



## Message from the Chairman

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**Lai Heng Lee**

Dear APSTH Members,

It is my pleasure to communicate with you once again via the APSTH newsletter.

It has been a relatively quiet time for our society, since the council last met in October 2012 in Melbourne. The main activity being the APSTH/Japanese Society of Thrombosis and Hemostasis (JSTH) joint symposium, held during the annual meeting of the JSTH from May 30 to June 1, 2013, at Yamagata, Japan. We received a total of 26 abstracts and after rigorous scorings from a panel of reviewers, we congratulate these four young scientists who were invited to give their presentations.

Author	Title of Abstract
Jasmine Tay (Australia)	miR-494 Down regulation of Protein S Expression in Oestrogen-mediated Acquired Protein S Deficiency
Zhanli Xie (China)	Role of Plasma High-molecular-weight Kininogen in Endotoxemia: an in vivo study
Jingyi Zhou (China)	Dysfibrinogenemia associated with obstetric complications in four unrelated female patients
Suryo Anggoro, (Indonesia)	Reduced Bone Density In Adult Hemophilia Patients in Indonesia and its related factors

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APSTH had also served as a publicity platform for announcement in support of regional activities such as "The Thai International Symposium of Thrombosis and Hemostasis" organized by the Thai Society of Hematology during May 24-26, 2013 in Bangkok and the "International Haemophilia Course for Haemophilia Treators" educational forum held on 16-18 May 2013 in Singapore.

An important upcoming event is the APSTH Focus Symposium, Thrombosis and haemostasis in the Asian-Pacific, at ISTH 2013 (Amsterdam) to be held on Wednesday, July 3, 13.00-14.15 pm. Drs. Ross Baker and Yoshihiro Fujimura will present their papers, and there will be four selected abstracts from the Asian-Pacific region. APSTH members attending the ISTH at Amsterdam please be there to support this event.

On another note, I strongly urge our members to encourage like-minded colleagues interested in thrombosis and haemostasis to join the APSTH. There is no membership fee and all members will only benefit from the collaborative efforts in education and research activities on this Asia Pacific platform. It is with increased membership and interactions with one another that we can build a strong society and contribute towards important health issues in our region. No recommendation is better than recommendations from our very own members, so please ask your colleagues to join the Society. To become a member of the APSTH, please go to [www.apsth.org](http://www.apsth.org), and click on "Join APSTH now" which is located at the right upper quadrant of our web page. I look forward to an increased membership in APSTH.

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## From the Editor

Dear Colleagues,

We are pleased to present in this issue of the newsletter, accounts written by the four outstanding young scientists who won the "Selection for Young Investigator Award for the APSTH / Japanese Society of Thrombosis and Hemostasis (JSTH) Joint Symposium" for the 24th Congress, May 30 to June 1, 2013, at Yamagata, Japan. These articles are impressive not only in outlining the research accomplishments of these four young investigators, but also in revealing some of the motivation for their doing their research. A common thread of all four articles is the importance of our Young Investigator Award program to the winners of the award. That confirms to us the value of the APSTH/JSTH sponsorship of this program with its accompanying travel grant. Countries represented this year by the young investigators are Australia, China (two representatives), and Indonesia.



Turning to another article featured in this newsletter, Dr. Ross Baker briefs us on the new oral anticoagulants (NOACs) which include dabigatran (direct thrombin inhibitor), rivaroxaban and apixaban (anti-Xa). These NOACs may replace warfarin for the prevention of thromboembolism in patients with atrial fibrillation and venous thromboembolism.

Another new study is described by Dr. Yi Wu. Observations made in this study provide a novel insight into the connection between the coagulation system and immunity. This system could be a pharmaceutical target for treatment of inflammatory and autoimmune diseases.

In our news section, there's an update on the Asian Pacific Microangiopathic Thrombocytopenia Research Network (APMAT Research Network). Also, there is an item about Prof. Hatem Salem, Immediate Past President of APSTH, who delivered two excellent lectures on Novel Oral Anticoagulants in VTE treatment at the 10th Annual Convention of the Philippine Society of Vascular Medicine in Iloilo City, Philippines on April 19, 2013.

