



# APSTH

Asian - Pacific Society on Thrombosis and Hemostasis

[www.apsth.org](http://www.apsth.org)

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## Message from the Chairman



**Lai Heng Lee**

Dear APSTH members,

Half a year has flown by very quickly.

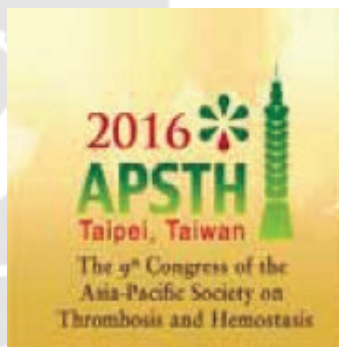
Our young investigators from APSTH have presented their work in June at the APSTH-JSTH Congress in Japan and they have shared their experiences in this newsletter.

Going forward, I will like to draw our attention to two events in the latter part of this year.

I urge our members to continue supporting the World Thrombosis Day (WTD) 13th October 2016, initiated by the International Society of Thrombosis and Hemostasis (ISTH). That date is Rudolf Virchow's birthday and has been designated as World Thrombosis Day. With its mission to increase global awareness of thrombotic diseases, particularly venous thromboembolism and atrial fibrillation associated thromboembolic stroke, WTD seeks to reduce the mortality and morbidities associated with these thrombotic diseases. It would be good if our member countries can lend their support of WTD for this worthy cause.

Our highlight of 2016 is the much anticipated 9th Congress of Asian-Pacific Society on Thrombosis and Hemostasis to be held 6th to 9th October in Taipei, which was also the venue for our very first APCTH in 2000. The local organising committee from the Taiwan Society of Thrombosis and Hemostasis has put much effort into putting up an exciting and excellent programme. This APSTH Congress sees a vast array of world-renowned speakers from USA, Canada and Europe joining our regional speakers from Asia Pacific to share the latest developments and up-to-date knowledge on all topics pertaining to thrombosis and hemostasis. We also anticipate numerous high quality oral and poster presentations from the region.

I certainly look forward to meeting you very soon in Taipei.



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## From the Editor



Dear APSTH Members,

Welcome to our mid-year newsletter.

In this edition, we feature a look at what is being planned for this year's World Thrombosis Day 2016 (October 13th). With educational events planned in more than 70 countries around the world, WTD and its partners place a global spotlight on thrombosis as an urgent and growing health problem. As it enters its third year, the campaign is on track to include more

than 500 partners and reach more than 440 million people around the world. The aim of WTD is to educate and motivate people of all ages to know the risk factors as well as the signs and symptoms of thrombosis. For health care professionals, the objective of WTD 2016 is to ensure they conduct a blood clot risk assessment upon hospitalization of patients. The 2016 campaign platform, *Know Thrombosis: Keep Life Flowing*, emphasizes the need for health care professionals and patients to become educated about the condition.

Looking ahead to another upcoming 2016 event, the 9th Congress of the Asian-Pacific Society on Thrombosis and Hemostasis, we have an article by the President of that Congress, Professor Ming-Ching Shen. The 9th APSTH Congress 2016 will be held on October 6th - 9th, 2016 at the Taipei International Convention Center (TICC) in Taipei, Taiwan. The conference will cover a wide range of Thrombosis and Hemostasis topics with presentations by leaders in the field from around the globe.

Our four talented APSTH Young Investigators presented their research in June at the APSTH-JSTH Congress in Japan. In this newsletter, they share with us their feelings about being selected for the award and being able to present their work and meet outstanding people at that Congress.

The Research News is from Shogo Tamura of Japan. His article is "A novel megakaryopoietic microenvironment in the bone marrow: Podoplanin-positive peri-arteriolar stromal cells regulate megakaryocyte proliferation and proplatelet formation via CLEC-2 binding"

I hope you enjoy reading the newsletter and look forward to seeing you in Taipei in October.

