



Inside

Message from the Chairman	1
From the Editor	1
Review of the 8th APSTH Congress in Vietnam	3
Reports from Recipients of the APSTH 2014 Young Investigator Award	5
Research News	12
World Thrombosis Day Activities in Asia-Pacific	14
Do not miss the ISTH XXV Congress in Toronto!	16
Upcoming Meetings	17
2015 Highlights of ASH in Asia	18

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Message from the Chairman

Dear friends and colleagues at APSTH,

New Year Greetings! As we look forward to a brand new year, we are proud to remember our major highlights in 2014.

The joint meeting of APSTH and JSTH was held for the 9th consecutive year in May 2014 in Osaka. The travel funds provided by the Japanese Society of Thrombosis and Hemostasis enabled our young investigators to present their scientific works there and reports from the recipients of APSTH/JSTH were published in our July 2014 Newsletter. A very successful 8th APSTH Congress took place in October 2014 in Hanoi, with 41 international speakers and 2 local speakers addressing a wide range of clinical and laboratory topics on thrombosis and hemostasis to over 200 foreign delegates and about 800 Vietnamese delegates. Congratulations to Prof. Nguyen Anh TRI and his team from the Vietnam National Institute of Hematology and Blood Transfusion, for the successful organisation of this congress.

We also appreciate the work of the APSTH executive committee comprising of Prof. Pantep Angchaisuksiri, Prof. Christopher Ward, Prof. Doyuen Oh, Prof. Yukio Ozaki, Prof. Satoshi Fujii and Prof. Tetsumei Urano, in orchestrating such an enriching and applicable scientific programme. Indeed, I hear much positive feedback from people who had attended and benefitted from this congress.

As we continue to press on with developing the APSTH, I will like to begin this New Year by urging you to bring like-minded friends and colleagues to join us as members. The success of the interest group in "Thrombotic Thrombocytopenic Purpura" led by Prof. Ross Baker is a good example to inspire more interest groups sprouting from APSTH. Certainly more can be done if we get together as APSTH is an excellent platform for collaborations in research and education and in the process, enduring friendships are formed and treasured.

Best Wishes and Happy New Year.



Lai Heng Lee

From the Editor

Dear Colleagues,

My best wishes to you for the New Year. 2014 was a busy year for APSTH and that pace will continue in the New Year.

We are pleased to start this fifth year of our newsletter with coverage of the very successful 8th APSTH Congress held last October in Hanoi, Vietnam. We have views of the Congress from two different perspectives.

First, we have a report from Prof. Nguyen Anh TRI, M.D., Ph.D., President of the 8th APSTH Congress



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Ponlapat Rojnuckarin

Vietnam

Bach Quoc Khanh
Nguyen Anh Tri

2014 and Director of the National Institute of Hematology and Blood Transfusion, Vietnam. During the three-day conference, Vietnam welcomed more than 1,000 participants, including over 200 international attendances from 17 countries including Japan, Korea, Malaysia, Thailand, China, Singapore, Australia, and Germany.

Next, we present reports from each of the seven recipients of the APSTH 2014 Young Investigator Award. These investigators included one from China, one from Indonesia, and five from Malaysia. All of the award winners were unanimous in their gratitude for being offered the opportunity to attend this important international congress. The ability to exchange information with noted experts from around the world was invaluable and was an important highlight of their careers. They expressed interest in the APSTH and I am sure this will help the APSTH in growing the number of members in 2015.

Our next Congress will be in Taiwan at the Taipei International Convention Center during October 6-9, 2016. I hope to see you there.

In this newsletter's "Research News" section, we have an article on "New concepts in hemophilia therapy (bi-specific antibody mimicking VIII)" by Midori Shima M.D., Ph.D., Department of Pediatrics, Nara Medical University, Japan. This very interesting molecule might fulfill the unmet needs in the current hemophilia treatment.

A very major project of the APSTH in 2014 was the establishment of the first World Thrombosis Day (WTD), an initiative of the International Society of Thrombosis and Hemostasis, on October 13 in Asia-Pacific. In the inaugural year of WTD, more than 175 organizations from more than 50 countries organized hundreds of events, which reached millions of people. In Asia and Australasia, organizations spread the WTD message throughout many countries, translating materials into native languages and hosting creative events. In this newsletter, we describe some of those events in Asia and Australasia. In 2015, the WTD project will focus on prevention of hospital-associated venous thromboembolism and diagnosis of atrial fibrillation (Feel the Pulse Campaign). If you have any suggestions for the 2015 World Thrombosis Day, please contact me at pantep.ang@mahidol.ac.th.

Next, we have a preview of the ISTH XXV Congress, June 20-25, 2015, in Toronto by Sam Schulman, M.D., Ph.D. Congress President, McMaster University, Canada. As you may know, the ISTH Congress is the largest scientific event in thrombosis and hemostasis in every 2-year period. Whether you want to catch up on the latest advances in the field or to broaden your general knowledge, this is the congress to go to. In addition, you will meet colleagues from all around the world working on the same problems as you.

We round our newsletter with a schedule of upcoming meetings. In addition to this, you should know that the Japanese Society of Thrombosis and Hemostasis (JSTH)/APSTH is looking for nominations for the Young Investigators Awards for the 37th annual meeting of the JSTH during May 21-23, 2015 in Yamanashi, Japan.

I mentioned above that the Young Investigators Awards are a good way to increase the number of APSTH members. I would like to point out that you are also a valuable "resource" in furthering this aim. Please help us with this. And help us too by sending your comments and suggestions for this newsletter to me at pantep.ang@mahidol.ac.th.

I would like to take this opportunity extend my best wishes to you as we move into 2015.

