOKLAS as early as the early 90's, acting as assessor of microbiological testing for foods, toys and so on for the accreditation of private laboratories. She also participated in the World Health Organisation (WHO) accreditation programme in the 90's to comply with requirements for poliovirus testing. Dr. Chan's laboratory started to look into accreditation in the late 1990's, while it was 1997 for Prof. Lam's laboratory, December 1998 for Dr. Wong's laboratory, and around 2000 for Dr. Collins's laboratory.

Independent acknowledgement, by way of inspection, is essential to demonstrate that a laboratory provides a quality (accurate, timely and consultative) pathology diagnostic service (Dr. Collins). Laboratory accreditation is the trend for testing laboratories globally (Dr. Lim). In the public and academic settings, laboratory accreditation was undertaken to implement quality management and Good Laboratory Practice according to international standards (Dr. Wong), and to promote a culture of continuous quality improvement among staff members (Prof. Lam).

In the private sector, the quality of laboratory testing was very variable and there was virtually no benchmark for doctors and end-users to appraise their standards. Therefore laboratory accreditation was embarked upon for the purpose of improving quality in laboratory testing in this sector, in a similar manner to that of the public counterparts (Dr. Chan).

For academic departments, laboratory accreditation is one of the requirements for participating in international clinical trials (Dr. Collins and Prof. Lam).

For the public health laboratory, accreditation had been made compulsory for national laboratories doing poliovirus testing, when WHO started the accreditation programme in the 90's with the initiative of polio eradication in 1988 (Dr. Lim).

Independent acknowledgement, by way of inspection, is essential to demonstrate that a laboratory provides a quality (accurate, timely and consultative) pathology diagnostic service.

Question 2.
By which body is your laboratory accredited? Why did you choose this body?

The accreditation bodies include:

- CAP (Dr. Collins / Queen Mary Hospital)
- HOKLAS (Dr. Chan / Diagnostix Pathology Laboratories; Dr. Lim / PHLSB)
- NATA in conjunction with the Royal College of Pathologists of Australasia (RCPA) (Dr. Chan / Diagnostix Pathology Laboratories; Prof. Lam / CUHK, Dr. Wong / Queen Elizabeth Hospital)

The Virology Division, PHLSB is also accredited by WHO for poliovirus, measles and rubella testing (Dr. Lim / PHLSB).

NATA has a long history for laboratory accreditation since 1947, is one of the oldest accreditation bodies in the world and has an established reputation in laboratory accreditation having accredited over 500 medical laboratories in Australia (Prof. Lam and Dr. Chan). It is also an international accrediting body recognised by drug companies. Departments having staff with previous experience in NATA accreditation enjoyed a head-start in preparing for accreditation by this organization (Prof. Lam). Cost-sharing for assessment visits is also possible among several hospitals applying simultaneously for the NATA-run programme (Dr. Wong).

CAP is another highly regarded international body, accrediting a large number of medical laboratories and cited by numerous pharmaceutical companies as satisfying their needs for clinical trials laboratory services. Its choice by Queen Mary Hospital was also based on consensus with the Clinical Trials Centre of the University of Hong Kong (Dr. Collins).

Once the local scheme, HOKLAS, was established and offered laboratory accreditation

as a 'bridging scheme', it was most appropriate to support it (Dr. Chan). HOKLAS is a government-run scheme, free-of-charge for government departments. The PHLSB, being a laboratory under the Department of Health, naturally has to support this scheme (Dr. Lim).

Question 3.
Could you tell us something memorable (an incident, an achievement, major obstacles, etc.) about your journey towards laboratory accreditation?

Dr. Chan: During the process of accreditation, he was faced with the definition of laboratory directors. As defined by the Articles of Association of the Hong Kong College of Pathologists, an accredited laboratory should be directed by a pathologist or a top-grade medical scientist with a relevant PhD degree. To promote this concept, interested professionals assembled to form the Hong Kong Association of Pathology Directors (HKAPD) in 2003. Subsequently this definition of laboratory directors was proposed and adopted by HOKLAS and endorsed by the College, resolving the issue. Its mission fulfilled, the HKAPD was dissolved this year.

Dr. Collins: One of the most memorable aspects concerning the achievement and subsequently maintaining laboratory accreditation was the enormous culture changes at all levels in the organisation. The mainstream culture saw gradual transformation from considerable initial reluctance and lack of appreciation of the need or benefits of the exercise - "we are a teaching hospital laboratory and don't need to prove we are excellent" - to wholehearted belief in the on-going benefits of continued participation in all aspects of laboratory accreditation.

