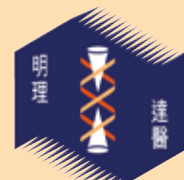


PATHOLOGUE

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



SCIENTIA ILLUMINAT MEDICINAM
香港病理學專科學院

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Message from the President

After nearly two years of hard work among Councillors, Honorary Advisor and the lawyer of the Company Registry, we are in the process of calling an Extraordinary General Meeting (EGM) in early June. A lot of work has been done on updating our Articles with modifications, including adopting a similar mechanism as the Academy on nomination of Honorary Fellow. The Registrar has, by the time of publishing this Newsletter, sent you the relevant information and invitation to attend the EGM held in the Academy Building in the evening on 10 June. I urge you to come and support the EGM which will only take a little bit of your time. If time permits, we may have a chat and you may let me know your thoughts on College matters. This is an important step for our College to move forward.

I am happy to announce that the structured training programme in Molecular Pathology is now established. Our Specialty Board chairpersons are instrumental in setting up individual programme in respective disciplines. Our laboratory inspectors have completed inspection of training centres. The Training and Examinations Committee reviewed all the inspection reports which have been endorsed by the Council. The new training curriculum will be effective for the new trainee intake this year.

One new topic in the Academy is the proposal on dual Fellowship. Recently the Hong Kong College of Physicians raised the discussion in the Education Committee of the Academy on whether the Academy would allow one to be registered in more than one Specialty in the Specialist Registry. However, many would agree that it is difficult for someone to work in more than one specialty in real practice; and there may be problems to work out the time split, and justification on the proportion of time spent in different specialties. The discussion is still in progress at present.

People who come to the Academy Building to use its facilities may see that renovation work is going on. There will be a major overhaul on the facilities including changes in layout of a few floors. There will be a Simulation Centre for professional training (in collaboration with Harvard University), improved dining facilities, increased dining areas, and more function rooms for meetings. Details are referred to the Academy Newsletter.

The Academy of Medicine is celebrating the 20th Anniversary this year, and will host the 20th Anniversary Congress from 8 to 10 December. Dr. Edmond Ma sits in the Organizing Committee. Professor Rossa Chiu represented our College to sit in the Scientific Committee, and has helped in setting up a session on "The Era for Medical Genetics and Molecular Medicine" with Dr. H.W. Liu (HAHO), Professor T.Y. Leung (Department of Obstetrics and Gynaecology, CUHK), and Professor Dennis Lo (Department of Chemical Pathology, CUHK) as speakers. I would urge your support to make it a successful event.

All these works cannot be accomplished without my Council. I thank specifically Alex and Victor, our Registrar and Deputy Registrar, for their unfailing support. I would also thank our TEC, laboratory convenors, inspectors, and Specialty Board members in making our new programme possible. Finally, I would thank Adrienne, our College Secretary, for her dedicated service.

Dr. Michael SUEN
The President
May 2013



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The 21st Annual General Meeting 2012 and the 21st T.B. Teoh Foundation Lecture

The 21st Annual General Meeting (AGM) was held after the 8th trainee presentation on 17th November, 2012. Three new Council Members, Dr. IP Pun Ching Philip, Dr. LAI Sai Chak and Dr. TSANG Ngai Chong Dominic were elected. We would like to take this opportunity to thank the immediate past Council Members Dr. LAM Wing Yin, Dr. POON Wai Ming and Dr. TSE Wing Sze Cindy for their contribution to the College.

In the conferment ceremony, one Honorary Fellow, 10 Fellows and three Members were admitted to the College. Prof. LEE Sum Ping was admitted as Honorary Fellow to the College. The honourable guests included Professor LIANG Hin Suen Raymond (President of the Hong Kong Academy of Medicine) and Dr. Hon. LEUNG Ka Lau (Member of the Legislative Council of Hong Kong, Medical Functional Constituency). The College President Dr. SUEN Wang Ming Michael shared with the audience the College plan on the setting up of a structured training programme in Molecular Pathology in different disciplines.

The 21st T.B. Teoh Foundation Lecture was delivered by Prof. BEH Swan Lip Philip, Clinical

Associate Professor (Forensic Pathology), Department of Pathology, Li Ka Shing Faculty of Medicine, The University of Hong Kong. In the lecture titled "Extending Boundaries", Professor BEH enlightened the audience on issues of homicides, suicides and sexual assault victims. The guests, senior fellows, new fellows and members enjoyed the subsequent Chinese banquet dinner.

We would like to thank Professor CHIU Wai Kwun Rossa for being the Mistress of Ceremonies in the AGM. We thank Dr. CHUNG Ah Yu Ivy, Mr. LAW Chi Kit and Ms. LIU Wing Yan Wynnee for taking photos during the Trainee Presentation Session, AGM, conferment ceremony, T.B. Teoh Foundation Lecture and the dinner. We would also like to express our gratitude towards our College Secretary, Ms. Adrienne YUNG, as well as Ms. Maizie CHAN and Ms. Heidi CHU, for their continuous support in organizing the AGM.

Looking forward to seeing you all in the coming AGM.



▲ *The Presiding Group on Stage.*

◀ *The Incoming Council.*



◀ *Past President and Other Senior Fellows in Anatomical and Forensic Pathology.*

▼ *Senior and Young Chemical Pathologists.*



◀ *Professor S. P. Lee, Honorary Fellow, and the President.*



◀ *Past Presidents and Senior Fellow.*

▼ *Professor Philip Beh Delivering the T. B. Teoh Foundation Lecture.*



◀ *The Head Table at the Banquet.*



The 8th Trainee Presentation Session

The Trainee Presentation Session is an annual event held before the College Annual General Meeting (AGM). The aim of this event is to encourage our trainees to participate in research and development in their daily practice and give them a chance to present their work in front of College Fellows and trainees. It is a College requirement that *all trainees registered on or after 16 October 2008 must make two presentations within their six years of recognized training, one of which must be at the Trainee Presentation Session or conferences organized by the College*. For each Trainee Presentation Session, a judging panel is formed by at least five College Fellows coming from different subspecialties. Best Presentation Award is granted to the participant who scores the highest mark based on the marking scheme which focuses on medical relevance, originality and study design, scientific content, findings and conclusions, and finally presentation skill.