I'd like to encourage you to share information with our readers by submitting an article for publication in this newsletter to me at [pantep.ang@mahidol.ac.th](mailto:pantep.ang@mahidol.ac.th).

**Pantep Angchaisuksiri, Editor**

Officer of Public Relations and Communications APSTH



## Challenges with the New Oral Anticoagulants (NOACs) and the Ares Collaborative

**Ross Baker**

Centre for Thrombosis and Haemophilia, Royal Perth Hospital, Murdoch University, Perth, Australia

The new oral anticoagulants (NOACs) which include dabigatran (direct thrombin inhibitor), rivaroxaban and apixaban (anti-Xa) are now or soon to be approved in Australia and internationally to replace warfarin for the prevention of thromboembolism in patients with atrial fibrillation and venous thromboembolism. Unlike the INR which is used as a measure for reversal of warfarin, there is great uncertainty as how to monitor the use of haemostatic agents in NOACs

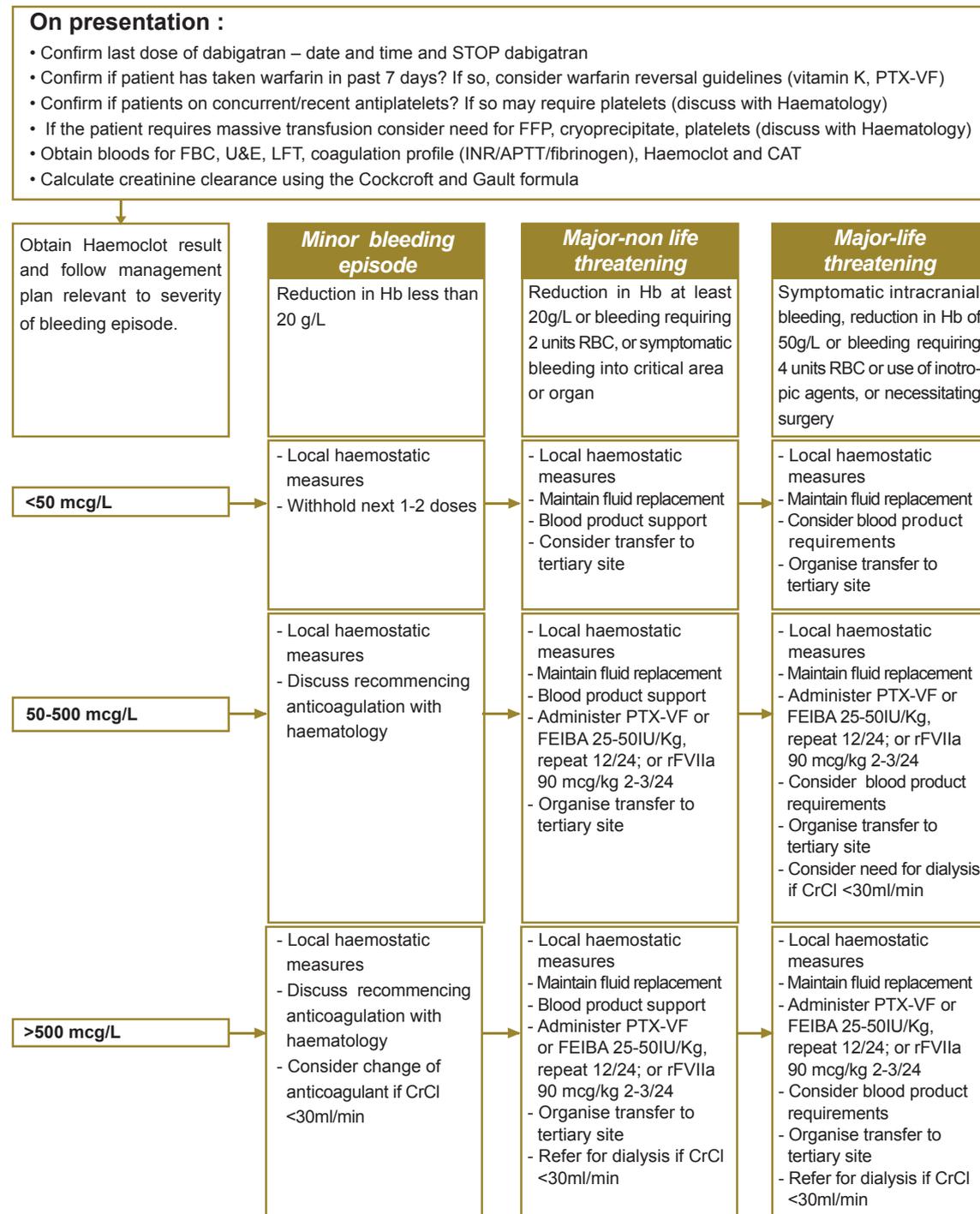
patients when they have major haemorrhage.