Prof. Lam: A memorable achievement is his department's success in achieving accreditation in March 2002 of the point-of-care (POC) blood gas analysis in the Intensive Care Unit, Neonatal Care Unit, Accident & Emergency, Operating Theatre, and Labour Ward of the Prince of Wales Hospital (PWH) and the Medical Ward of the Shatin Hospital with local area network (LAN)-based connectivity to the central laboratory in PWH Chemical Pathology. This was based on the advice of NATA and facilitated with special funding support by the then PWH Hospital Chief Executive Prof. Allan Chang. Such a quality concept initiated by Dr. Michael HM Chan has since April 2004 been extended to POC blood glucose analysis (85 wards and outpatient locations) that is well appreciated by clinicians and nurses in the New Territories East Cluster.

Dr. Lim: The process of building the quality system and culture in the laboratory takes many years. She quotes the example of continuous improvement requests (CIRs), which staff at first did not feel comfortable to raise, but with time, came to be perceived as opportunities for improvement rather than a fault-picking exercise.

Dr. Wong: It is a memorable moment every time his laboratory is granted accreditation status, since success proves that hard work pays off. He notes, on the other hand, that the major difficulty is to persuade and align the whole pathology team (management and frontline) in the commitment to laboratory accreditation; it is sometimes difficult or even impossible to comply with the requirements set by the assessors because of either resource limitation or need of change in habit.

Question 4.
What is your advice to a laboratory contemplating to undergo laboratory accreditation?

Planning and preparation should begin several years in advance of enrolment in an accreditation programme. It is critical for the laboratory to actively participate in proficiency testing and other external quality assurance programmes for at least 1-2 years before applying, and the laboratory should ensure that these programmes are acceptable to the planned accreditation body (Dr. Collins).

Laboratory accreditation or, in other words, attainment of quality, entails cost and more paper work (Dr. Chan). These are however worthwhile, as is the hard work involved in the process (Dr. Chan & Dr. Wong). Laboratory accreditation should be seen as the responsibility of every member of the laboratory. Everyone should contribute in one's own way to achieving the required standards (Dr. Lim). The process of preparing for accreditation confers as much

benefit on the laboratory as its attainment (Prof. Lam). It is educational in its own right. It stimulates review of existing practices and benchmarking against other institutions (Dr. Collins).

Although laboratory accreditation often starts as a top-down directive (Dr. Wong), frontline colleagues and even minor staff members should be motivated by involvement in the core team for preparation. They will take ownership of the project and can often provide clever and practical solutions to the problems encountered (Prof. Lam). A culture of quality finally develops (Dr. Wong). Accreditation ensures quality control standards are maintained at the highest level (Dr. Collins). The laboratory staff themselves are the first to benefit (Dr. Chan).

The process of preparing for accreditation confers as much benefit on the laboratory as its attainment. It is educational in its own right.

Question 5.
In your opinion, what should be the future of laboratory accreditation in Hong Kong?

Laboratory accreditation is an irresistible force for change and improvement in the medical laboratory (Dr. Collins). It is a global trend. All laboratories carrying out medical testing would need to be accredited to prove that they have attained recognised standards (Dr. Lim).

On the local scene, the future of medical laboratory accreditation is bright, especially when the healthcare reform is heading towards shared care with the private sector and enhancement of primary healthcare (Dr. Wong). Laboratory accreditation should be used as a means to level the playing field in the medical testing industry. More effort should be put into promoting and educating the end-users of the private sector about the benefits for laboratory accreditation. This is especially pertinent in the private sector, where doctors may choose from a variety of laboratories to refer their specimens (Dr. Chan).

Although currently many laboratories in major hospitals are accredited by overseas organisations, the medical laboratory accreditation programme run by HKAS has proved to be one of the most successful programmes in the world, promoting the use of ISO 15189 to accredit medical laboratories. It has gained wide acceptance, including that from the private sector. In the coming couple of years, it is hoped that laboratories currently accredited by overseas accreditation bodies will gain more confidence in the local programme (Dr. Wong).

When nearly all laboratories are accredited, the government should consider enacting legislation mandating accreditation of clinical laboratories which provide medical testing and linking accreditation status to practice license (Prof. Lam).

Question 6.
What do you think is the role of the College in laboratory accreditation?