The prize of the 8th Trainee Presentation Session included a plaque, a Certificate of Best Presentation, and HK\$2,000.

Since the first Trainee Presentation Session in year 2005, eight years have passed. Eight years ago, I was one of the participants. In 2012, I became the organizer of this event! This task would have been much more difficult if there had been no previous organizers who already built a good foundation. So I would like to give my salute to Dr. Janice LO and Dr. Wei Kwang LUK. Both of them had paid a lot of effort on this event in the past. Also, I would like to give my special thanks to Adrienne, our College Secretary, who did all the preparation work nicely.

The number of participants reached a record high this year (Table 1). I was very excited at the beginning and thought "the new policy works"! However, this excitement was quickly replaced by a frown. When I tried to fit in the presentations into our time table, I discovered that we utterly did not have enough time! This really created a bit of a headache to the Education Committee (EC) members – time allocated to this event had been fixed in mid-2012 when the venue was booked. Very limited flexibility was allowed as the Trainee Presentation Session would be followed immediately by the College AGM. Various possible solutions were raised and discussed by the EC members. After a bit of struggle, it was finally decided to cut down the presentation time from 15 minutes to 12 minutes for each participant (Table). The EC will review this arrangement and hopefully can come to a solution for the future.

This event would not have succeeded without active participation from our judges Dr. Albert CHAN, Dr. Vincent CHENG, Dr. Wah CHEUK, Dr. Raymond CHU and Dr. Sai Chak LAI. A big round of applause to all of them!



YUEN Yuet Ping Liz
Vice-Chairman
Education Committee

Dr. Elaine CHEUNG presenting to the audience.

Participant (in order of presentation)	Title of presentation	Subspecialty
1) Dr Elaine CHEUNG	EWSR1-CREB3L1 gene fusion: a novel alternative molecular aberration of low-grade fibromyxoid sarcoma.	Anatomical Pathology
2) Dr Chin Yeung TSANG	Disaster management and victim identification.	Forensic Pathology
3) Dr Ka Ki KWOK	Sexual development of Hong Kong teenage girls - in a forensic aspect.	Forensic Pathology
4) Dr Alexander Hin Ning TANG	A pilot study on HER2 status in gastric adenocarcinoma using immunohistochemistry and brightfield in situ hybridization.	Anatomical Pathology
5) Dr Ka Shing SHUM	Uncommon but potentially fatal presentation of ovarian teratoma.	Anatomical Pathology
6) Dr Hoi Kei WONG	Vasovagal reaction among young first-time blood donors: prediction by body dimension and reduction by less collection.	Haematology
7) Dr Chun Yin PANG	An approach to resolve the diagnostic dilemma between malignant mesothelioma and reactive mesothelial hyperplasia using 3 immunohistochemical markers.	Anatomical Pathology



Group photo of presenting trainees, judges and organizers of Trainee Presentation Session.

The Winning Abstract

Title:

EWSR1-CREB3L1 Gene Fusion: A Novel Alternative Molecular Aberration of Low-Grade Fibromyxoid Sarcoma

Abstract:

Low-grade fibromyxoid sarcoma (LGFMS) is an uncommon sarcoma with a deceptively bland-looking morphology that disguises its malignant clinical behavior. It shows distinctive chromosomal translocations resulting in fusion of FUS with CREB3L2 gene in most cases, and CREB3L1 in rare cases. Thus molecular studies are particularly helpful in the diagnosis of this bland-looking sarcoma. We report two cases of LGFMS serendipitously found to harbor a novel alternative EWSR1-CREB3L1 gene fusion, as confirmed by DNA sequencing of reverse transcriptase-polymerase chain reaction products and fluorescence in-situ hybridization. One patient was a child who presented with a subcutaneous nodule on the lower leg, and the other was a middle-aged woman who had a mass lesion over the proximal thigh. Morphologically, one case showed a spindle cell tumor with hyalinization and giant rosettes, while the other showed classical histology of LGFMS with focal metaplastic bone formation. Immunostaining for MUC4 showed extensive positive staining. Our findings therefore expand the spectrum of gene fusions that characterize LGFMS, and suggest that EWSR1 gene may substitute for the function of FUS in gene fusions of sarcoma.

Experience of Participation in the 8th Trainee Presentation Session

Participating in the College's 8th Trainee Presentation Session was a challenging yet memorable experience. Whilst I do recall the long nights devoted to the honing of my own presentation on the topic "*EWSR1-CREB3L1 Gene Fusion: A Novel Alternative Molecular Aberration of Low-Grade Fibromyxoid Sarcoma*", I also recall having spent an enjoyable Saturday afternoon listening to a potpourri of excellent presentations delivered by trainees from different pathology sub-specialties and the practical advice our experienced adjudicators impressed upon us. This invaluable experience allowed me to gain more knowledge in pathology and skills essential for research and presentation. I wish to take this opportunity to thank my colleagues who took the trouble to guide and inspire me throughout the preparation process. I also wish to thank the College for organizing this meaningful activity and I encourage trainees to actively participate in the upcoming Trainee Presentation Sessions.



▲ Dr. Janice LO, Chairman of Education Committee, presenting Certificate of Appreciation to Dr. Elaine CHEUNG.