If you have something to share with our members, please send an article to me at [pantep.ang@mahidol.ac.th](mailto:pantep.ang@mahidol.ac.th)

**Pantep Angchaisuksiri, Editor**

*Officer of Public Relations and Communications APSTH*

# World Thrombosis Day 2016 Campaign - World to **Know** Thrombosis



**Barbara Krolak**

*International Society on Thrombosis and Haemostasis (ISTH)*

## World Thrombosis Day 2016

It's a troubling fact that 1 in 4 people die of conditions related to thrombosis around the world each year. Recognized on 13 October, World Thrombosis Day (WTD) focuses attention on the often overlooked and misunderstood condition of thrombosis. With thousands of educational events in more than 70 countries around the world, WTD and its partners place a global spotlight on thrombosis as an urgent and growing health problem. As it enters its third year, the campaign is on track to include more than 500 partners and reach more than 440 million people around the world.

This year, the WTD campaign has launched a new creative suite of materials to educate and motivate people of all ages to know the risk factors as well as the signs and symptoms of thrombosis. Many materials are also intended for health care professionals to ensure they conduct a blood clot risk assessment upon hospitalization of patients. Clear, open dialogue is critical for health care professionals and their patients. The 2016 campaign platform, **Know Thrombosis: Keep Life Flowing**, emphasizes the need for health care professionals and patients to become educated about the condition. It also employs a universal analogy and compelling imagery to make thrombosis feel relevant.

The campaign is also excited to announce the appointment of two new members to its scientific steering committee, including one new member from Japan. Dr. Tetsumei Urano was appointed to the WTD Steering Committee in May. He is Vice President of Hamamatsu University School of Medicine in Hamamatsu, Japan. His leadership and expertise in Japan's thrombosis and hemostasis community is an important asset to the WTD campaign. In addition, the campaign also welcomed a Steering Committee member from Uganda, Africa, Dr. Henry Ddungu.



## Join the conversation online!

Follow WTD on Facebook, Twitter, LinkedIn, Instagram, YouTube and Pinterest. Don't forget to use the following campaign hashtags: #WorldThrombosisDay, #WTD16, #KnowThrombosis, #KeepLifeFlowing, #StopDeadlyClots and #AwarenessMatters. Please also update your social media images and banners to show your support!



### News in the Asia-Pacific Region

The importance of raising awareness about blood clots is more timely than ever in the Asia-Pacific region. The topic of blood clots as a major health concern has been a top news item in Japan following the devastating earthquakes in Kumamoto. Recent news has shared the dangerous after-effects of the earthquakes, with many survivors left to sleep in their cars. Some of these survivors have since been diagnosed with economy-class syndrome, or blood clots. This tragic news puts a spotlight on the issue of blood clots in the Asia-Pacific region and across the world.



### Getting Started: Preparing for WTD 2016

Last year, the Asia-Pacific region played a crucial role in the overall success of the WTD campaign. Activities spanned across countries throughout the Asia-Pacific region and the WTD message of awareness spread across languages and

cultures. Globally, the campaign featured more than 6,500 activities organized by 320 partner organizations representing 70 countries. Following such exciting engagement and participation, this year is the perfect time to continue to boost awareness and increase activities to support WTD.

With WTD 2016 only a few months away, start planning your awareness events and activities. For WTD partners, creativity and capacity are crucial to engaging the public on WTD. Awareness activities are great opportunities to invite the public into your hospital or institution, engage with patients and their families, hold workshops with other health care professionals and work with the local media to build awareness of thrombosis. Events educate, motivate and help save lives. To help you brainstorm the best event or activity to hold in your community, see a comprehensive list of ideas and events on the WTD website that have been successfully executed by other organizations in previous years. Stay tuned for more updates on upcoming events in the Asia-Pacific Region.

To complement the new campaign platform, valuable new resources are now available to the WTD community, including social media graphics and badges, flyers, partner toolkit, posters, slide templates and more. To use the resources, first join the campaign for free at [www.worldthrombosisday.org/join/](http://www.worldthrombosisday.org/join/). In addition, you can also get involved by sharing your story with the WTD community. Submit a personal story for consideration to be added to the WTD website. Email [wtd@isth.org](mailto:wtd@isth.org) for more information.

Now is also an important time to reach out to local organizations and businesses to discuss sponsoring your WTD activities and/or involvement. To learn more about local sponsorship considerations, review the Awareness-to-Action Partner Toolkit.