The College should be more proactive in promoting laboratory accreditation (Dr. Wong). College Fellows, the ultimate experts in the various fields of medical laboratory accreditation, should play a more active advisory and consultative role in the local accreditation programme. They are also the key personnel in the inspection and accrediting process (Dr. Collins). The College should set standards without fear of disenfranchising sector interests. In particular, it should uphold the principle that Pathologists should direct all medical laboratories, assisted by technologist colleagues (Dr. Chan). It should monitor the standards and ensure professional requirements are incorporated in the standards; this should be done in collaboration with the accreditation body (Dr. Lim). It may arrange regular seminars for members and fellows to address their queries and concerns for such exercise (Prof. Lam).

Question 7.
Do you want to comment on other areas related to laboratory accreditation not covered by the above questions?

Dr. Chan: "The medical profession is not yet fully aware of the importance of laboratory accreditation. In the private sector, doctors have a variety of choices of laboratories to

refer samples and specimens. The process of laboratory accreditation will be promoted by the support doctors show in referring their cases only to accredited laboratories. Laboratories lagging behind will inevitably try to catch up. Ultimately, patients will benefit."

Dr. Collins: "Laboratory accreditation can be achieved with current laboratory resources and utilising the goodwill and expertise of existing staff; however, the ideal is to acknowledge the importance of the key elements leading to and maintaining laboratory accreditation and then employ specific suitably equipped staff to set up and maintain a quality system. A Quality Manager, as defined by ISO 15189, will prove to be an essential part of a laboratory hierarchy."

Prof. Lam: "Currently six colleagues in the Department of Chemical Pathology of the CUHK are HOKLAS assessors appointed by HKAS. They participate in laboratory assessment and give advice to laboratories preparing for accreditation. We hope our efforts will contribute the improvement of pathology service in Hong Kong."

Dr. Lim: "Resources must be allocated to build quality systems. It is not a one-off process. Without resources and cooperation of staff, maintaining the quality system will be a challenge."

Laboratory accreditation is an irresistible force for change and improvement in the medical laboratory. It is a global trend.

Concluding Remarks

The interview assembled a group of veritable local experts in the field, sharing with us their invaluable experience and outlook on laboratory accreditation. They explored the philosophy behind the concept, expounded the methodology leading to success, and envisioned the future of the programme in Hong Kong. This article, we believe, presents an authoritative and comprehensive overview of the topic. It expresses the contributors' commitment to and knowledge of continuous quality improvement. All readers, be they upholding or planning for laboratory accreditation, should hopefully find it enlightening.

Timetable of the 17th Annual General Meeting 22nd November 2008 (Saturday)

Venue:
HKAM Jockey Club Building, 99 Wong Chuk Hang Road, Aberdeen, Hong Kong.

3:00 pm – 5:00 pm	**The 4th Trainee Presentation Session**
5:00 pm – 5:30 pm	**AGM**
5:30 pm – 6:00 pm	**Reception**
6:00 pm – 7:00 pm	**Conferment Ceremony**
7:00 pm – 8:00 pm	**The 17th T. B. Teoh Foundation Lecture** **Title:** **Haemoglobin Genetics, from Diagnosis to Treatment** **Speaker:** **Prof. KAN Yuet Wai,** **Louis K. Diamond Professor in Hematology,** **University of California, San Francisco, CA.**
8:00 pm – 10:00 pm	**Chinese Banquet Dinner**

THE HONG KONG COLLEGE OF PATHOLOGISTS:

TOPICAL UPDATE

Volume 3, Issue 2 2008

Editorial note from the Education Committee:

In this issue of Topical Update, Dr. Janette KWOK introduced to us on the immunogenetics. This is an area of great potential in understanding the immune response which is encoded in our genetic makeup and therapeutic choices. We welcome any feedback or suggestions. Please direct them to Dr. WK LUK (e-mail: lukwk@ha.org.hk) of Education Committee, the Hong Kong College of Pathologists. Opinions expressed are those of the authors or named individuals, and are not necessarily those of the Hong Kong College of Pathologists.

Immunogenetics: MHC and non-MHC

KWOK, SY Janette
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Queen Mary Hospital, Hong Kong

Introduction

Immunogenetics is the study of the immune response in relation to genetic makeup. The immune system protects the vertebrates from all potential harmful infectious agents such as bacteria, virus, fungi and parasites. The growing understanding of the immune system has influenced diversified biomedical disciplines, and is playing a significant role in the study and treatment of many diseases such as cancer and autoimmune conditions.

The launch of immunogenetics could be traced back to the demonstration of Mendelian inheritance of the human ABO blood grouping in 1910. Major developments leading to the emergence of immunogenetics were accounted by the rediscovery of allograft reactions during the Second World War and the formulation of the immunological theory of allograft reaction and the clonal selection hypothesis by Burnett in 1959.