Dr. CHEUNG Tin-yan Elaine
Resident Trainee in Anatomical Pathology
Department of Pathology
Queen Elizabeth Hospital



◀ The plaque for the winning trainee.

TOPICAL UPDATE

Volume 8, Issue 1 January 2013

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

Editorial note: A severe form of encephalitis associated with antibodies against NR1–NR2 heteromers of the anti-N-Methyl-D-Aspartate receptor (NMDAR) was recently identified. It is increasingly recognised as a reasonably common and treatable cause of acute psychosis. Dr Richard Wong, a specialist Immunologist in Queensland, and his team have provided a detailed analysis of the anti-NMDAR testing for autoimmune encephalitis and have kindly shared their experience in HSSA-Pathology Queensland on the performance of anti-NMDAR kits. We welcome any feedback or suggestions. Please direct them to Dr. Janette Kwok (e-mail: kwoksy@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.

Laboratory Testing For Anti-NMDAR In Autoimmune Encephalitis: The HSSA-Pathology Queensland Experience



◀ *Authors (from left to right):
Bob Wilson, Kerri Prain, David Gillis, Richard Wong*

*Bob Wilson MSc, FFS(RCPA), Kerri Prain, BSc, David Gillis, FRCPA FRACP FFS(RCPA) and Richard Wong GDM FRCPA FRACP FRCP.
Division of Immunology, Central Laboratory, HSSA-Pathology Queensland, Royal Brisbane and Women's Hospitals, Herston, Brisbane, 4061, Australia.*

Introduction

The spectrum of antibodies against intracellular, cell surface and synaptic neuronal antigens has expanded rapidly in recent years. The antigenic targets include ion channels, receptors involved in neurotransmission across synapses and proteins associated with them. There are now more than twenty anti-neuronal antibodies detected in association with neurological diseases. These antibodies may be associated with underlying malignancies and are commonly referred to as paraneoplastic antibodies (PNAs). Many PNAs have been correlated with neurological manifestations and fall into two groups: those that are cytotoxic for example anti-purkinje cell antibody-I (PCA-I/Yo) and anti-neuronal nuclear antibody-I (ANNA-I/Hu); and others that have functional activity, such as anti-N-Methyl-D-Aspartate receptor (NMDAR) and anti-Voltage-gated potassium channel (VGKC). Recently there has been a marked interest in both anti-NMDAR and anti-VGKC antibodies as the presence of these antibodies identify patients with treatable neurological disease.

Anti-NMDAR was initially described as a paraneoplastic antibody associated with ovarian teratoma, with a characteristic clinical picture of encephalitis with psychiatric features, cognitive dysfunction and seizures.^{1,2} Although subsequent case series have confirmed that ovarian teratoma is a frequent association, it has become apparent that many patients who are positive for anti-NMDAR do not have evidence of an associated malignancy.

There is also some evidence supporting the need for rapid identification of anti-NMDAR. Patients who are diagnosed and treated with immuno-suppressive/immunomodulatory therapy within 40 days of disease onset, have been reported to have a better clinical outcome than those treated after 40 days.²

Given the common finding of psychiatric features in patients with positive anti-NMDAR, there has been interest in the prevalence of anti-NMDAR in patients presenting with their first episode of psychosis. Zandi et al reported

that 6.5% (3 of 46) patients recruited prospectively from a cohort of patients with a first episode of psychosis were positive for anti-NMDAR positive in their serum.³ As discussed below, if the CSF of these patients was also tested, it is likely that the prevalence of anti-NMDAR would be even higher. However it is clearly difficult to obtain informed consent and also actually perform lumbar punctures in acutely psychotic patients.

Finally, it is likely that some patients suspected of having viral encephalitis (including herpes simplex and enterovirus) actually have anti-NMDAR associated autoimmune encephalitis. In the prospective UK multicentre study⁴ and a retrospective study from the California Encephalitis Project,⁵ the prevalence of positive anti-NMDAR was 10/203 (4.9%) and 32/761 (4.2%) respectively, compared to 28/203 (13.8%) and 7/761 (0.9%) for herpes simplex virus, and 3/203 (1.5%) and 30/761 (3.9%) for enterovirus respectively.^{4,5}

Detection of anti-NMDAR

Initially described as a novel neuropil (grey matter) antibody detected by immunohistochemistry on sagittal sections of paraformaldehyde-fixed rat brain,⁶ the target antigen was first characterised in 2007. For the next three years, only two laboratories performed testing for anti-NMDAR, namely those of Josep Dalmau (Philadelphia, USA) and Angela Vincent (Oxford, United Kingdom). The initial 2005 paper described the difficulties of detecting the antibody by immuno-histochemistry, and mentioned that the rat brain had to be fixed in 4% paraformaldehyde at 4°C for 10 days prior to cryosectioning.⁶ Our experience is that anti-NMDAR could not be detected on fresh frozen mouse brain sections by indirect immunofluorescence.