Pantep Angchaisuksiri, Editor

Officer of Public Relations and Communications APSTH



Review of the 8th Congress of Asian-Pacific Society of Thrombosis and Hemostasis



Prof. Nguyen Anh TRI, M.D., Ph.D.

President – 8th APSTH Congress 2014

Director – National Institute of Hematology and Blood Transfusion, Vietnam

For the Asian-Pacific Society of Thrombosis and Hemostasis, we were proud to be the host of the 8th Congress of APSTH during October 9 – 11, 2014 at the Calidas Convention Center, Keangnam Landmark 72, Hanoi, Vietnam. After three interesting and hardworking days, the conference has closed with success and congratulations from international friends.



During conference time, we were proud to welcome more than 1,000 participants including over 200 international attendances from 17 countries including Japan, Korea, Malaysia, Thailand, China, Singapore, Australia, and Germany. The conference also attracted about 800 local people from the thrombosis and hemostasis fields, including health authorities and people from hospitals throughout the country. Organized in three days with 15 sessions, the conference was covered by 42 lectures and 31 oral presentations focusing on:

1. Anticoagulant
2. Platelet in healthy and illness
3. Blood product and coagulation
4. Women and coagulation disorders
5. Deep vein thrombosis & pulmonary embolism
6. Disseminated intravascular coagulation (DIC)
7. Clinical platelet disorders
8. Other thrombosis disorders (TTP/HUS)
9. Other bleeding disorders
10. Laboratory hemostasis and coagulation
11. Congenital bleeding disorders: "Hemophilia"
12. Fibrinolysis
13. Coagulation in tropical diseases
14. Arterial thrombosis



One whole-day session on 9th October 2014 was an education session specifically for thrombosis and hemostasis. Supported by ISTH, the Education Day was organized with seven lectures made by experienced international experts to provide attendees with state-of-the-art information and updates.

By inviting 43 international speakers not only from the Asian-Pacific region but also from the rest of the world, content of the congress included a wide range of information. This was a forum for people to learn and choose the most suitable applications.

The 8th Congress of APSTH has closed with outstanding

success. This is a large international conference which brings benefits not only to thrombosis and hemostasis but also to other related fields as cardiology, surgery, and obstetrics.

The conference was a valuable chance for Vietnamese medical staff to exchange experiences with other local colleagues and international experts. It was also a chance to extend international collaboration and introduce the image of Vietnam, a country with diversified cultures and traditions. We would like to show our gratitude for the great support from APSTH, ISTH, local authorities, and participants of the conference. We hope to welcome you another time in Vietnam to share our point of view and culture.



Reports from Recipients of the APSTH 2014 Young Investigator Award



From China: The 8th APSTH Congress 2014 Experience

Fengwu Chen
 Cyrus Tang Hematology Center
 Soochow University, Suzhou
 China

This summer, my supervisor advised me to write an abstract to summarize my research work and send it to the 8th Congress of APSTH. Six weeks later, I was overjoyed to receive an email from Dr. Nguyen Trieu VAN saying that my abstract was approved for poster presentation and I was selected as a candidate for a young researcher grant. I was so exhilarated because it would be my first time to go aboard and it would be my first time to attend an international conference.

After arriving at Noi Bai Airport on the night of 8th October, I easily found the hotel the congress organizing committee booked for me, not far from the congress venue. 9th October was ISTH education day and I attended most of the sessions. At night, a fancy opening ceremony of the 8th congress of APSTH was held at Calidos Gardium, the Keangnam Landmark 72. Besides the great art performance program and delicious food, I was further pleased to meet LiTeng Khoo from Malaysia, who also received a young researcher grant. We had many conversations and soon become good friends.



With Prof. Yukio Ozaki (Japan)

10th October was the first day of the congress of APSTH. I attended several interesting sessions on the topic of platelets in healthy and illness and was very impressed by these



From left to right –Nurul Huda (Malaysia), Azlina Muhsin (Malaysia), Zetty Nadia (Malaysia), Prof. Pantep Angchaisuksiri (Thailand), Fengwu Chen (China), Cherry P. P. Jukim (Malaysia), Li Teng Khoo (Malaysia)

informative sessions which broadened my horizons. At the tea break, thanks to the introduction of LiTeng, I was delighted to meet the other four young researcher grant recipients. They were very polite and friendly. At night, we were invited to a gala dinner party held on the 71st floor of the Keangnam Landmark 72, the largest and highest building in Indochina region. At the party, we appreciated an art performance by professional artists and watched fireworks in honor of the 60th year of the liberation of Hanoi. I mingled with the other conference attendees, most of whom were Vietnamese. They were all very friendly and hospitable. Our dinner conversation ranged from professional research experience to nuances of different cultures. They taught me some Vietnamese and together we took pictures. The atmosphere was euphoric. This was really a memorable experience for me. On the afternoon of 11th October, Professor Pantep Angchaisuksiri came to see all the young researcher grant recipients and photos were taken.

It was a great honor for me to attend the 8th Congress of APSTH and I really enjoyed the valuable experiences in Hanoi. Besides gaining a lot of professional knowledge I have learnt from other investigators' work, the experience has given me the confidence and motivation to keep my research career going. I would like to express my sincerest gratitude to all the organizers of the congress. Their kind invitation and warm welcome made the congress an unforgettable one for me.



From Malaysia: The 8th APSTH Congress 2014 Experience

Azlina Muhsin

*Universiti Kuala Lumpur – Institute of Medical Science Technology
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Firstly, I would like to express my sincere gratitude to the organizing committee of the 8th APSTH Congress 2014 for giving me the golden opportunity to present and share my research work at the Congress in Hanoi, Vietnam. I had never been in Vietnam and it was a privilege to be able to attend the Congress under the Young Researcher grant. The experience gained was definitely invaluable.