Immunogenetics has poised on the brink of a new era, driven by new technologies and shaped by discoveries about regulatory mechanisms within the immune system.

The field of immunogenetics has exploded during the last 25 years, thus expanding the range of concepts with the potential to improve the field of medicine with regard to transplantation, immunotherapy and the study of immune polymorphisms. Immunogenetics has poised on the brink of a new era, driven by the development of new technologies and shaped by fundamental discoveries about the mechanisms that regulate interactions between the adaptive and innate immune systems. Technologies are developed to revolutionize genetic analysis and providing new strategies for elucidating the genetic mechanisms that influence immune responsiveness and autoimmunity.

The most relevant influence on the development of immunogenetics is the studies of the highly polymorphic gene family well known as the major histocompatibility complex (MHC). These genes was first studied as antigens of the white blood cells and hence named human leukocyte antigens (HLA). They have influenced both the donor choices in organ transplantation and the susceptibility of an organism to chronic diseases. The MHC is also linked with many important autoimmune diseases such as rheumatoid arthritis and diabetes.

The explosion in immunogenetics studies of these molecules was ultimately resulted from the discovery in 1972 that these MHC molecules are intimately associated with the specific immune response to viruses. This has led to the construction of very detailed genetic and physical maps of this complex and its complete sequence in an early stage of the great human genome sequence project.

The target for this update is to bring out a brief

overview of some of these new areas that are of clinical importance to the field of HLA and immunogenetics, and hopefully provide some thought into the future of modern methods and their potential importance in understanding the immune response.

Non-classical MHC Class I

The impact of non-classical HLA molecules in the immune response has been investigated only in these recent years. Humans encode three "non-classical" MHC Class I genes, HLA-E, F, and G. These relatively new class I genes and molecules were first described by Koller and colleagues in 1989. In general, these non-classical HLA molecules are considered immune "tolerization" molecules, which not only interact with natural killer (NK) cells but also with T lymphocytes and other cells. These non-classical class I molecules are similar in sequence and structure to MHC class I molecules but do not show the striking polymorphism seen for their classical relatives and may be encoded outside the MHC. These molecules are characterized by unique patterns of transcription, protein structure and immune function.

Studies on non-classical HLA molecules suggest they play important roles in immune recognition, immune response modulation, and tumour progression.

The study of HLA-E in transplantation has yielded information regarding the pattern of HLA-E expression suggesting its important role in immune recognition. HLA-E molecules may present some peptides, such as MHC signal sequences, to T lymphocytes and this recognition is mediated by the interaction of HLA-E with the CD94/NKG2 receptor and can result in either 'inhibition' or 'activation" of the NK cell.

Several recent studies have shown how HLA-E and HLA-G act as potential powerful modulators of the innate immune response with regard to susceptibility to infectious processes. HLA-F was identified at the same time as HLA-G and HLA-E but there is little information to date about its expression and function. HLA-F is only slightly detectable on the cell surface of trophoblast, some B and mononuclear cell lines and occurs predominantly as an intracellular, empty and unstable class I protein. On peptide binding, HLA-F is expressed and can interact with immunoglobulin-like receptors ILT2 and ILT4, leading to an altered activation of immune effector cells. The unusual characteristics of the predicted peptide-binding groove of HLA-F, together with its predominantly intracellular localization, raises the possibility that HLA-F might be capable of binding only a restricted set of peptides.

Tumour cells have been found to express the non-classical HLA molecules. Evidence suggests a possible role of these molecules in immune recognition. Abnormalities in non-classical MHC expression have been found in human tumours and might lend insight into clinical outcome. Implications that a delicate balance needs to exist between stimulating and suppressing signals among cells expressing non-classical MHC suggest that studying this immune response could provide information regarding possible tumour progression.

MHC Class I-related chain genes

In 1994, two new polymorphic families of MHC class I-related genes, termed MHC class I-related chain A (MICA) and B (MICB) which were ccontained within the MHC region, were described and already sparked a new area of interest in the HLA community in relation to transplantation. These genes are located near the HLA-B locus on chromosome 6 and encode cell surface glycoproteins that do not associate with β -2 microglobulin. These molecules function as restriction elements for intestinal γ/δT cells and they behave as cell stress molecules. MICA is expressed in endothelial cells, keratinocytes and monocytes, but not in lymphocytes, thus making them potentially important in solid organ transplant. It is likely that the polymorphic MICA molecule may be a target for specific antibodies and T cells in solid organ grafts or in graft vs. host disease (GVHD).