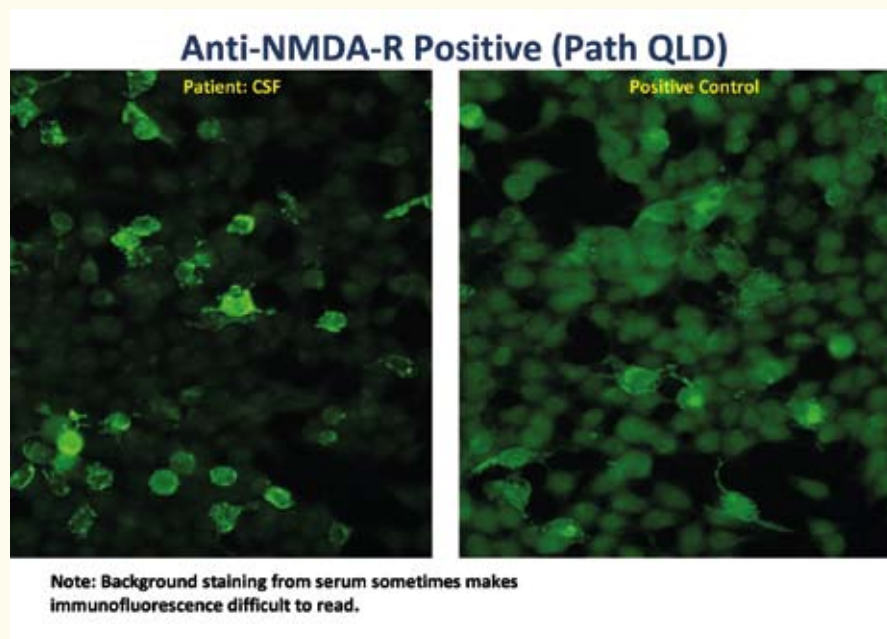
In 2010, Euroimmun (Lubeck, Germany) released the first commercial assays for anti-NMDAR testing using transfected HEK (human embryonic kidney)-293 cells (Figure 1). Two different slide configurations are currently available: one configuration being a 4 "Biochip" mosaic of transfected HEK-293 cells, non-transfected HEK-293 cells, rodent cerebellum and rodent hippocampus sections; while the second configuration comprises only of transfected and non-transfected HEK-293 cells.

Issues with testing:

There is ongoing controversy as to whether serum or CSF is the best specimen type to test for anti-NMDAR. Dalmau et al reported that none of the 412 paired serum and CSF specimens that were positive of anti-NMDAR, was positive only in the serum specimens.⁷ In addition, the level of anti-NMDAR was higher in CSF than serum in 53 patients that were analysed.⁸ These findings have also been taken to support the hypothesis that there is intrathecal production of anti-NMDAR.^{7,8} Dalmau has therefore strongly recommended that CSF should always be tested in patients suspected of having anti-NMDAR associated encephalitis, especially if their serum is negative for anti-NMDAR.

In contrast, Irani and Vincent⁹ reported that in 7 paired specimens, serum levels of anti-NMDAR were higher or the same as CSF levels. These authors therefore attributed the finding of "isolated" CSF positivity for anti-NMDAR reported by Dalmau's group, to the relatively high dilution of serum (1/200) used by the Dalmau group (compared to 1/20 in Vincent's laboratory).

Considerations on method-dependent factors are important in interpreting anti-NMDAR testing results



▲ Figure 1: Positive anti-NMDAR in CSF (left) and positive serum control (right) on NR1 transfected HEK-293 cells on "Euroimmun Glutamate Receptor Mosaic 3" slides (40x Objective).

	HSSA-Pathology Queensland (Euroimmun Glutamate Receptor Mosaic 3 slide)	Dalmau et al (2008) ⁸	Irani et al (2010) ²
Serum Dilution	1/10	1/200	1/20
CSF Dilution	Neat/undiluted	1/10	1/1
NR1:NR2B composition used to transfect HEK-293 cells	NR1 only	NR1:NR2B ratio of 1:1	NR1:NR2B ratio of 3:1
Permeabilization/fixation	Permeabilized/Acetone fixed	Permeabilized / fixed	Non-permeabilized / non-fixed

▲ *Table 1: Comparison of available methods for anti-NMDAR testing (modified from Irani and Vincent 2011).⁹*

These findings illustrate the important fact that, as is the case with most other autoantibody assays, there are crucial method-dependent factors to be considered for anti-NMDAR testing. The laboratories of Dalmau and Vincent, both utilize in-house transfected HEK-293 cells as their primary screening assay. However, there are important differences between these two laboratories (see Table 1).⁹ Specifically, Dalmau's laboratory uses fixed permeabilized cells with a NR1:NR2B cDNA ratio of 1:1 in the transfected cells, compared to the use of unfixed, un-permeabilized cells with a NR1:NR2B cDNA ratio

of 3:1 in Vincent's laboratory. The commercially available transfected HEK-293 cells from Euroimmun, are acetone fixed permeabilized cells that are only transfected with NR1 (see Table 1). These differences are highly likely to affect diagnostic performance, and produce different results with some specimens. The screening serum dilution also varies 10-fold between Dalmau's (1/200 dilution) and Vincent's (1/20 dilution) which is likely to lead to differences in the ability to detect low levels of anti-NMDAR between these two laboratories.

	HSSA-PATHOLOGY QLD	DALMAU J ET AL, (2008) ⁸
Positive Anti-NMDAR	37/1253 (3.0%)	n/a
Number of Paired Serum and CSF specimens = 174		
Positive in serum and/or CSF	25/174 (14.4%)#	58
Positive in serum only	1/174 (0.6%)*	0/58 (0%)
Positive in both serum and CSF	13/174 (7.5%)	53/58 (91%)
Positive in CSF only	11/174 (6.3%)#	5/58 (9%)
Age range of patients with positive anti-NMDAR	4 to 77 years (median 25 years)	5 to 76 years (median 23 years)

▲ *Table 2: HSSA-Pathology Queensland Anti-NMDAR Testing (November 2010 to December 2012).*

* This 68 year old female patient had an atypical clinical presentation (progressive memory loss and confusion), diffuse white matter changes on brain MRI, and was subsequently diagnosed with cerebral diffuse large B-cell lymphoma on brain biopsy.
Of the 25 anti-NMDAR positive patients in whom paired serum and CSF samples were received, 11 patients (44%) had detectable anti-NMDAR only in CSF

It should also be noted that other autoantibodies are associated with autoimmune encephalitis including anti-VGKC (anti-LGI1 and/or anti-CASPR2), anti-AMPA 1/2, anti-GABA_BR and anti-glutamic decarboxylase (GAD).^{10,11} It has been reported that anti-GAD antibodies define a form of autoimmune encephalitis that is non-paraneoplastic, chronic and often unresponsive to treatment with immunosuppression and anti-convulsants.¹² Anti-GAD may be more commonly associated with autoimmune encephalitis (3%) than other antibodies such as anti-GABABR and anti-AMPA 1/2.¹³

How should levels of NMDA-R antibodies be determined and reported?