During the two days of the Congress, I grabbed the chance to meet all the young researchers and get to know each other. Most of us were from Malaysia but Fengwu was the only person from China. Listening to the lectures given by all the well-known distinguished speakers was motivating and inspiring. I was glad that those who were there shared the same passion to contribute in every possible way in the area of thrombosis and hemostasis.

I attended the Gala Dinner together with Li Teng and Cherry, the other young researchers. Despite the crowd, it was enjoyable and all the food served was delicious with a lot of variation. I truly enjoyed the live cultural arts performances during the dinner and I only wished that there had been more. From



Li Teng, Azlina, Cherry and others at Gala Dinner

the 71st Floor of Keangnam Tower, we also could view the night scenery of Hanoi city. Everything looked so small yet beautiful!

Towards the end of the Congress, we had a quick photo session. I could see from everyone's face, a feeling of joy and satisfaction as the Congress was a great success. Latest technologies were shared, new knowledge learnt and new friends connected.

Right after the closing ceremony, I made a quick sightseeing trip to Hoan Kiem Lake and also went to the Old Quarter with my friends. It was unique to see how the street vendors were set up along the way.



“Well done!” to the organizing committee for making the Congress an unforgettable and wonderful event. I also would like to thank my research supervisors, Dr. Eusni and Dr. Sabariah for their endless encouragement and support during the research work.



From Malaysia: The 8th APSTH Congress 2014 Experience

Cherry Prissie Philip Jukim
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I would like to extend my sincere gratitude to the organizers of the Congress, Asian Pacific Society of Thrombosis and Hemostasis (APSTH), for trusting me and sponsored me as young researcher. It was my privilege and honour that I was given a chance to participate amongst the eminent people in such international congress. I also want to thank my friends, especially my supervisors P.M. Assoc Prof. Dr. Lee Ping Chin and P.M Dr. A. Thiruchelvam for giving me a chance to attend the APSTH Congress.

I learned a lot of new things during the congress in Hanoi. The APSTH education day and congress was very informative and it has broadened my mind to discover new things in thrombosis and hemostasis. The speakers were very enlightening, giving us many facts. It was good sharing with people who share the same interests. I was very impressed by our meeting with Professor Pantep Angchaisuksiri (Officer of Public Relations and Communication APSTH). His comments motivated us to continue educating ourselves and to be active participants in APSTH.



I enjoyed seeing Hanoi because it is much different from my country. The city is very historical and the people there are very friendly. I felt very lucky that we had a chance to celebrate Vietnam Independence day during the gala night together with the local people. The view of the fireworks from the 71st floor of Kaengnam Tower was really amazing. Also, I took my parents to visit Halong Bay, a UNESCO World Heritage Site, and we found it to be truly beautiful.





From Malaysia: The 8th APSTH Congress 2014 Experience

Zetty Nadia Mohd Zain, Ph.D.
 Faculty of Medicine and Health Sciences
 Universiti Sains Islam, Malaysia

The long awaited APSTH 8TH Congress finally arrived when the first announcement was made in the mid-year 2014. I had been waiting to attend this congress since last year. My abstract was submitted long before I knew that there is a travel grant award dedicated to young researchers. I remembered feeling enthusiastic following an email from Prof. Satoshi Fuji encouraging young researchers to apply for a Young Researcher Award, thus I sent my application straight away. I was proud when I went through the list of award recipients.

The flight from Kuala Lumpur to Hanoi took almost 3 hours. Hanoi is a beautiful city with mixture of old and new buildings. I managed to experience Hanoi city at night by cab. Surprisingly, the city is still alive at night where the traffic is busy and the city is crowded with people doing various activities. There was a booth at the conference exhibiting and selling various Vietnam souvenirs. Following my seeing the quality of Vietnam silk, I headed to a silk village one morning, about 35 minutes from Cau Giay District to see the production of Vietnam silk. Named "Van Phuc Village", it is a traditional village producing the largest amount of silk in Vietnam.

The successful three day conference started with ISTH Education Day. The purpose of this session was to educate researchers with various significant topics and updates including NOAC, DIC, hemostatic problems in tropical disease and pregnancy, APS, platelet biology and haemophilia. I personally found this session to be very beneficial to me as young researcher, especially a lecture about platelet function, which was delivered by Dr. Yukio Ozaki.

As a pharmacologist, updates on NOAC, clinical trials and current management of bleeding are valuable to increase my knowledge for teaching purposes. It was a pleasant experience to meet notable researchers, most of whom are familiar from my references.

Conference programs also included updates of antithrombotic therapy by Prof. Satoshi, heparin-induced thrombocytopenia by Prof. Chris Ward, selection of anticoagulant in pregnancy by Prof. Lee Lai Heng and the use of FFP by Dr. Jameela Sathar. Prof Ozaki also presented his research about the newly identified platelet-activating receptor, CLEC-2 that is involved in the mechanism of platelet-induced tumor metastasis. In addition, Prof. Pantep Angchaisuksiri delivered a lecture on management and hypercoagulability state in thalassemia. Almost all topics in symposium sessions and poster presentations were interesting, with topics ranging from diagnostic tools to natural product with antithrombotic potency.

I would like to thank all scientific committee of 8th APSTH Congress 2014 for accepting my abstract and awarding me with Young Researcher Award. This has given me the opportunity to update myself with current research pertaining to thrombosis and hemostasis. In addition to that, I also managed to network with researchers from various parts of Asia-Pacific. Congratulations should also be given to the organizing committee as well. Last but not least, I'm looking forward for the next APSTH congress. Terima kasih dan jumpa lagi! (Thank you and see you again)



After the closing ceremony with other award recipients, Dr. Jameela Sathar, and Prof. Nguyen Anh Tri.