Have a question or need help? Contact the WTD team at [wtd@isth.org](mailto:wtd@isth.org). The team appreciates your support and is dedicated to helping you. For more information and/or to join the WTD movement, visit [www.worldthrombosisday.org](http://www.worldthrombosisday.org). You can make a difference!





## Preview of the 9th Congress of the Asian-Pacific Society on Thrombosis and Hemostasis

**Ming-Ching Shen**

*President of the 9th APSTH Congress 2016*

The 9th Congress of the Asian-Pacific Society on Thrombosis and Hemostasis (9th APSTH Congress) will be held on October 6th – 9th, 2016 at the Taipei International Convention Center (TICC) in Taipei, Taiwan. The conference will cover a wide range of Thrombosis and Hemostasis topics with presentations by leaders in the field from around the globe. We look forward to seeing all of you in October in Taipei, Taiwan!

### Scientific Program

The 9th APSTH Congress features a rich scientific program that includes 7 intriguing and inspiring plenary speeches, more than 50 invited speakers from over 15 countries, in addition to many thematic oral and poster presentations.

The conference begins on October 6th with two educational programs sponsored by ISTH and WFH, and offered by eight leading experts from various fields of Thrombosis and Hemostasis. Following the educational program there will be an opening ceremony, a celebration of World Thrombosis Day, and a welcoming reception party for all conference attendees.



The key goal of APSTH 2016 is to facilitate the exchange of scientific information and the discussion of current issues in Thrombosis and Hemostasis research among participants from around the world. We would like to thank the many authors who have contributed their outstanding work to this 9th APSTH Congress. At last count, more than 130 papers have been submitted to the conference which will make it an exciting and enriching experience for all in attendance.

### More Information

Details and more information can be found on the conference website at [www.apsth2016.org](http://www.apsth2016.org).

### Accommodation

Arrangements have been made with several hotels near the conference venue for special rates to be offered exclusively to APSTH 2016 participants. Please make your reservation using the registration form on the APSTH website to ensure you get these special conference rates.



### Today's Taipei

Modern Taipei is a city of contrasts which can be vividly experienced through the exploration of both its urban and natural settings. Only a few minutes from the heart of the city you can soak away the cares of the world in mineral-rich hot springs nestled in the lush mountain foothills which ring the Taipei Basin, while throughout the city itself are numerous trails, parks, and oases of tranquility that will lift and invigorate your spirits. Taipei's cultural heritage is on display through its world renowned National Palace Museum, its exciting architecture, and its many fine restaurants and markets which have led CNN, The New York times, and the Lonely Planet tour guide all to recognize Taipei as one of the world's premier food destinations.

Taipei is a multi-faceted treasure that will call you back again and again. Discover the heart of Asia in beautiful Taipei!





## Thursday, Oct. 6

Time/Venue	1F	102	201
9:00-12:05	Registration (8:00-18:00)		E1 Educational Program with support of ISTH
12:05-14:00		L1 Lunch Symposium 1 (Werfen)	L2 Lunch Symposium 2 (Novo Nordisk)
14:00-17:05			E2 Educational Program with support of WFH
17:30-18:30			Opening Ceremony / Celebration of World Thrombosis Day
18:30-20:00	Welcome Reception (3F Banquet Hall, TICC)		

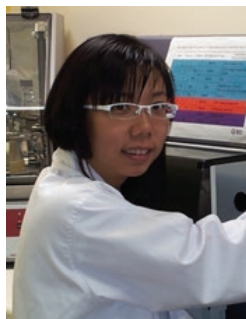
## Friday, Oct. 7

Time /Venue	1F	101	102	201	VIP Room, 4F
08:30-10:10	Registration (08:00-17:00)	Exhibition (08:00-17:00)	S1 Symposium 1 PNH and aHUS	S2 Symposium 2 Hemophilia (I)	S3 Symposium 3 APS and ITP
10:10-10:30			Coffee Break		
10:30-12:00				P1 Plenary Lecture 1 <i>Sam Schulman</i> <i>Frits Rosendaal</i>	
12:00-13:30			L3 Lunch Symposium 3 (Baxalta)	Lunch Symposium 4 (Stago)	Lunch Symposium 5 (Novo Nordisk)
13:30-15:10			S4 Symposium 4 Anticoagulants, Cardiovascular and Cerebrovascular Disorders	S5 Symposium 5 vWD and Rare Bleeding Disorder	S6 Symposium 6 Platelets Biology
15:10-15:30			Coffee Break		
15:30-17:10			O1 Oral Communication 1	O2 Oral Communication 2	O3 Oral Communication 3
17:10-18:30		Poster Session 1			
18:30-20:00			SS1 Satellite Symposium 1 (Bayer)	SS2 Satellite Symposium 2 (Baxalta)	SS3 Satellite Symposium 3 (Pfizer)