We describe the experience in standardising laboratory testing and observing clinical haemostatic management in 9 patients with dabigatran related major haemorrhage over a 6 month period. We also explored the clinical use of a global haemostatic assay (calibrated thrombin generation - CAT) in response to dabigatran and rivaroxaban and investigated in vitro

the potential for restoration of haemostatic function using Prothrombinex VF (PTX), FEIBA and rVIIa. In patients presenting with major haemorrhage on dabigatran, the validated APTT, TCT, dabigatran level, creatinine clearance and time since last dose are all required to determine appropriate management. Whilst it is uncertain which haemostatic agent to use in patients on dabigatran, CAT analysis may guide subsequent therapy.

Based on this limited experience a management algorithm is suggested but reliable information is lacking.

### Proposed Management of Patients Presenting with Haemorrhage whilst Taking Dabigatran



Post administration of haemostatic agent (10 mins) repeat APTT, Haemoclot and CAT (3 citrates)

In order to address this practice gap, the Anticoagulant Reversal and Event Study collaborative (ARES Collaborative) has been initiated and supported by the Australian Society on Thrombosis and Haemostasis to investigate patients on oral anticoagulants who present with significant haemorrhage or thrombo-embolic adverse events in Australia and New Zealand over the next 3 years.

Its primary aim is to observe and contrast the haemostatic or thrombo-embolic management of people on warfarin or the new oral anticoagulants (NOAC). The protocol has been finalised, the data collection tool accepted, and ethics submission approved at various sites in Australia and New Zealand.

## Reports from Recipients of the APSTH/JSTH 2013 Travel Grant



Far left- Prof. Satoshi Fujii, far right- Prof. Yukio Ozaki, with award winners from left to right- Zhanli Xie, Jingyi Zhou, Jasmine Tay, Suryo Anggoro.



### APSTH/JSTH Joint Symposium: An Experience and an Event to Remember

**Suryo Anggoro**  
 Department of Internal Medicine  
 University of Indonesia, Indonesia

I first received the information on JSTH travel grant through my mentor Dr. Lugyanti Sukrisman and she asked me to submit my paper to apply for it. At first to be honest I felt pessimistic because I thought there must be a lot of researchers with excellent papers also pursuing that opportunity and I thought my chance of being chosen was slim. But then I submitted my paper and I already prepared myself that I would not make it. Days passed and I didn't think about it again. Then suddenly I received an email from Prof. Satoshi Fujii stating that my paper was selected to be presented in Japan. I was really surprised, proud and happy that I could make it but at the same time also afraid because this would be my first oral presentation outside of my country at a prestigious forum. I also amazed by the generosity of the committee in providing me all the arrangements for my travel to Japan. I then tried to prepare my best so that I would not embarrass myself during the presentation.

At the JSTH, I met other young investigators from China and Australia. It was a really nice experience to know colleagues from other countries and it provided opportunities to link with research community from abroad. The first evening in Japan other young investigators and I met Prof. Fujii and Prof. Ozaki and we had a really nice dinner. It warmed my heart that Prof. Fujii and Prof. Ozaki were warmly welcomed us. That helped me to reduce my anxiety before the presentation. The study that I presented was a clinical study on reduced bone density in hemophilia patients. It was a simple clinical

study that gave another side from sophisticated studies on basic science presented by other investigators.