From Malaysia: The 8th APSTH Congress 2014 Experience

Li Teng, Khoo

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Universiti Putra Malaysia, Serdang, Malaysia*

I still remember how delighted I was when my supervisor informed me that my abstract had been accepted by the Congress. I always thought that there was a high possibility that my abstract might not be accepted. This was due to the fact that there are a lot of excellent researchers and clinicians who take part in the Congress.

Full of gratitude and anticipation, I participated in the ISTH Education Day on 9th October, 2014. Through this event, I was given opportunities to open up my mind in many aspects of thrombosis and haemostasis, especially on the topics of anticoagulant and antiplatelet therapy as well as haemostasis in pregnancy. That night, I was welcomed by the organiser's heart-warming opening ceremony. I liked the Vietnamese cuisine and their art performances. Besides, the opening ceremony also gave me a chance to get to know the young scientific grant recipients.

On the day of the Congress, I was given the opportunity to deliver a speech on a part of my research, "Anticoagulant effects of bioactive fractions from *Melastoma malabathricum* Linn. leaf extract". In this study, *Melastoma malabathricum* Linn., a traditional medicinal plant, which exhibited anticoagulant activity was subjected to a series of bioassay guided fractionation and chemical characterisation. As a result, polyphenolic glycoconjugates were identified as active ingredients for the anticoagulant activity of *Melastoma mal-*

abathricum Linn. leaf hot water extract. I was pleased that my research received positive feedback from the audience. During the rest of the Congress, I was able to attend many interesting talks. My knowledge in the field of thrombosis and haemostasis was widened. One unforgettable memory was the social event on the first day of the Congress, the Gala dinner.

The night of the Gala dinner, 10th October 2014, we also celebrated Vietnam's 60th year of the Capital City Liberation on the 71st floor of the Keangnam Landmark 72 - the highest tower in Vietnam. Besides enjoying the party, I also had a chance to see the fireworks from different places in Hanoi city, which had beautiful scenery. Throughout the Congress, I was happy to be able to get to know some of Asia-Pacific's distinguished researchers. We shared our knowledge and experiences. We also exchanged contacts, hoping to be able to keep in touch in the future.

I would like to express my deepest gratitude to the organizers of the 8th APSTH, especially Prof. Nguyen Anh TRI and Dr. Nguyen Trieu VAN, for giving me the opportunity to participate in this congress. Furthermore, I also would like to thank all of the organizing committee for being so kind to me. It was a truly great learning experience. I am looking forward to participating in the next thrombosis and haemostasis meeting.





From Malaysia: The 8th APSTH Congress 2014 Experience

Nurul Huda Mohd Nor
 Faculty of Medicine and Health Sciences
 Universiti Putra Malaysia, Serdang, Selangor, Malaysia

The APSTH Congress was my first international conference and to achieve the Young Researcher Award in the conference was truly bliss. One major thing that I liked the most was to meet, listen and learn directly from speakers that people were queuing to meet in person. Among them were Dr. Raymond Wong from Hong Kong and Dr. Maria Teresa Abola from Philippines who explained the updates about anticoagulants and antiplatelets while AP Dr. Martin Krause from Australia, undoubtedly has increased my knowledge regarding fibrinolysis and stroke. All of the speakers were eye-opening and awe-inspiring.



After my oral presentation with Dr Maria Teresa Abola, Miss Li Teng Khoo, Miss Thien Ngo, Dr Raymond Wong.



Picture of me and the chairpersons during my oral presentation.

To have my family together with me at Hanoi was wonderful. My daughters and husband enjoyed it so much that we indulged ourselves with sightseeing of the perplexing skyscrapers, and breathtaking scenery. The flavor of food was astounding. My only regret was that the trip was too short.



Picture of me and my family at the airport.

I can't emphasize enough how lucky I was to attend to this APSTH congress. Many thanks to my supervisor for advising me and strongly encouraging me to submit my paper. Also, thanks to the organizer for introducing me to a whole new level of expertise. I will definitely not forget this congress.



From Indonesia: The 8th APSTH Congress 2014 Experience

Kiking Ritarwan, M.D., Ph.D.

*Department of Neurology, Medical Faculty of Sumatera Utara
Medan, Indonesia*

My research adviser, Rosita J Sembiring MD, PhD, Chairman of Thrombosis and Hemostasis of Columbia Hospital in Medan, Indonesia, suggested that I enter my research for the APSTH Young Researchers Award. It turned out that I was selected for an award along with researchers from Malaysia, and China. I was very surprised when I learned of my selection. My research was about the effect of beta- fibrinogen gene polymorphism -455 G/A on Barthel Index (BI) score and modified Rankin Scale (mRS) of ischemic stroke patients treated with aspirin by age group in the Department of Neurology, Medical Faculty of Sumatera Utara.

Stroke, a leading cause of disability and death, generally attacks older people, but currently there is a rise incidence of stroke in younger people. An elevated fibrinogen level is one of risk factors of ischemic stroke. Carriers of the A allele of the beta-fibrinogen -455 G/A polymorphism is associated with an increase of plasma fibrinogen level. There is no data mentioning the beta-fibrinogen gene polymorphism -455 G/A in the Indonesia population. Aspirin has been commonly used as a primary agent for secondary prevention of ischemic stroke. Therefore, it is needed to determine the effect of beta-fibrinogen gene polymorphism -455 G/A on BI score and mRS of ischemic stroke patients treated with aspirin by age group.

The study was conducted in a cohort during the period July 2013 to November 2013. One hundred and thirty-six patients with acute ischemic stroke, consisting of 61 men and 75 women participated in this study. Ischemic stroke patients were divided according to age groups, namely young age (<55 years) and elderly (> 55 years). Patients received a single dose of aspirin (300 mg followed by 100 mg once daily). Plasma fibrinogen levels were measured by the Clauss method. Hyperfibrinogenemia was defined as plasma fibrinogen levels > 375 mg/dl. Levels of plasma fibrinogen measurement was performed at baseline (day 0)

and end of the study (day 90).