MHC class I-related chain A and its encoded antigen are potentially important in solid organ transplant as well as transplant rejection.

MIC molecules interact with both T cell and NK cell receptors. MIC antigens have been implicated in transplant rejection because anti-MIC antibodies are often found in transplant recipients, reminiscent of the classical anti-HLA antibodies. These antibodies may facilitate some complement-mediated cytotoxicity against endothelial cells from the graft well documented in a four year follow up study of a prospective trial in kidney transplants have provided strong evidence that HLA and MICA antibodies are associated with graft failure. The anti-MICA antibodies were found to induce a prothrombotic state, characterized by a loss of surface heparan sulphate and thrombomodulin from cultivated endothelial cells.

Minor Histocompatibility Antigens

A different set of polymorphic non-MHC proteins have been identified that are important in provoking transplant rejection, they were defined by Snell and colleagues as minor histocompatibility antigens (mHAg), as the rejection reactions they induced in mice were slower. Peptides from these proteins are presented to T cells in an MHC class I or class II restricted manner. The role of mHAg as the facilitators of GVHD as well as the targets for immunotherapy of cancer was well studied by Prof. Els Goulmy. The number of possible mHAgs in transplants performed between genetically unrelated, MHC-matched individuals is very large. However, the reactions seem to be restricted to a few epitopes, thus dubbed immunodominant. The molecular basis for this phenomenon is incompletely understood, although it has recently been shown that both the duration of individual mHAg presentation and the avidity of T-cell antigen recognition influence the magnitude of the cytotoxic response that ensues. Though mHAgs are named minor, and the frequency of responders to these antigens is very low, after transplantation, a single immunodominant mHAg can induce GVHD. Apart from gene polymorphisms, homozygous gene deletions can also serve as mHAgs as it has recently been described for an autosomal gene in the UDP-glycosyltransferase 2 family. mHAgs were originally identified as a plausible explanation for the cause of graft rejection or GVHD in HLA-matched allogeneic haematopoietic stem cell transplants (HSCT).

Molecular identification has revealed that most mHAgs are short peptide fragments encoded by genes, which are polymorphic due to single nucleotide polymorphisms (SNPs). Disparity at the genotypic level between donor and recipient gives rise to mHAgs as non-self antigen differences for both the donor and recipient. Thus, information gathered from both solid organ and HSCT could provide information regarding the importance of this system's immune function. Identification of mHAgs currently employs PCR-based methods.

Information gathered from both solid organ and haematopoietic stem cell transplants could reveal the importance of this system's immune function; monitoring of HA-1 responses provides a potential strategy for optimizing immunosuppressive therapy.

When minor antigens are tissue restricted, they can be considered an adjunct for graft vs. tumour responses in HSCT. This strategy is currently under investigation in phase I/II clinical trials in which post-transplant recipients are boosted with donor lymphocyte infusions using tumour-specific minor peptides. There are trials for hematologic malignancies using mHAg HA-1 and HA-2, and for breast and renal cell carcinoma using HA-1. The integration of clinical practice of the tolerizing potential of minor antigens in solid organ transplantation is well demonstrated by the HA-1-specific alloimmune responses may lead to allograft tolerance in renal transplantation. HA-1-specific T regulator cells can be identified in long-term transplant recipients and correlate with HA-1-specific cytotoxic T-lymphocyte responses and microchimerism. As such, they provide a potential strategy for optimizing immunosuppressive therapy by monitoring HA-1 responses.

Projects in the field of mHAg have been continued in 13th, 14th and the soon-to-be 15th International Histocompatibility and Immunogenetics Workshops (IHIWS). Data is being gathered to formalize information pertaining to this system.

Killer Cell Immunoglobulin-like Receptors

The killer cell immunoglobulin-like receptor (KIR) genomic region displays extensive diversity through variation in gene content and allelic polymorphism within individual KIR genes. Family segregation analysis, genomic sequencing and gene order determination proven that genomic diversity have already given rise to more than 20 different KIR haplotypes and 50 KIR genotypes. The importance of this recognition stems from the fact that in the clinical setting of mismatched HSCT, donor vs. recipient NK cell alloreactivity has been associated with better outcome. This alloreactivity derives from a mismatch between inhibitory receptors for self-MHC class I molecules on donor NK clones and the MHC class I ligands on recipient cells. NK cell function is regulated by clonally distributed inhibitory receptors that are specific for self-MHC class I molecules. Lack of engagement of these receptors results in target cell lysis (missing self-recognition), which has the potential to eliminate the remaining malignant recipient-originated cells. The National Marrow Donor Program (NMDP) high-resolution KIR typing pilot project was initiated to evaluate the efficacy of performing allele level KIR typing.