Using an ELISA-based method in which lysates of HEK-293 cells both expressing and not expressing NR1 subunits of NMDA-R, Dalmau et al determined the concentration of anti-NMDA-R in patients' CSF and serum.⁸ However, it is important to note that the use of the term "titre" in this paper is misleading. The method described is based on subtracting the absorbance of the non-transfected cell lysate from that of NR1-transfected lysate. Hence the results for anti-NMDA-R are expressed as an absorbance unit, which is not a true serial dilution-based titre.

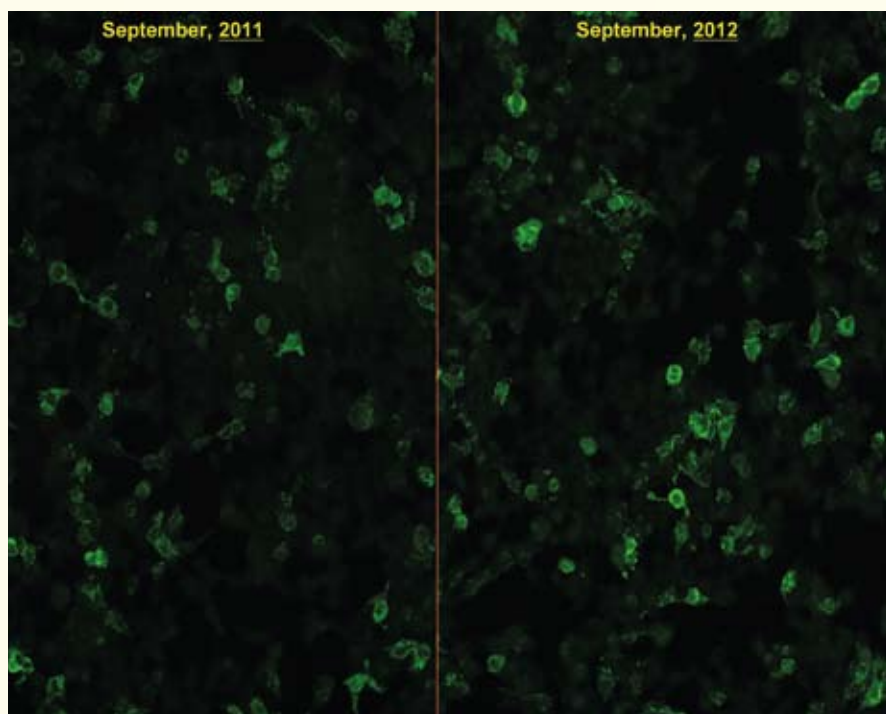
True serial dilution-based titres could theoretically be performed with the transfected HEK-293 cells. Indeed, the Euroimmun kit insert for the Glutamate Receptor Mosaic 3 slides recommends an initial screening dilution of 1/10 for serum specimens, followed by two further serial dilutions of 1/100 and 1/1000. However, discerning the end-point dilution on transfected cells is problematic, in terms of defining the criteria for a negative result. This includes the need to define the number of transfected cells per field, the precise magnification to be used, and the minimum visual intensity that indicates a positive transfected cell. There is also the high likelihood of variation between different batches/lots of the transfected cells, which will affect the validity of comparing results obtained on different batches/lots of slides. For these reasons, it is not recommended to attempt to determine visual end-point titration for

other transfected antigens, such as for anti-60kD SSA/Ro on the 60kD SSA/Ro transfected HEp-2000 (Immunoconcepts, Sacramento, CA, USA) cells used for anti-nuclear antibody testing.

The cost of serial dilution is also an important consideration for laboratories that are using commercial slides for anti-NMDAR testing. The significant cost involved with routinely performing 3 dilutions (1/10, 1/100 and 1/1000) on all positive specimens will either have to be borne by the laboratory or passed on to the patient or requesting clinical department.

The laboratory of Angela Vincent reports the results of their anti-NMDAR testing as a score between 0 to 4, based on visual assessment of the intensity of immunofluorescent staining at a single serum dilution (1/20).¹⁴ A score of 0 indicates absent/negative staining while a score of 4 reflects very strong staining.

Optimal staining conditions are helpful to achieve high cost-effectiveness in anti-NMDAR testing



▲ *Figure 2: Comparison of anti-NMDAR testing on serum specimens from an 18 year old female diagnosed with autoimmune encephalitis. The original serum was collected on September 2011 (left image). The patient then received treatment with rituximab with clinical improvement, but experienced a relapse of symptoms thus prompting the repeat test in September 2012 (right image). Both specimens were tested in parallel at 1/100 dilution on the same run, and digitally photographed using a x20 microscope objective. There is a discernable increase in staining intensity and number of positive NR1-transfected HEK-293 cells in the 2012 specimen (right image) compared to the 2011 specimen (left image).*

Due to concerns regarding the effect of lot-to-lot variation on single dilution intensity scoring, our laboratory is currently evaluating an alternative approach. This involves concurrent testing of the latest specimen with the original (positive result) specimen at 1/100 dilution. Both specimens are digitally photographed with a 20x objective with identical exposure parameters. The number of positive transfected cells and the immuno-fluorescence staining intensity is compared visually using the digital photographs placed side-by-side on the same digital display. The results are classified and reported as follows:

- No discernable difference in staining intensity between specimens;
- A decline in staining intensity from the original specimen to the current specimen ;
- An increase in staining intensity from the original specimen to the current specimen (see Figure 2 for example).