Beta-fibrinogen gene polymorphism -455 G to A was determined by PCR and RFLP using HaeIII enzyme. Stroke outcome value was measured by the BI and mRS on day 1, day 14, and day 90.

In the younger age group, the frequencies of the GG, GA, and AA genotypes were 60.3%, 30.9%, and 8.8%, respectively. In the older age group, the frequencies of the GG, GA, and AA genotypes were 72%, 23.5%, and 4.4%, respectively. There was significant difference in polymorphism according to patient's age ($p < 0.05$), where the A allele was more prevalent in younger age patients with ischemic stroke. The absence of differences in plasma fibrinogen levels either before or after administration of aspirin ($p > 0.05$) was found. There were no differences between alleles of plasma fibrinogen levels, both before and after the administration of doses of aspirin ($p > 0.05$). A significant decrease in fibrinogen levels was found in ischemic stroke patients with the GG and GA genotypes.

Outcome assessment of ischemic stroke patients in this study was performed on days 0, 14, and 90. The assessment was based on the scale mRS and BI. In this study, there were differences in the value of BI and mRS according to fibrinogen beta gene polymorphism -455 G to A, in which ischemic stroke patients with the GG genotype experienced more clinical improvement, whereas ischemic stroke patients with the AA genotype experienced more clinical worsening. There was no significant difference in the value of BI, but there were significant differences by age of mRS score after administration of aspirin in ischemic stroke patients.

Based on multivariate analysis using logistic regression, the most influential variables on the outcome of ischemic stroke are age and fibrinogen (Table 1).

Table 1. The influence of genotype, plasma fibrinogen levels, and age on the outcome of ischemic stroke.

Variable	B	p Value	Relative Risk	CI 95% Min Max
Age	-0,920	0.166	0.667	0.30 – 1.49
Fibrinogen	-2,203	0.083	0.778	0.37 – 1.63
Constant	5,949	0.000	0.02	0.00 – 0.03

Research News



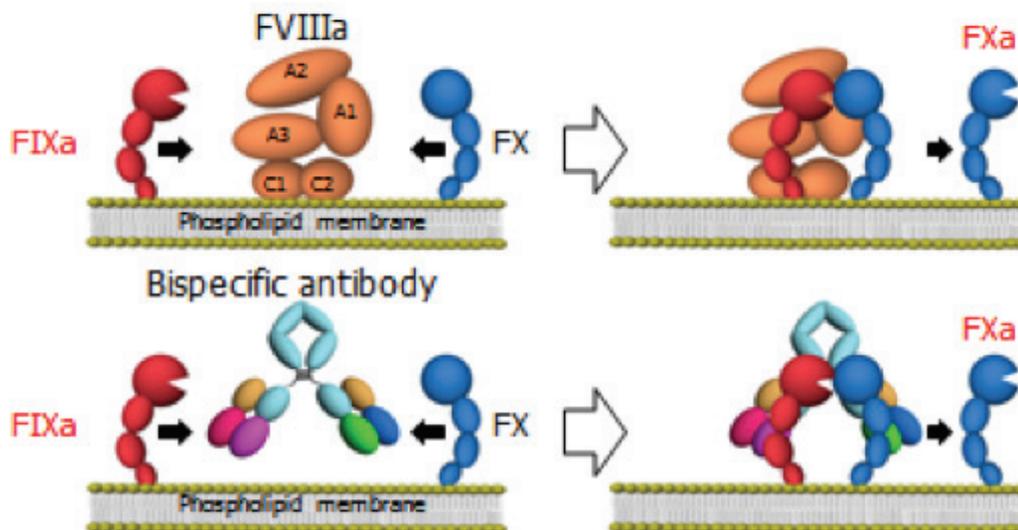
New concepts in hemophilia therapy (bi-specific antibody mimicking VIII)

Midori Shima M.D., Ph.D.
 Department of Pediatrics
 Nara Medical University, Japan

A principle treatment of hemophilia A is replacement therapy with FVIII concentrates. Recently, regular prophylaxis starting at early childhood has been regarded as an effective therapy not only for reduction of joint bleeding but also for protection from arthropathy. However, several issues still remain unsolved. One is physical and mental stress according to the frequent intravenous infusion of FVIII concentrates. Furthermore, the requirement of the frequent infusion may result in the decrease in the adherence especially for the

adolescence age group. The second issue is the development of alloantibodies against FVIII (inhibitor). Once inhibitor develops, the hemostatic and prophylactic control becomes extremely difficult. For hemostatic treatment in the patients with inhibitors, bypassing therapies with activated prothrombin complex concentrates (APCC) or recombinant factor VII (rFVIIa) are generally used. However, they are not always effective. Immune tolerance induction therapy with high dose of FVIII is effective for eradication of inhibi-

Concept of FVIIIa-mimetic bispecific antibody(ACE910)



Kitazawa, -- Shima, Yoshioka, Hattori . Nature Medicine 18 1570 (2012)
Sempei, et al. PLoS One 8 e57479 (2013)
Muta, -- Shima, Hattori . J Thromb Haemost 12 206 (2014)

• Bispecific antibody supports the interaction between FIXa & FX, thereby promotes FX activation and accelerates coagulation.

tor, however, this treatment is very expensive and does not always work. Therefore, the unmet needs in the current hemophilia treatment are longer acting products, easier infusion, and effectiveness regardless of inhibitor and economically competitive. In order to overcome these criteria, we produced a series of humanized bi-specific antibodies against FIXa and FX (Fig 1). We found that the antibody mimicked FVIII cofactor function by placing FIXa and FX into spatially appropriate positions (Nat Med 2012). Recently, a more potent bi-specific antibody, ACE 910, was produced by multidimensional optimization for clinical application. A single bolus intravenous infusion of 1 or 3 mg/kg of ACE 910 demonstrated a hemostatic effect corresponding to that by infusion of recombinant porcine FVIII at 10 U/kg twice a day against on-going bleeding in a short-term primate model of acquired hemophilia A (J Thromb Haemost 2014). Recently, we successfully established a long-term

acquired hemophilia A model exerting spontaneous joint bleedings. Weekly subcutaneous infusion of ACE910 significantly protected the monkeys from bleeding (Blood 2014 Nov 13;124(20):3165-71).