During the conference, I attended several interesting lectures from recognized speakers. I was astonished by excellent presentation and advance techniques presented in the meeting. It really opened my eyes that Indonesia really needs to catch up with the gap and the only way to keeping up with other countries is to start doing the research and take the opportunity to upgrade our knowledge. This experience in presenting a paper abroad and seeing how research community in other countries works, really gives me motivation to keep doing research despite the clinical work that we have to do. I was also impressed by the commitment of the Japanese scientific community to keep looking for new information despite the advance knowledge they already have. I felt really honored that some of the spectators of my presentation asked questions even though I only presented a simple observational study.

This event also provided us the opportunity to experience the beauty of Japan and their people. I met Dr. Kokame and Dr. Tamura and we had a really nice chat and dinner. I can only thank the committee, Prof. Fujii, and Prof. Ozaki for all the great memories, opportunity and experience. I also want to thank all of my mentors for my current paper. I suggest that other young investigator apply for this opportunity because this event really enriched me scientifically and personally.



## APSTH/JSTH Joint Symposium Report

**Jasmine Tay**

*Department of Haematology, Coagulation Research  
Royal Perth Hospital, Perth, Australia*

Visiting Japan has always been at the top of my bucket list, and being able to represent the laboratory and share our research investigating miRNAs in oestrogen-mediated acquired Protein S deficiency at the APSTH-JSTH Joint Symposium alongside three other brilliant young scientists – Jingyi Zhou and Zhanli Xie from China, and Suryo Anggoro from Indonesia is certainly a great honour.



This year's Annual JSTH Meeting was held in the beautiful Yamagata prefecture approximately 240 kilometres north of Tokyo city. Famous for its numerous natural hot springs and cherry fruits, I was pleasantly surprised to find out that Yamagata was off the beaten track for many of the local attendees, and that they were as much a tourist as I was. With sunny skies forecast and the famous Yamagata cherry harvest season in full swing, all signs bode for a great meeting ahead. Although the meeting was in Japanese, there were a number of excellent English lectures by invited prominent international scientists. Professor Wolfgang Korte from St Gallen, Switzerland presented their clinical research data which showed that the imbalance of Factor XIII availability and prothrombin conversion was a major cause of acquired coagulopathy in surgical patients. This finding led to the development of a highly successful management strategy for identifying surgical patients at a high risk of post-surgical bleeding. Professor Korte's clinical lecture was well complemented by Professor Khalid Naseem from Hull York Medical School, United Kingdom, who spoke about the central role of Factor XIII in platelet action. The work in his laboratory demonstrated that Factor XIII has vital functions beyond its transaminidase activity, and is involved in platelet secretion, filapodia, lamelapodia and Src kinase pathway activation processes.

We were generously hosted by Professor Satoshi Fujii and Professor Yukio Ozaki, who initiated us in various types of traditional (and exotic) Yamagata/Japanese cuisine, and candidly shared with us the progression of their careers and their experiences as post docs overseas. We also had the pleasure of meeting research fellows, Dr Shogo Tamura and Dr Koichi Kokame, exchanging our personal stories about working scientists in different parts of the Asia-Pacific region. By the end of the meeting, and I am sure I speak for all four of us who presented at the APSTH/JSTH Joint Symposium, we were well fed in every possible way – scientifically, gastronomically, culturally, socially, you name it. I sincerely thank the organisers, especially Professor Satoshi Fujii and Professor Yukio Ozaki for this wonderful opportunity. It has been immensely enriching and a great experience for any young scientist. I look forward to visiting Japan again and also catching up with many of the wonderful new friends at the upcoming ISTH2013 in Amsterdam.



## My Unforgettable Experience of Attending APSTH/JSTH Joint Symposium



### Zhanli Xie

*Cyrus Tang Hematology Center,  
Soochow University, China*

I am currently a graduate student at the Cyrus Tang Hematology Center at Soochow University. My ongoing project is the role of the plasma kallikrein-kinin system in innate immunity. During my study in the last three years, I enjoyed the thrombosis and hemostasis research and discovered the APSTH. Also, I have read many high quality research papers submitted by the Japanese scientists. Last year, I submitted my abstract to this 24th Congress of the ISTH -APSTH joint symposium. Four months ago, I received an e-mail - "Selection for Young Investigator Award for the APSTH/JSTH Joint Symposium". I was so happy to get this award, because this is my first time to present my work at an international meeting and my first time to go abroad.