In the clinical setting of mismatched HSCT, donor vs. recipient NK cell alloreactivity has been associated with better outcome; the importance of the KIR system, such as impact on many disease states and the risk of viral function, is under investigation.

The role of NK cell alloreactivity in solid organ transplantation is less known. Results in animal models show that NK cells are neither necessary nor sufficient for acute immune rejection - which does not exclude an NK cell contribution to the rejection process. In addition, work continues in determining the importance of the KIR system in many aspects important to medicine, such as impact on many disease states and the risk of viral function. Recent work on the KIR system with regard to viral function could provide information on how to combat certain viruses. These areas of interest have pushed the field forward to develop different commercial methods for KIR typing.

Cytokine Polymorphism

Cytokine polymorphism and signaling is also becoming a major focus for understanding and interpreting the immune response. Cytokines are secreted molecules which act on their surrounding environment to help provide cell-to-cell signaling, affecting not only in HSCT but also other immune modulated environments.

The "cytokine storm" which occurs when subjecting cells to different conditioning regimens in HSCT or solid organ transplant must have diverse effects on this microenvironment. The monitoring of this environment could be essential in adjusting the post-transplant immunotherapy. Individual differ in the amounts of cytokines secreted in response to the triggering stimulus due to the cytokine polymorphisms and some polymorphisms appear to have consistent alteration in cytokine production. Studies are being conducted to determine whether associations exist between cytokine gene polymorphisms and susceptibility to particular diseases. The positive associations with cytokine SNPs in human diseases have been described.

The monitoring of this environment could be essential in adjusting the post-transplant immunotherapy.

The expanding list of candidate genes linked with GVHD includes cytokines, chemokines and their receptors. The physiopathology of GVHD provided the rational to prioritize which gene to study first. The main cytokine gene polymorphisms that have been linked to GVHD or transplant-related mortality (TRM) include TNF, IL-10, IL-6, IFN-g, IL-1 and TGF-b, and studies are being conducted on IL-2, IL-4, IL-13 and CTLA4 amongst others.

Summary

The question arises as to what is the most efficient method for gathering this information in these new areas of immunogenetics. Immunogenetic profiling can be defined as the process of extrapolating the information encoded in one's genetic makeup, which will help unlock the mystery of the immune response. With increasing evidence concerning the complexity of immune polymorphisms and the significant role these polymorphisms play in the immune response, it is imperative to gather not only the expected information but also the hitherto unknown information.

As the diversity of the HLA system and other similar systems continues to emerge, we may expect further evolution in the immunogenetics field.

With the rapidly expanding wealth of genetic, biological and functional information, we are faced with the challenges of making scientific complexity more productive and optimizing its translation into medicine and public health. The expanding knowledge could benefit from an integrated systems biology approach. MHC/HLA systems biology will foster the emergence of a truly scientifically based holistic pathway for MHC/non-MHC immunogenetics.

Out of the Whitecoat:

From 'COS' to 'cos'

I was much honoured to be a pathologist in the first half of my life and I feel the same to be able to work as a pastor preacher for the rest of my life. I "retired" from the post of COS in 2004. On leaving the department I brought with me sweet memories, precious friendships and wonderful working experience. Now I am facing new challenges to work, in certain sense, again as a "cos" **(Carer of souls in a caprice of situations through a combination of services).** *I work in Hong Kong Swatow Baptist Church located in Kennedy Town HK Island.*

▲ *The church that I belong to.*

▶ *The main hall of the church.*

The change was a decision made after a ten-year period of waiting, ruminating and observing. Observing the human plight; ruminating over the price that I have to pay, my motive to change, the possibility of doing this job well and waiting for the direction from the God I believe. I did not rush into any decision as it involved not only me but also my immediate family. Will they accept a less secure and simpler lifestyle? I waited till I had the full support from my wife, my children and last but not least my parents who labored to provide me with the possibility of studying medicine. The VER scheme was an added bonus to my decision.

You might think that being a pastor is very different from a COS. It's quite true from the work nature and activities. I have to preach; to teach; to counsel and to conduct ceremonies. However apart from this, there is a basic similarity between pastor and COS that is to interact with people. In a church with 4 full time pastors and over 400 members of different age groups, I have to look after around 100 members. The number is similar to the number of staff in UCH Pathology department. From my previous working experience, I learned how to stay close to my colleagues, sharing and caring their problems, appreciating and developing their talents and enjoying their company. Now I do my job with the same attitude.