The phase I study was conducted in 64 Japanese and Caucasian healthy adults by single subcutaneous infusion of ACE910. The half-life of the ACE910 was approximately 1 month. There was no safety issue in the clinical and laboratory findings including thrombotic parameters such as FDP and D-dimer. The hemostatic effect was also suggested by the results that APTT was shortened and thrombin generation was increased in the artificial FVIII-deficient plasma samples of each subject spiked with two anti-FVIII neutralizing antibodies. The phase I study in the patients with/without inhibitor is ongoing for the objectives of prophylactic effect as well as safety, PK and PD.

Outline of Phase 1 study ~ PK, PD and Safety ~

Jepic CTI-121934

Healthy subjects

: Placebo-controlled, randomized, double-blind, inter-individual dose-escalation study

Part A

Step	ACE910 dosing group		Placebo group
	Single SC	N	
A-1	0.001 mg/kg	6	2
A-2	0.01 mg/kg	6	2
A-3	0.1 mg/kg	6	2
A-4	0.3 mg/kg	6	2
A-5	1 mg/kg	6	2

Part B

Step	ACE910 dosing group		Placebo group
	Single SC	N	
B-1	0.1 mg/kg	6	2
B-2	0.3 mg/kg	6	2
B-3	1 mg/kg	6	2

Severe Hemophilia A patients
with or without FVIII inhibitors
**Once weekly subcutaneous
administration × 12 weeks**

: Open label, inter-individual dose-escalation study

+ Prophylactic efficacy (exploratory endpoint)

Part C

Step	ACE910 dosing group	
	Multiple SC	N
C-1	1*, 0.3** mg/kg	6
C-2	3*, 1** mg/kg	6
C-3	3 mg/kg	6

*: 1st dose (Loading dose),

** : 2nd and subsequent dose

2

World Thrombosis Day Activities in the Asia-Pacific Region



WORLD THROMBOSIS DAY
OCTOBER 13

Louise Bannon

ISTH Director of Marketing and Membership

OVERVIEW

According to a global burden of disease article published in the *Journal of Thrombosis and Haemostasis (JTH)*, thrombosis causes nearly one in four deaths worldwide. In order to combat this epidemic, World Thrombosis Day (WTD) was established on October 13 as an annual campaign to raise awareness and develop better systems of care and prevention for those at risk of thrombosis. Seeking to improve preventative measures, WTD focuses on venous thromboembolism (VTE), encouraging patients and health systems to implement evidence-based preventative measures.

In the inaugural year of WTD, more than 175 organizations from more than 50 countries organized hundreds of events, which reached millions of people. In Asia and Australasia, organizations spread the WTD message throughout many countries, translating materials into native languages and hosting creative events. Some of those events in Asia and Australia are described below.

AUSTRALIA



The Australasian Society on Thrombosis and Haemostasis (ASTH) partnered with Bayer, Covidien and other Australian based pharmaceutical companies to develop media materials, including the recent Bayer survey results from about public knowledge of blood clots. The ASTH nominated a spokesperson in different states to help with media interviews and identified suitable case studies. Then, they ap-

proached national and suburban media, plus medical media across the country to secure coverage in both consumer and medical media. The ASTH encouraged their members to conduct events in their workplaces by providing posters, pamphlets and T-shirts to assist in highlighting the key messages of WTD locally. In addition, the ASTH highlighted World Thrombosis Day at HAA (the joint scientific meeting of the ASTH, the Haematology Society of Australia and New Zealand, and the Australia and New Zealand Society of Blood Transfusion) through a breakfast seminar. The organization also supported the Royal Australian College of General Practitioners accredited meetings for GPs in the run up to WTD, and they provided information packs to GPs for use with patients.

At the Royal Hobart Hospital, organizers held a VTE prevention dinner on Oct. 9 for junior medical staff in addition to two more educational presentations for medical and nursing staffs. The Hospital secured appearances on two state-wide TV stations servicing a population of 520,000 as well as a radio interview. On WTD, the staff created several displays to raise awareness for patients and staff about preventing VTE. The displays were part of a competition amongst wards in which the winner received a mini iPad. There was also a staff quiz competition in which first and second place won gift cards. They also produced a patient education video featuring "Tom Brosis," a private detective who solved the case of the deadly blood clot, which was well received by consumers.

Other groups and organizations throughout Australia posted information on websites, social media and set up information tables at regional hospitals throughout the country.

CHINA

The Chinese Society of Hematology launched the first WTD in China on the afternoon of October 12 at the Suzhou Summit on Hematology 2014 at the Suzhou Conference Center.

INDIA

Health Science professional students of the Hemostasis and Thrombosis Division of Kasturba Hospital in Manipal performed a dance drama on hemostasis and thrombosis. See here: <https://www.youtube.com/watch?v=AsSys5AJwcc>. The event took place at the Path Theatre in Manipal, Karnataka, South India. Additionally, the organization held an open to the public event to launch World Thrombosis Week on October 13 in conjunction with the Manipal Haemophilia Society of Manipal University. Scholarships for patients with bleeding disorders were also given.