From multiple resources such as TV, movies and the Internet, I have learned that Japan is a very beautiful country with many friendly people. Thus it has been my dream for a long time to visit Japan. On May 29, Jingyi Zhou from Shanghai and I arrived at Haneda Airport in Japan. We soon saw Ms. Yumiko Kobayashi, who was waiting for us. She accompanied us to Yamagata by bullet train. She is a very kind and patient lady, we really appreciated her help, otherwise we would have had a hard time to get to the venue. At our first night in Yamagata, Prof. Yukio Ozaki and Prof. Satoshi Fujii came to see us and other two speakers, Jasmin Tay from Australia and Suryo from Indonesia. They invited us to a dinner at a traditional restaurant. I truly enjoyed the Japanese cuisine.

On the day of the symposium, I presented my work on the role of plasma high-molecular-weight kininogen (HK) in endotoxemia. We have spent more than 3 years on this project, and have come up with a set of data demonstrating that HK, which is a key component of plasma kallikrein-kinin system, is a critical inflammatory mediator in endotoxemia. I felt greatly honored to present this work. Besides, I also learned a lot from other

young speakers and many high quality presentations by the Japanese scientists. One more thing I want to mention is that I also enjoyed the lecture of Dr. Earl W. Davie, who is the greatest scientist in our field. From his talk, I learned that it was he who cloned almost all of the coagulation factors, including HK, prekallikrein and FXII. So I learned a good lesson on the history of these molecules I am working on. During the meeting, we also met many Japanese scientists and graduate students and we shared our ideas about science and culture. The APSTH-JSTH is indeed a wonderful platform for me to understand our society and the new progress of thrombosis and hemostasis.

I want to express my sincere appreciation to everyone who helped me to attend this meeting, especially Professor Ozaki and Professor Fujii, as well as the APSTH-JSTH. I really enjoyed my experience in Yamagata, and I am so happy to make friends with many young scientists in this meeting. My experience of attending this meeting will certainly encourage me to continue my research in science, and will be unforgettable.





## Amazing experience in Yamagata, Japan

**Jingyi Zhou**

*Department of Clinical Laboratory,  
Ruijin Hospital affiliated with  
Shanghai Jiaotong University School of Medicine, China*

It was my great pleasure and honor to be invited to attend 2013 APSTH/JSTH Conference held in Yamagata, Japan in the end of May, 2013. I think that the stay in Japan was one of the most valuable treasures of my life.

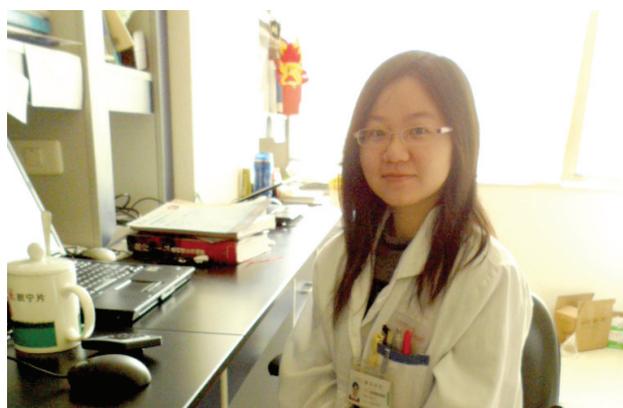
When I first arrived at Haneda Airport, I met Yumiko Kobayashi, who is a very nice woman with kind smile. She arranged for us to take a bus from Haneda Airport to Tokyo station and said goodbye to us when we got on the JR to Yamagata. During my stay with her, she showed me the Tokyo Tower and the Rainbow Bridge, so although I didn't have time to stay in Tokyo, I still had the opportunity to have a glance at this beautiful city. And here, I want to thank Ms. Yumiko Kobayashi again.

The first day when we arrived at Yamagata, Zhanli Xie and I met Professor Yukio Ozaki and Professor Satoshi Fujii, as well as another two speakers, Jasmin Tay from Australia and Suryo from Indonesia in a traditional Yamagata restaurant. There we not only enjoyed the delicious traditional Yamagata food, including the well-known Yamagata beef, sashimi, saki and so on, but also the traditional Yamagata dance. We talked a lot with these two professors and other two invited speakers, from science to culture in Japan and all over the world, and I really gained a lot from these conversations and I really enjoyed the life in Yamagata.