This approach significantly reduces the cost of testing and also removes the issue of lot-to-lot variation. However, very occasionally the current and original specimen have to be repeated at a higher dilution (1/1,000) if the immuno-fluorescence staining intensity is very strong at 1/100 dilution, and no discernable difference in staining intensity can be demonstrated between the specimens at the 1/100 dilution.

Pathology Queensland Experience:

Pathology Queensland commenced anti-NMDAR testing in November 2010. We currently receive specimens from public and private laboratories from most states in Australia, one centre in Indonesia and one centre in Singapore. We use the Euroimmun "Glutamate Receptor Mosaic 3" slide; each well of this slide comprises a 4 "bio-chip" mosaic of transfected HEK-293 cells, non-transfected HEK-293 cells, rodent cerebellum and rodent hippocampus sections. We have chosen these 4 "Biochip" Mosaic slides over the alternative slides that only contain transfected and non-transfected HEK-293 cells, even though the former 4 "biochip" mosaic slides are more expensive. This is because we have found the additional sections of rodent cerebellum and hippocampus to be very useful in confirming the presence of anti-NMDAR (via the typical staining appearance in the cerebellar granular layer and dentate gyrus of the hippocampus), and also enable the detection of other antibodies including anti-GAD, and other paraneoplastic anti-neuronal antibodies (e.g. anti-PCA-I, ANNA-I).

Serum samples are tested at 1/10 dilution while CSF samples are tested neat/undiluted. All anti-NMDAR results are reported as positive or negative. Testing is performed daily with a typical turn-around-time of 24-48 hours from the time of the specimen arriving in our laboratory. Our immunopathologists (who are also qualified clinical immunologists with experience in the clinical management of patients with autoimmune encephalitis syndromes) routinely contact referring clinicians (if contact details are provided) regarding positive anti-NMDAR results and/or other coincidentally detected anti-neuronal antibodies.

Over 1000 patients underwent anti-NMDAR testing in Pathology Queensland, with a prevalence of 3%

Since November 2010, anti-NMDAR testing has been performed on 1,578 requests from a total of 1,253 patients. From these 1,253 patients, there have been 37 positive anti-NMDAR results, corresponding to a prevalence of 3.0% (see Table 2). Of these 37 positive patients, both serum and CSF were received from 25 patients, only serum was received from 9 patients, and only CSF was received from 3 patients. The age range of the patients with positive anti-NMDAR ranges from 4 to 77 years of age, with a median age of 25 years. This relatively young median age is comparable to that obtained by Dalmau et al⁸ and the prospective UK encephalitis study,⁴ in which the median age was 23 years (range 5 to 76 years) and 30 years (range 0 to 87 years) respectively. These findings emphasize the fact that anti-NMDAR encephalitis is a disease that typically affects children and young adults, in comparison to autoimmune encephalitis associated with other antibodies (anti-AMPA 1/2, anti-GABA_B, anti-LGI1 and anti-CASP2) which typically affect older adults (median age 60 to 62 years).¹⁰

To date, we have received paired serum and CSF samples from 174 patients. Of these 174 patients, 11 patients (6.3%) were only anti-NMDAR positive in CSF while 13 patients (7.5%) were anti-NMDAR positive in both serum and CSF. These findings would suggest that even at a serum dilution of 1/10, approximately two fifths (40%) of patients with anti-NMDAR autoimmune encephalitis would be incorrectly considered as anti-NMDAR negative if only their serum was tested. **We therefore recommend to our clients that if the serum is negative and**

there is strong clinical evidence for NMDAR-encephalitis, a CSF sample should be submitted for testing.

Interestingly, we have detected one patient that was only anti-NMDAR positive in serum and negative in CSF. However, the clinical presentation (progressive memory loss and confusion, with diffuse white matter changes on brain MRI) of this older (68 year old) female patient was not typical for encephalitis, and she was subsequently diagnosed with a cerebral diffuse large B-cell lymphoma on brain biopsy. It could therefore be argued that this represents a false positive anti-NMDAR result, possibly induced by augmented exposure of NMDAR to her immune system in the setting of her cerebral lymphoma.

Conclusion

Anti-NMDAR associated encephalitis is an important and treatable autoimmune disease, which is underappreciated due to the variable spectrum of clinical presentation. It is likely that there are also cases with

milder clinical presentations than the original case series. A prompt diagnosis is crucial as early immuno-suppressive/immunomodulatory treatment appears to be associated with better clinical outcomes than delayed treatment.

Testing for anti-NMDAR is becoming increasingly available. However, there are important differences in the assays currently utilized to detect anti-NMDAR, including the serum dilutions employed. Testing for anti-NMDAR in CSF should always be performed if there is strong clinical evidence for NMDAR-encephalitis and the serum specimen is negative for anti-NMDAR.

To maintain expertise and shorter turnaround times, anti-NMDAR testing should be limited to one specialized laboratory per region, and this laboratory should have established experience with the detection of other neuroimmunological antibodies. This is important as all patients with suspected autoimmune encephalitis should also be tested for the other autoantibodies (including anti-VGKC (anti-LGI1 and anti-Caspr2) and anti-GAD) reported to be associated with autoimmune encephalitis.

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Out of the Whitecoat:

Theatre and I (since 1991): a pictorial review

By Amy Bik-Wan Chan

(All photo credits except Fig 2B: Amy Bik-Wan Chan.

Fig 2B photo credit: Victor Chun-Wai Siu.)

THE BEGINNING OF MY THEATRE LIFE

Fig 1



I still remember the rehearsal and the performance were in the summer holiday after my HKCEE exam. There was only very little support from my Alma mater for our production, but all the five performers (including me) as well as our director and producer worked very hard for the production and rehearsed every day. Finally, every one of our performers was awarded the prize of "Outstanding Performer". (There were a total of eight "Outstanding Performer" winners in the whole drama festival.) Urban Council, the organizer, has long gone, but the memory and the influence last forever.