From October 13 – 18, Kasturba Hospital held free clinics for testing of inherited thrombophilia and lupus, in addition to monitoring by D-Dimer. To conclude all WTD activities, on October 18, Manipal University held an update and case discussion by Dr. Rajasekharan Warriar, pediatric hematology oncologist.

JAPAN

Despite the approaching typhoon which hit Japan from October 12th to 14th, the DVT awareness seminar of WTD in Tokyo was held on October 13th and had 520 participants out of 1000 applicants. There would have been more if the typhoon had not come.

The live broadcasting of the DVT checkup, held in the Sanriku area where some people who suffered from the Tsunami three years ago and who still live in makeshift housing units, was highly appreciated.

Additionally, more than a thousand booklets on VTE were distributed at the Haneda International Airport, along with the stage performance of the physical exercise to prevent DVT. There was also coverage by a number of nation-wide mass-media outlets.



KOREA

The Korean Society on Thrombosis and Hemostasis (KSTH) held a World Thrombosis Day event on October 13 in Seoul, Daegu, Kwangju. Awareness information was shared and some media outreach was conducted.

NEW ZEALAND

The New Zealand Health Quality and Safety Commission participated in WTD activities. The Thrombosis Service at North Shore Hospital and the Waitemata District Health Board in Auckland, New Zealand, promoted WTD via a local press release, patient experience video, a thrombosis kiosk in the hospital foyer and with staff education presentations. The Thrombosis Service team was in the hospital wearing Stop the Clot T-shirts and giving information to staff, patients and the public. Lakes District Health Board shared public awareness information with patients at the hospital as well as caregivers.

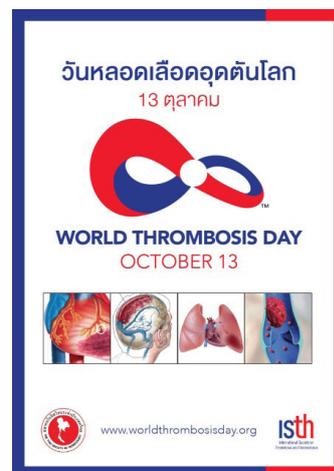
TAIWAN

The Taiwan Society of Thrombosis and Hemostasis (TSTH) held a presentation at National Taiwan University Hospital in Taipei. Patients with VTE, the health authority, general public and journalists were invited. The event featured educational presentations as well as patient testimonials and entertainment. TSTH President Ming Ching Shen opened the ceremony, and a press conference followed.



THAILAND

The Thai Society of Hematology sent articles to Thailand newspapers and country health magazines about the importance of VTE and the date of WTD. They also developed and printed posters about WTD to post in all University hospitals and provincial hospitals in Thailand in the month of October. The organization posted materials, including the WTD poster, on the Thai Society of Hematology website. They announced WTD and discussed VTE as part of all educational activities for health care professionals hosted by the Thai Society of Hematology including its annual meeting and the ASEAN Federation of Hematology Meeting.



Do not miss the ISTH XXV Congress in Toronto!

Sam Schulman, M.D., Ph.D.

Congress President

McMaster University, Canada

The ISTH Congress is the largest scientific event in thrombosis and hemostasis in every 2-year period. It starts traditionally with 1½ days of scientific working group meetings, filled with information on planned and ongoing studies, preliminary data, work in progress on definitions, standardization projects. There are also educational sessions. Immediately following these SSC meetings is the scientific congress for 3½ days – days filled with Plenary lectures from world-renowned scientists, State-of-the-Art symposia with 2-3 invited speakers that are top experts in their field, Abstract symposia with one invited speaker presentation framed by oral presentations of the highest scoring abstract, Oral Abstract presentations, Poster Sessions, Master Classes, and Corporate Satellite Symposia.

Whether you want to catch up on the latest advances in the field or to broaden your general knowledge, this is the congress to go to. In addition, you will meet colleagues from all around the world working on the same problems as you. There will be plenty of opportunities for networking – from the Poster Sessions to the Welcome Reception and the coffee and lunch breaks.

We also encourage nurses and allied health professionals (pharmacists, physiotherapists, occupational therapists, medical technologists, etc.) to take the opportunity of very low registration fees to attend the congress and to submit abstracts, either earmarked for the specific Nurses and Allied Health Professionals oral or poster sessions or to the general scientific program.



The abstract submission site has opened on December 1, 2014 and the deadline is February 4, 2015.

Toronto is welcoming the delegates in many ways. There are direct flights from all inhabited continents in the world to Toronto. In the spring of 2015 a rapid train – the UP Express – will start running from the airport to downtown Toronto. The Metro Toronto Convention Center is located downtown,

within walking distance from the UP Express and from many hotels. There are hundreds of restaurants and entertainment options in this part of the city. End of June is the time of the year with very comfortable weather.



The novelties at the ISTH XXV Congress in Toronto are:

- Career Mentorship Small Group Sessions
- A formal scientific half-day session for Nurses and Allied Health Professionals abstract presentations
- Satellite Symposia during the lunch break without any competing programs but with the alternative option of taking the complimentary lunch box and visiting the poster exhibition of the industry booths.
- A final Highlights of ISTH session that will summarize the highest scoring abstracts



You will get excellent value for your time, efforts and money by attending this conference. Visit the www.isth2015.org website to learn more about the details of the congress. Registration has already opened and if you plan to come, remember that “early registration” ends on March 11, 2015, thereafter the fees increase. And why not plan on combining the congress with a family vacation in Canada! Toronto has on its own many tourist attractions. In the region are also the wine routes in the Niagara Peninsula and of course the Niagara Falls, the Niagara-on-the-Lake Shaw Festival and the Stratford theatre festivals and a little further away the enormous Algonquin Park for those who like wildlife.