On the day of symposium, I presented my study on dysfibrinogenemia associated with obstetric complications in five unrelated female patients. This was my first time to present my work at an international congress, which was my great honor. I also listened to the presentations made by the other three speakers, and the lecture made by Professor Earl W. Davie, from which I learned a lot. In the evening, Professor Fujii arranged for us to meet students to exchange our ideas with each other. I want to express my deep appreciation to Professor Ozaki and Professor Fujii for their invitation and warm welcome to us, and for the opportunity they gave us to attend this congress.

After the congress, Jasmine, Zhanli Xie and I also went to Zao Onzen to experience the famous hot spring in Yamagata. This was my first time to experience the outdoor hot spring, and I think that it was really amazing. I enjoyed the fresh air and natural hot spring in the mountain, and felt relaxed after that. All of us liked it

very much. After that, we went shopping and the sales people in the shop were so helpful that we finally found everything that we wanted to buy with their help.



All in all, I really enjoy my stay in Yamagata, and I am so happy to make friends with so many young scientists at the APSTH/JSTH congress. I really learned a lot from this congress. I want to thank Professor Ozaki and Fujii again for their kind invitation and welcome. The travel grant really means a lot to me as a student. This travel grant provides me with an opportunity to go abroad and to communicate with young scientists from all over the world. It also provides an international platform for me to present my work. This kind of experience will inspire me to work harder in the future. And I would also encourage more and more young investigators to apply for this grant to present their work in this international platform.



# Research News



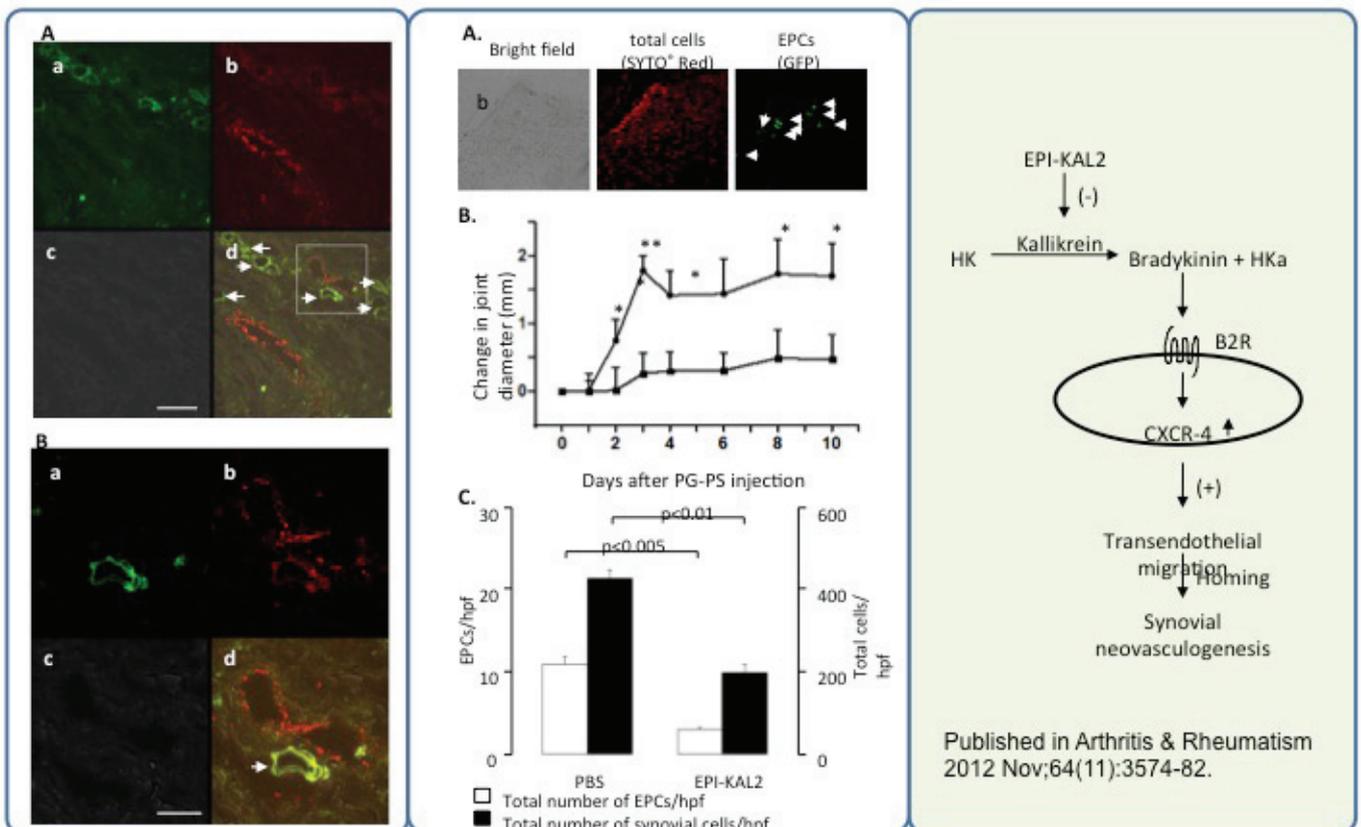
## Role of Plasma Kallikrein-Kinin System in the Pathogenesis of Arthritis