▲ *My eldest daughter, wife, youngest daughter, myself and son (left to right).*

▲ *Leading a baptism ceremony.*

◀ *Group singing in a district programme open to all in a district park.*

▲ *Next to me is my younger brother, he is my 'senior' colleague working in the same church.*

Besides this, my church also worked with other local churches in central and western districts to conduct program and services to the community. For example we distributed "rice dumplings" to the poor and needy during the Dragon Boat Festival. We visited old age homes and families that can be reached in the community to share their problems and our faith.

Every now and then I met and chatted with previous colleagues who reminded me of those good old days. I am sure that we all share the same conviction of maximizing our knowledge and abilities to serve and to live well.

Dr. Andrew Chung-Ho CHOI

Memento

On a beautiful Saturday afternoon, we were honoured to have the presence of all presidents, past and current, of the Hong Kong College of Pathologists. The photos taken on that day reminded us of their influential contributions to the College, as well as the milestone achievement at various stages. This photo-taking occasion also served as a precious opportunity for a brief but delightful reunion. We thank Dr. Victor TANG for his hard work in organizing this event.

▲ *From left to right: Dr. NG Wing Fung, Dr. Robert John COLLINS, Professor Faith HO, Dr. MAK Wai Ping and Dr. LEE Kam Cheong.*

Fellows' Laurels

Loke Yew Professorship in Pathology

Professor Irene O.L. Ng, one of our College Council members, was elected Loke Yew Professor in Pathology for her prominent contributions to the study of liver disease, especially on liver cancer and hepatitis. The University of Hong Kong celebrated its Third Inauguration of Endowed Professorships on April 17, 2008, with the inception of the Loke Yew Professorship in Pathology. This Professorship was established through the generosity of Mr. Loke Yew's grandchildren, Ms. Ruby Loke Yuen-Kin and Professor Loke Yung-Wai, as a testimony of the strong ties between the University of Hong Kong and the Loke Family. Significantly, this Endowed Professorship in Pathology is first of its kind in Pathology in Hong Kong. For those interested in Professor Ng's research, please refer to the following web site: http://www.hku.hk/patho/staff/list/ing.html

Congratulations, Irene! We are proud of you!

▲ *Ms. Amanda Loke (left), the great-grand-daughter of Mr. Loke Yew, presenting the honour to Professor Irene Ng (right).*

Smart State Fellowship of Australian Queensland Government

Professor Alfred K.Y. Lam, our overseas College Fellow and Chair Professor of Pathology in Griffith University, was awarded Smart State Fellowship in 2008 for his research in thyroid cancer. The Smart State Fellowship is part of the Australian Queensland Government's Smart State Innovation Funding Programme, which aims to build world-class research facilities, attract top-quality scientists to Queensland and stimulate cutting-edge research projects.

Bravo, Alfred!

◀ *Professor Alfred Lam working hard at his microscope.*

CONGRATULATIONS!!

We are pleased to announce that the following candidates have passed the membership examination/fellowship assessment. Please join us to congratulate them on their success.

ANATOMICAL PATHOLOGY:

Dr. YIU Kwan Ho
(Fellowship assessment)

Dr. HUI Yin
(Membership examination)

Dr. LAU Wing Hung
(Membership examination)

Dr. LO Cheuk Lam Regina
(Membership examination)

Dr. TSANG Koon Ho
(Membership examination)

CLINICAL MICROBIOLOGY AND INFECTION:

Dr. CHAN Chi Wai Rickjason
(Fellowship assessment)

Dr. LAM Ho Shiu Bosco
(Fellowship assessment)

Dr. TANG Siu Fai
(Fellowship assessment)

FORENSIC PATHOLOGY:

Dr. CHIAO Wing Fu
(Fellowship assessment)

HAEMATOLOGY:

Dr. LIANG Yu Shan
(Fellowship assessment)

Dr. WONG Lap Gate Michael
(Fellowship assessment)

NEW EXAMINATION SCHEME OF CLINICAL MICROBIOLOGY AND INFECTION AND VIROLOGY

Please be informed that the formats of Clinical Microbiology and Infection and Virology fellowship examinations have been revised. You can download the addendum from the College website.