Upcoming Meetings:

- 1 **Maastricht Consensus Conference on Thrombosis**
11-13 February 2015 – Maastricht, Netherlands
www.mcct.eu
- 2 **The 6th International Symposium on Women's Health Issues in Thrombosis and Haemostasis**
13-15 February 2015 – Berlin, Germany
www.whith.org
- 3 **The 17th Annual Scientific Meeting of the Australasian College of Phlebology (ACP)**
15-19 February 2015 – Noosa, Queensland, Australia
www.phlebology.com.au/acp2015
- 4 **2015 Highlights of ASH[®] in Asia**
28 February-1 March 2015 – Bangkok, Thailand
www.hematology.org/Highlights/Asia.aspx
- 5 **2015 Hemostasis & Thrombosis Research Society (HTRS) Scientific Symposium**
16-18 April, 2015 – New Orleans, USA
www.hemedicus.com/meetings/htrs
- 6 **14th WFH International Musculoskeletal Congress**
7-10 May 2015 – Belfast, Northern Ireland
www.wfh.org
- 7 **37th Annual Meeting of the Japanese Society of Thrombosis and Hemostasis**
21-23 May, 2015 – Yamanashi, Japan
<http://www.jsth2015.umin.jp>
- 8 **20th Congress of the European Hematology Society**
11-14 June 2015 – Vienna, Austria
www.ehaweb.org
- 9 **ISTH 2015 Congress**
20-25 June 2015 – Toronto, Canada
www.isth.org




ACP 2015
 THE AUSTRALASIAN COLLEGE OF PHLEBOLOGY

ACP 17TH ANNUAL SCIENTIFIC MEETING AND WORKSHOPS
 15 - 19 FEBRUARY 2015
 SHERATON NOOSA RESORT AND SPA
 NOOSA SUNSHINE COAST, QLD
www.phlebology.com.au/acp2015

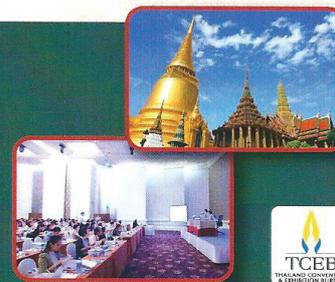
Mark Your Calendar

The only official
2015 Highlights of ASH®
 Bangkok, Thailand
 February 28 - March 1, 2015
 in Asia



- Examine advances in clinical and translational hematologic research
- Evaluate the role of new diagnostic techniques and therapeutic approaches as applied to the care and management of people with blood diseases
- Discuss new patient management and care strategies and emerging drug therapies with leading faculty in the field

Registration opens November 2014
www.tsh.or.th/2015HOA
www.hematology.org/Highlights/Asia.aspx



Saturday, February 28

7:30 a.m.	Registration and Exhibits Open Poster Session Setup
8:30 a.m.	Welcome and Introductions
8:45 a.m.	Acute Myeloid Leukemia John DiPersio, MD, PhD Washington University in St. Louis
9:15 a.m.	Pediatric Acute Lymphoblastic Leukemia Sarah Alexander, MD Toronto Sick Kids
9:45 a.m.	Panel Discussion with Drs. DiPersio and Alexander
10:15 a.m.	Coffee Break, Exhibition, and Poster Viewing
10:40 a.m.	Immune Thrombocytopenia David J. Kuter, MD, DPhil Massachusetts General Hospital
11:10 a.m.	Pediatric Red Cell Disorders Including Thalassemia Haewon C. Kim Children's Hospital of Philadelphia
11:40 a.m.	Panel Discussion with Drs. Kuter and Kim
12:10 p.m.	Lunch with Experts
1:30 p.m.	Adult Red Cell Disorders: Hemolysis, Iron, Infection, and Pheresis Michael L. Linenberger, MD Fred Hutchinson Cancer Research Center
2:00 p.m.	Aplastic Anemia David A. Williams, MD Boston Children's Hospital
2:30 p.m.	Panel Discussion with Drs. Linenberger and Williams
3:00 p.m.	Hematopoietic Stem Cell Transplantation Sergio Giralt, MD Memorial Sloan-Kettering Cancer Center
3:30 p.m.	Myeloproliferative Neoplasms Including Chronic Myeloid Leukemia Michael J. Mauro, MD Memorial Sloan-Kettering Cancer Center
4:00 p.m.	Panel Discussion with Drs. Giralt and Mauro
4:30 p.m.	Announcements
4:45 p.m.	2015 Highlights of ASH in Asia Poster Presentation
6:00 p.m.	Adjournment

Sunday, March 1

7:00 a.m.	Registration, Exhibition, and Poster Viewing
7:30 a.m.	Welcome and Recognition of Highlights of ASH Partner Organizations
7:45 a.m.	Hodgkin Lymphoma: PET Scans and Other Treatment Strategies Ranjana Advani, MD Stanford University
8:15 a.m.	Non -Hodgkin Lymphomas Including T-Cell Lymphoma Jonathan Friedberg, MD University of Rochester
8:45 a.m.	Panel Discussion with Drs. Advani and Friedberg
9:15 a.m.	Coffee Break, Exhibition, and Poster Viewing
9:40 a.m.	Disorders of Hemostasis Nigel S. Key, MBChB, FRCP University of North Carolina
10:10 a.m.	Thrombosis: Cancer -Related Treatments Kenneth A. Bauer, MD Harvard Medical School
10:40 a.m.	Panel Discussion with Drs. Key and Bauer
11:10 a.m.	Myelodysplastic Syndromes Mikael A. Sekeres, MD, MS Cleveland Clinic
11:40 a.m.	Multiple Myeloma: What is the Role of Transplant? Sagar Lonial, MD Emory University
12:10 p.m.	Panel Discussion with Drs. Sekeres and Lonial
12:40 p.m.	Closing Remarks
12:50 p.m.	Adjournment