Yi Wu, M.D., Ph.D.

Cyrus Tang Hematology, Soochow University, China

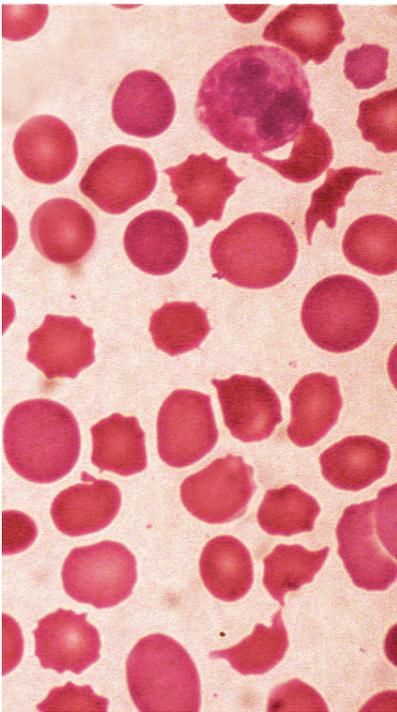
Plasma kallikrein-kinin system (KKS) is also known as intrinsic coagulation system and plasma contact activation system. This system consists of four plasma proteins, plasma prekallikrein, FXII, FXI and high molecular weight kininogen (HK). Our research interest is the role of plasma KKS in vascular biology and immunity. Previous studies have suggested that the activation of plasma KKS is involved in the pathogenesis of arthritis, however, the underlying mechanisms remain unknown. We recently found that the activation product of plasma KKS regulates the function of endothelial progenitor cells in vitro (J Thromb Haemost 2010;8:185-93 and Arterioscler Thromb Vasc Biol 2011;31:883-9), suggesting a novel link between plasma KKS and vasculogenesis. Since the pathogenesis of rheumatoid arthritis (RA) is critically dependent on neovascularization of the synovium, occurring before clinical symptoms appear, we asked whether the participation of plasma KKS in arthritis is associated with synovial homing of endothelial progenitor cells. In Lewis rat model of arthritis, we found that exogenously-injected endothelial progenitor cells homed to inflamed synovial tissues

and formed de novo vessels (see the left panel of figures). When the rats were treated by specific inhibitors of plasma kallikrein, the recruitment of endothelial progenitor cells to the synovium and the development of disease were significantly inhibited, demonstrating that the activation of plasma KKS mediates synovial neovasculation (see the middle panel of figures). Furthermore, we identified that the receptor of bradykinin Type 2 is involved in the home process of endothelial progenitor cells; its downstream effects include the upregulation of major homing receptor CXCR4 (see the right panel of figures, Arthritis & Rheumatism 2012;64:3574-82). In a mouse model of anti-collagen antibodies-induced arthritis, our more recent observation has shown that the deficiency of bradykinin receptors protects mice against arthritis (Rheumatology, in revision). Taken the above together, plasma KKS activation stimulates synovial neovasculation by activating bradykinin receptors. These observations provide a novel insight into the connection between coagulation system and immunity. This system could be a novel pharmaceutical target for treatment of inflammatory and autoimmune diseases.