TWO GIRLS FROM NGAU TAU KOK

Fig 2A



All the books and products related to "Two Girls from Ngau Tau Kok"

Fig 2B



The latest performance of "Two Girls from Ngau Tau Kok" in 2009 in a little restaurant in the to-be-demolished lower Ngau Tau Kok Estate.

Since 1991, I devoted myself into theatre in my spare time. I worked in many posts, including director, playwright, performers, stage manager, set designer and lighting designer, in various kinds of productions. Among the many different productions, "Two girls from Ngau Tau Kok" is definitely the most important one to me. I was the co-playwright, co-director, performer and

lighting designer of this original play. It has been re-run, revised and performed in various venues throughout 9 years since 2001. The play was adapted into comic book in 2002 and an English radio play broadcasted in the BBC Worldplay Series 2003. The original Chinese script and the translated English script were included in "Hong Kong Drama 2001" (IATC) and "City Stage" (HKU Press) respectively. The play is important not only because of the achievements which it has attained, but also because it explores the beauty and the "her-story" (versus "his-story") of ordinary people in a local community. Nonetheless, this is the story about the place where I grew up, my mother and I.

LIGHTING DESIGN

Fig 3A



From the draft of design concept...

Fig 3B



To light plan and all the technical details...

Fig 3C



To realization on stage. (Lighting design for drama production "The Scholar and the Executioner", Hong Kong Academy for Performing Arts, 2012)

Since 1995, I have gradually shifted my focus to theatre lighting design. Lighting design is an interesting specialty of performing arts. It requires a refined balance of both technology and arts. As a good lighting designer, one must have thorough knowledge about electricity, optics, visual perception, the technology of the stage and lighting instruments, design theories, theatre history and genres, scripts and literature, and performance styles. Lighting design is the specialty most closely related to the performances on stage. Sometimes, I can feel my lighting performing like an actor on stage with the whole company. Up till now, I have designed lighting for almost 50 productions in Hong Kong and overseas.

OUT OF THE THEATRES

Fig 4A



My lighting design and I in Hong Kong Museum of Art (Hong Kong Contemporary Art Biennial Awards, 2003). Setup of an installation was not easy. It was almost midnight when I took this photo.

Fig 4B



Lighting design for the permanent lighting installation of a gallery in Central.

In 2003, I was invited by an artist to collaborate and design lighting for her visual art installation. This installation, together with my lighting design, was one of the award winners of Hong Kong Contemporary Art Biennial Awards 2003, so I had the chance to set up lighting in Hong Kong Museum of Art. Seeing my lighting design surrounded by other artworks in the museum was amazing and memorable. The installation together with my lighting design is now the purchased collected artwork of the museum. From that time onward, I also design lighting for installations, exhibitions and interior of gallery.

WHY LIGHTING DESIGN? WHY THEATRE? WHY ARTS?

Let me share with you an experience. Last year, I spent two weeks in the pathology department of UMC St Radboud in Nijmegen of the Netherlands to study dental pathology under the guidance of Prof. Pieter Slootweg. Firstly, I found this artwork at the end of the corridor of the department.

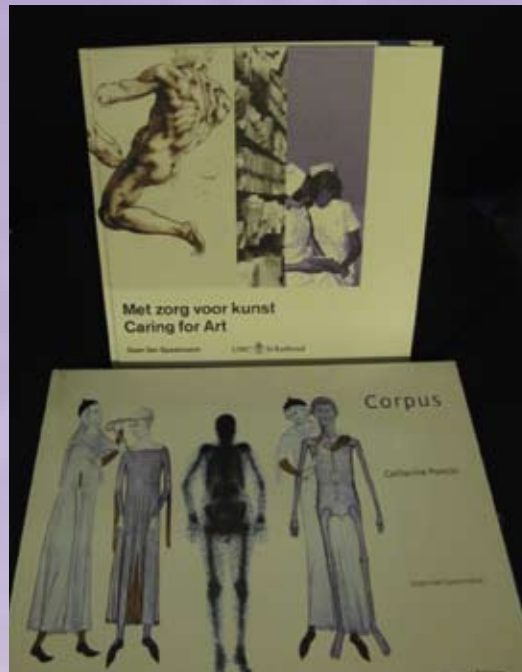
Fig 5A



I was also amazed to find out that the whole hospital was in fact full of various artworks, such as paintings, photography, sculptures and installations, in every corner and corridor. All the artworks were of high quality and were by renowned contemporary artists. Then I found these two art books published by the hospital.

Look familiar, right? It was the artwork on the cover of Journal of Pathology in 2008.

Fig 5B



As stated clearly in the introduction of the books, “every leading hospital in the Netherlands has an art collection.” Other than creating a pleasant, attractive environment for the patients, the staff and the students and helping to put the hospital on the map, many of the works on display in the hospital are ‘in dialogue’ with medicine, in all its various aspects - not just treatment, but also training, research and reflections on the human body. (I encourage you to browse through the site dedicated to hospital-owned visual arts collection and activities in the hospital official website: <http://www.umcn.nl/OverUMCstRadboud/Beeldendekunst/Pages/default.aspx>)

To me, arts and medicine have never been on the two extremes. The ultimate goal of both arts and medicine is the exploration of human nature and the world surrounding human being. They are the inquiry into life. This is what I truly believe and am always pursuing.



Fellows' Laurels

*Congratulations once again to Prof. CHIU Wai Kwun,
Rossa of the Department of Chemical Pathology at
The Chinese University of Hong Kong.*

Prof. Chiu was recently awarded the Chinese Young Women in Science Fellowship for her research and development of non-invasive prenatal diagnostic approaches in successfully developing and applying DNA testing of maternal plasma for Down syndrome.