Saturday, Oct. 8					
Time /Venue	1F	101	102	201	VIP Room, 4F
08:30-10:10	Registration (08:00-17:00)	Exhibition (08:00-17:00)	S7  Symposium 7 Hemophilia (II)	S8  Symposium 8 Thrombotic Disorder	S9  Symposium 9 Acquired Bleeding Disorder
10:10-10:30			Coffee Break		
10:30-12:00			P2  Plenary Lecture 2 Kenneth Kaushansky Rolf Ljung		
12:00-13:30			L4  Lunch Symposium 4 (Novo Nordisk)	L5  Lunch Symposium 5 (Baxalta)	L6  Lunch Symposium 6 (Pfizer)
13:30-15:10			S10  Symposium 10 Unusual Bleeding, Thrombosis and Hemostatic Therapy	S11  Symposium 11 DIC and TTP	S12  Symposium 12 Snake Venom and Fibrinolysis
15:10-15:30			Coffee Break		
15:30-17:10			O4  Oral Communication 4	S13  Symposium 13 Laboratory Issue	O5  Oral Communication 5
17:10-18:30				Poster Session 2	SS4  Satellite Symposium 4 (CSL Behring)
19:30-21:30	Banquet (Grand Hotel Taipei)				

Sunday, Oct. 9		
Time/Venue	1F	201
8:30-10:45	Registration (8:00-10:00)	P3 Plenary Lecture 3 Midori Shima Tetsumei Urano Ming Chen
10:45-11:15		Coffee Break
11:15-12:00		Award Ceremony
		Closing Remarks

# Reports from Recipients of the APSTH/JSTH 2016 Travel Grant



## APSTH/JSTH Joint Symposium Experience

**Xiaowei Wang**

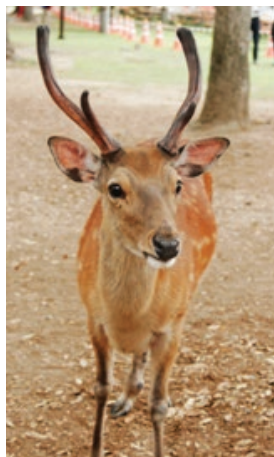
*National Heart Foundation Postdoctoral Fellow  
Atherothrombosis and Vascular Biology Laboratory  
Baker IDI Heart and Diabetes Institute  
Melbourne, Australia*

I felt very privileged and honoured to be invited to present my research at the 2016 APSTH/JSTH joint symposium in Nara Japan. Therefore I would like to take this chance to thank Prof. Satoshi Fujii, and the organisers of the JSTH for this wonderful opportunity.

I am a postdoctoral fellow working at the Atherothrombosis and Vascular Biology Laboratory, at the Baker IDI Heart and Diabetes Institute, situated in Melbourne, Australia. My research interests are thrombosis, molecular imaging, targeted drug delivery and theranostics so I was very honoured to be selected as one of the recipients of the travel award for JSTH. This experience has provided me with a chance to foster regional collaborations with researchers from Japan and other countries in the Asia Pacific region.

The symposium was exceptionally well organised and our travel plans were well thought out. Prior to departure, I was given clear and detailed instructions on how to get from Kansai Airport to Nara, including the location of the bus stop and its timetable. Therefore even though I do not speak any Japanese, I had no issues getting to my hotel in Nara.