For Clinical Microbiology and Infection:
Fellowship Assessment
(1) Written component – one written paper AND
(2) Oral component – consisting of a comprehensive viva with a practical component, which may include questions on clinical virology.

For Virology:
Fellowship Assessment
(1) Written component – one written paper AND
(2) Oral component – consisting of a comprehensive viva with a practical component, which may include questions on clinical microbiology.

This change will only be applied on new trainees **registered on or after 1 July 2008**. Existing trainees (i.e. registered before 1 July 2008) are welcomed to opt for this examination format during their examination application.

For enquiry, please contact Dr. Chloe MAK, TEC Secretary, at 2990-1882.

NOTES TO FELLOWS ON THE NEW CONTINUING MEDICAL EDUCATION / CONTINUOUS PROFESSIONAL DEVELOPMENT (CME/CPD) SCHEME

According to the new Continuing Medical Education / Continuous Professional Development (CME/CPD) scheme started on 1 January 2008, Clinicopathological Conference and Morbidity & Mortality Meeting (CPC & M&M meeting) had been included as a new Formal College Approved Activity (category 5.7), and fellows are eligible to score a maximum of 30 CME/CPD points for this new category in each 3-year-cycle. Since this change could affect CME/CPD scoring regulation on a number of regular activities named “CPC or M&M meeting” in different institutes, the Education Committee had sent out a letter to various activity organizers to remind them about the changes and encourage them to update the activity titles whenever appropriate.

The essence of the new scheme is to provide more varieties of CPD programmes for participants, which is in line with the spirit of CME/CPD. We would like to remind all our fellows to observe the for maximal claimable CME/CPD points set for each activity category in a 3-year-cycle.

POLICY ON DISTRIBUTION OF NON-COLLEGE-RELATED ANNOUNCEMENTS

The following policy related to the distribution of non-College-related announcements is now in effect, and it has been endorsed by the Council:

1. For activities not organized by the College, but are of potential interests to our Fellows, the College can help to disseminate the announcement by various means.

2. Announcements can be made in the College newsletter and the College website free of charge, at the discretion of the Chief Editor/Webmaster, or the Registrar, or the Chairman of the PGA Committee.

3. The College can help to distribute ready-to-go packages (already with stamps) at a charge of $1,000 per service, at the discretion of the Registrar or the Chairman of the PGA Committee.

4. The College can help to disseminate the announcement through e-mail at a charge of $1,000 per service, at the discretion of the Registrar or the Chairman of the PGA Committee.

5. For announcement of activities co-organized by the College, no charge will be applied.

If member/fellow wishes to opt out of receiving non-College-related announcement by either post or e-mail, please notify College Secretary via hkcpath@hkam.org.hk (e-mail), 2871 8756 (tel) or 2871 8755 (fax).

AWARDEES OF THE CHAN WOON CHEUNG EDUCATION AND RESEARCH FUND 2008

This year, the CHAN Woon Cheung Education and Research Fund was awarded to **Drs. WONG Shun and LUK Shik** with HK$25,000 to each applicant to support their research proposals on "the prognostic significance of allelic losses of chromosomal arms 1p and 9q in atypical meningioma" and "the local prevalence, genotypes and antibiotic susceptibility profiles of plasmid-mediated AmpC beta-lactamases in *Klebsiella pneumoniae, Escherichia coli, Proteus mirabilis* and *Salmonella* species in blood culture", respectively. Congratulations !

MEETING ANNOUNCEMENTS

HKIAP Annual Scientific Meeting 2008

Oct 31 - Nov 2, 2008
Postgraduate Education Centre,
Prince of Wales Hospital, Hong Kong.
http://www.hkiap.org

Hong Kong Academy of Medicine 15th Anniversary Congress: Grand Rounds: *'Working together: the Power of Collaboration'*

Nov 15 - 16, 2008
HKAM Jockey Club Building, Aberdeen, Hong Kong.
http://www.hkam.org.hk/hkam15

17th Annual General Meeting of the Hong Kong College of Pathologists with 17th T.B. Teoh Foundation Lecture: *'Haemoglobin Genetics, from Diagnosis to Treatment' by Prof. Kan Yuet Wai*

Nov 22, 2008
HKAM Jockey Club Building, Aberdeen, Hong Kong.
http://www.hkcpath.org

The XXV Congress of the World Association of Societies of Pathology and Laboratory Medicine (WASPaLM) in conjunction with Pathology Update 2009 (the Royal College of Pathologists of Australasia)

March 12 - 15, 2009
Sydney, Australia.
http://www.rcpa.edu.au/pathologyupdate2009