The Chinese Young Women in Science Fellowship was jointly founded by the All-China Women's Federation, China Association for Science and Technology, the UNESCO China National Committee, and L'Oreal China. The award aims to reward elite female scientists aged below 45 in all fields of science and to encourage young females to engage themselves in science research and contribute to the welfare of mankind. All the 10 selected awardees for 2012 have made significant innovative research accomplishments in their fields which included physics, geography, genetics and applied mathematics.



Prof. Rossa CHIU (left) received the award from Ms. LAN Zhenzhen, Vice President of L'Oreal China (right).

OBITUARY: DR. SUSAN LEONG JP



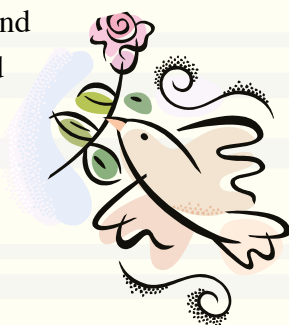
**Dr. Susan LEONG JP, MBBS (RANGOON),
FRCPATH , FRCPA, FRCP (EDINBURGH),
FHKAM (PATHOLOGY)**

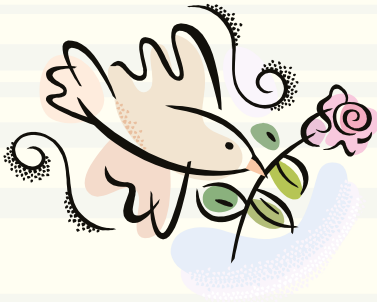
Susan passed away peacefully on 21 December 2012 after a period of illness in Vancouver, Canada.

Susan was born on 23 January 1930 in Rangoon, Burma and graduated from the University of Rangoon. She received training in United Kingdom at the Hammersmith Hospital before arriving Hong Kong to join the Government Health Service in the early 1960s. She joined the Government Pathology service and, with the opening of Queen Elizabeth Hospital, worked in the Department of Haematology. She was a dedicated clinician who was generous with her time and always ready to serve the medical community (Chair of Hong Kong Society of Haematology).

Susan was extremely hard working but it was her determined nature that led to her assignment to develop a territory-wide blood transfusion service for Hong Kong. From the early limited beginnings at the Red Cross center in Tamar, Hong Kong, she established the foundation for a quality service. As the first Director of the HK Red Cross Blood Transfusion Service, she established a program that provided safe blood for all patients in both the public and the private sector without prejudice. Under her leadership, the Hong Kong Red Cross Blood Transfusion Service came to be recognized as one of the leading centers in Asia, if not the world.

She received world-wide recognition for her pioneering work, and as a WHO consultant, she was in demand throughout Asia to advise and consult on blood transfusion matters constantly. She was recognized by the International Society of Blood Transfusion for all her work as its President (1992~1994). She was also honoured for her inspiring service with numerous awards, including the Badge





of Honour (Queen Elizabeth II), the British Red Cross Badge of Honour for Distinguished Service, and the Justice of Peace appointment in Hong Kong.

Susan mentored many generations of young professionals, from nursing staff to laboratory technicians, to doctors. A consummate professional whose varied interests in life (nature, cooking, eating, traveling, family and seeing people excel in their gifts), her network of friends both professional and personal is wide. A devoted Christian, she has served also with Christian Aid and numerous other non-governmental humanitarian organizations in various roles.

Her friends describe her as a gentle, sincere, kind and helpful person. When approached for advice, on personal or work issues, she was always attentive and gave sound and practical advice. As a person, she was always optimistic and courageous; able to face and overcome difficult situations (personal and professional) with a steely will.

She was a devoted mother to her children, always a constant guiding light for them. She will be sadly missed by her family -- Chris, Tim, Kim and Matt, Jon and Kate, her grand children, Rebecca, Isaac, Natasha, and Harlan.

Acknowledgement:

The Editorial Board would like to thank Dr. James Kong, MBBS FRCS FRACS FHKAM (Surgery), specialist Plastic Surgeon, for contributing the above article.

P.S. Dr. Susan Leong was admitted as founder fellow of the Hong Kong College of Pathologists on 14 June 1991. She was invited to deliver the 1995 TB Teoh Foundation Lecture during the College AGM.

EXTRAORDINARY GENERAL MEETING

Date: 10 June 2013 (Monday)
Time: 6:30 p.m.
Venue: Meeting Rooms 903-4,
The HKAM Jockey Club Building,
99 Wong Chuk Hang Road,
Aberdeen, Hong Kong

An Extraordinary General Meeting (EGM) will be held on 10 June 2013 (Monday), aiming to pass the Special Resolutions related to the revision of the Memorandum and Articles (M&A) of our College.

The original purpose of the revision was to address the nomination and election process of Honorary Fellows. However, when we submitted our proposal to the Companies Registry, we were advised to revise other components of the M&A, to bring the M&A up to date to the current Companies Ordinance. Eventually, we also took this opportunity to revise the whole M&A, clarifying some existing practice.

The EGM notice with details of the proposed revision has already been sent to you, and we look forward to seeing you at the EGM.

Dr. CHAN Chak Lam, Alexander
Registrar, HKCPATH

REVISION OF COLLEGE EXAMINATION FEES

With effect from 17 April 2013, the College examination fees (and examination exemption fee) have been revised as follow:

Type of Examination	Examination/Exemption Fee
Fellowship Assessment	\$16,000
Membership Examination	\$12,000
Membership Examination Exemption	\$12,000
Supplementary Examination	\$10,000

Dr. CHAN Chak Lam, Alexander
Registrar, HKCPATH