On the evening of my arrival, Prof. Fujii organised a Japanese dinner for all the recipients of the APSTH/JSTH travel award and this gave me an awesome chance to meet other international early career researchers. Prof. Fujii and Dr. Shogo Tamura met us at our hotel lobby and walked us to the restaurant. I was delighted to meet two brilliant young scientists, Dr. Hui-Ju



Tsai and Fangmiao Jing (both of whom also received the travel awards). They were both knowledgeable and passionate about their research. In person, they were friendly and fun-loving. We were all keen to exchange contact details and keep in touch. We were also introduced to Prof. Yukio Ozaki and Prof. Tetsumei Urano, both excellent senior researchers who offered much advice. We had an enjoyable and delicious dinner, where Prof. Yukio Ozaki encouraged young researchers to be more involved in the APSTH.

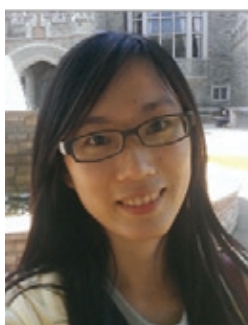
During the conference, I attended all the English sessions. I was very impressed with the work carried out by the early career researchers and I enjoyed the very insightful lectures given by the international speakers. Therefore, this conference has been a very fruitful experience for me. The conference centre was located in the middle of Nara Deer Park. The deer are surprisingly tame and walked straight up to me. It was one of the most wonderful experiences one can have with nature and these beautiful animals.

On the first evening of the conference, the organisers prepared a banquet for all the invited speakers, where we were served delicate French/Japanese fusion cuisine at the Nara Hotel. On top of the excellent meal, the dinner also provided a perfect opportunity for me to speak to the senior Japanese researchers, as well as the two outstanding scientists Prof. Björn Dahlbäck and Prof. David Lillicrap.

On the second evening of the conference, there was an impeccable banquet of Japanese cuisine and fine sake. I took this chance to mingle with the other awardees and got to meet the other conference attendees.

I would like to thank Prof. Fujii, Prof. Ozaki as well as all the organisers of JSTH for giving me this golden opportunity to learn from the brilliant scientists and clinicians present at this conference. Thank you for your hospitality. I really enjoyed myself in Japan.





## APSTH/JSTH Joint Symposium Experience

**Hui-Ju Tsai**

*Department of Medical Biotechnology and Laboratory Science  
Chang Gung University, Taoyuan, Taiwan*

In this summer, I had a special and wonderful experience at the APSTH/JSTH 2016 joint symposium in Nara, Japan. Thanks to the committees of the 38th Congress of the Japanese Society on Thrombosis and Hemostasis (the 38th JSTH), which accepted my application, provided the travel award and let me have this opportunity to attend the APSTH/JSTH 2016 joint symposium and present our study.



Our research topic was “Thrombin-stimulated phosphorylation of Disabled-2 causes its dissociation with CIN85 and activation of integrin in human platelets”. In this study, we address the functional role of phosphorylated Disabled-2 (Dab2) in human platelets. We have quite exciting data and demonstrate that Dab2 Ser723 is identified as the substrate of protein kinase C (PKC) during thrombin-stimulated inside-out signaling by using a newly generated phospho-Ser723-specific anti-Dab2 antibody. Dab2 Ser723 phosphorylation is associated with a decrease in the Dab2-CIN85 interaction leading to integrin  $\alpha IIb\beta 3$  activation during thrombin stimulation.

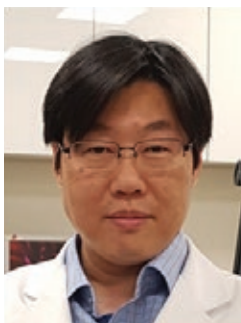
The organizers of this symposium were Prof. Satoshi Fujii and Prof. Tetsumei Urano. They were very nice and warm. They gave us an introduction for the 38th JSTH, the process of the APSTH/JSTH 2016 joint symposium, the notifications of presentation and responded fully to our questions. They had a welcome casual dinner before the starting of the 38th JSTH. It's my pleasure to know the leading scientists, Prof. Satoshi Fujii, Prof. Tetsumei Urano, Prof. Yukio Ozaki and Dr. Shogo Tamura, in the field of haemostasis and thrombosis and other Young Investigator Award recipients such as Dr. Xiaowei Wang and Dr. Fangmiao Jing. We exchanged the information about the areas of research and culture from our respective countries.