## News

# Asian Pacific Microangiopathic Thrombocytopenia (APMAT) Research Network



In Melbourne, at the recent October Scientific Meeting of the Asia Pacific Society on Thrombosis and Haemostasis, the APMAT Research Network International Steering and Executive Strategic Implementation Committees met to review progress and consolidate the APMAT network. Most member countries of APSTH are interested and well represented. We were honoured to have AP leaders in MAT to discuss and present their work including Professor Changgeng Ruan and Ziqiang Yu from Suzhou, P.R.China, Professor Yoshihiro Fujimura, Nara, Japan and Professor Doyeun Oh, Seongnam, South Korea.

It was recognised that MAT is a rare yet fatal disease, clinical management is difficult and there are major information gaps in registry data and clinical diagnostic testing.

It was agreed to;

1. Develop the APMAT Research Network Protocol
2. Formation of a AP medical advisory panel of APMAT experts for individual clinical advice and problem sharing for MAT in AP
3. Establishing a clinical adjudication committee to independently classify patients with MAT with standardised criteria for the APMAT study
4. Standardise laboratory testing for ADAMTS13 and any other novel assays in the AP region
5. Facilitate basic science and translational clinical research into MAT

We welcome all APSTH members to consider their involvement and contact me directly if you have further questions. It is a great opportunity for APSTH to establish the APMAT research network for better care and improved understanding of our patients with MAT.

### **Professor Ross Baker**

Chairman APMAT  
 Email: ross@wahaem.com.au

APMAT is supported by the Asian Pacific Society on Thrombosis and Haemostasis (APSTH) and the Australasian Society of Thrombosis and Haemostasis (ASTH) and now has a live website [www.apthn.org](http://www.apthn.org) for communication, information and data entry.



Prof. Hatem Salem, Immediate Past President of APSTH, delivered two excellent lectures on Novel Oral Anticoagulants in VTE treatment at the 10th Annual Convention of the Philippine Society of Vascular Medicine in Iloilo City, Philippines on April 19, 2013. His first lecture was on "Managing Bleeding complications in Patients on New Anticoagulants" as he shared recommendations on measures to prevent bleeding, identifying patients at high risk for bleeding and selecting the most appropriate anticoagulant. Prof. Salem also gave a lecture on the new anticoagulants for the treatment of Acute Venous thromboembolism. Both lectures were very well received and the subsequent open forum raised several issues.

**Dr. Maria Teresa Abola**  
 Philippine Heart Center, the Philippines



## 1 XXIV Congress of the International Society on Thrombosis and Haemostasis

29 June – 4 July 2013 – Amsterdam, Netherlands  
[www.isth2013.org](http://www.isth2013.org)

### Focus Symposium on Thrombosis and Haemostasis in the Asian-Pacific Wednesday, July 3, 2013 (13:00 - 14:15) Emerald Room

- Asian-Pacific Microangiopathic Thrombocytopenia Network (APMAT)  
*Ross Baker (Australia)*
- Registry of congenital atypical HUS in Japan  
*Yoshihiro Fujimura (Japan)*
- SMTP-7, a novel thrombolytic with an anti-inflammatory potential, improves primate thrombotic stroke with reduced hemorrhage risk: a role of soluble epoxide hydrolase inhibition  
*Eriko Suzuki (Japan)*
- ACTN 1 mutations cause congenital macrothrombocytopenia  
*Shinji Kunishima (Japan)*
- Impaired haemostasis in Reelin-deficient mouse: a potential role of plasma Reelin in thrombin generation and fibrin clot formation  
*Wei-Lien Tseng (Taiwan)*

## 2 HAA 2013 A Joint Scientific Meeting of the Haematology Society of Australia and New Zealand, Australia and New Zealand Society of Blood Transfusion, Australasian Society of Thrombosis and Haemostasis

20-23 October 2013 – Queensland, Australia  
[www.fcconventions.com.au/haa2013](http://www.fcconventions.com.au/haa2013)

## 3 2013 ASH Annual Meeting and Exposition

7-10 December 2013 – New Orleans, LA, USA  
[www.hematology.org](http://www.hematology.org)