In addition, after the end of the APSTH/JSTH 2016 joint symposium, Prof. Midori Shima, the president of the 38th JSTH, invited us to participate in the social events. There, I met other kind and warm researchers, Prof. Yoshiaki Tomiyama, Prof. Toshiyuki Miyata and Dr. Kazuyo Yamaji-Kegan. Prof. Yukio Ozaki gave us encouragement for our work. I really enjoyed the Welcome Party at the first day of the congress and the Banquet at the second day of the congress. The traditional Japanese performance was wonderful and the food was delicious.

Finally, I deeply appreciated that my advisor, Prof. Ching-Ping Tseng, supported my study and encouraged me to attend this congress. By attending, I shared our study with the international scientists and was inspired by the leading scientists in the field. It's a very important event and experience for me to pursue my career in the research field of haemostasis and thrombosis. I'm looking forward to the future collaborations. Thank you for your help along the way.





## APSTH/JSTH Joint Symposium Experience

**Jaewoo Song**

*Dept. Laboratory Medicine, Yonsei University College of Medicine  
Seoul, Korea*

I was very pleased to be given the opportunity to present our results in APSTH-JSTH joint symposium. My presentation for the meeting was entitled "Improved sensitivity and discriminative power of factor VIII assay by applying turbidimetric clotting curve analysis" and was addressing the analysis of the whole process of clot formation by coagulometers commonly used in clinical laboratories. It was the first presentation to officially introduce our results on this topic in such a detail. The clotting process continues far beyond the time point that is measured to be assigned to the clotting time. We were trying to find if there exist meaningful patterns in turbidimetry curves of prothrombin time and/or activated partial thromboplastin time that could be exploited to provide clues and/or aids in clinical decision making. As a preparatory step we tried to fit each turbidimetry curve by a common mathematical model. We were surprised that the Gompertz model that originally was developed for ecological studies fitted most turbidimetry curves so well. Measuring factor VIII activity was an example of applying those efforts to the practice of clinical laboratory.

I hope that our results will awake a renewed interest of other researchers in this revisited but rather untouched topic in the era of flooding laboratory data. Every talk held in that session was fascinating and Dr. Wang's works on the application of microbubbles to theranostic ultrasound in fibrinolytic therapy, especially was impressive to me. I didn't know that the diagnostic performance of ultrasound in visualizing the mural thrombi can be enhanced so much by pharmaco-physical methods rather than by advanced electromechanical engineering.

I want to express my deepest thanks to Prof. Ozaki, Prof. Fujii and the organizing committee for their warm treat.

Without their caring help, I could barely have managed to get to Nara in time. Also, my short stay in Nara, a calm city with many inspiring sceneries was really a wonderful experience. I've been told many times that the JSTH is a large and very active society. And now after I've attended the 38th Congress of the JSTH I could understand what it meant. Having a glimpse at the program, what stood out to me was that the scientific aspects of hemostasis and thrombosis are strongly emphasized along with many clinical issues. It probably reflects the amount of scientific research done by the members of this society. The topics and titles of presentations generally were unique. Personally, my attempt to data-mine the turbidimetry curves of coagulometers was originally inspired by the studies of several Japanese researchers. Their results and the idea then were very unique as such I often feel with many other results and findings from Japanese groups.

Also notable was the participation of the pharmaceutical and diagnostic companies in academic activity. I don't know if that means active cooperation between industry and academia in Japan. Maybe it's related to the fact that there is strong effort to develop drugs and diagnostics of hemostasis and thrombosis. The last impression was that the wide scope of the topics covered in this meeting and the diverse backgrounds of the participants. It looks like a web structure of fibrin clot. The idea that the biologic background of hemostasis differs between populations advocates the regional cooperation in studying the unique pathophysiology of hemostasis and thrombosis. It seems to me that JSTH now is contributing much in organizing those collective efforts in Asia Pacific region, giving a hand to researchers for cooperation, which I really appreciate.





## APSTH/JSTH Joint Symposium Experience

**Fangmiao Jing**

Department of Hematology, Oncology Center  
Qilu Hospital, Shandong University, Shandong, P. R. China

This year, it was indeed a great opportunity for me to present our team's research at the 38th APSTH/JSTH Joint Symposium held in Nara, Japan. Also, it was an amazing experience for me to attend this meeting. I appreciated that I was sponsored as a young researcher by the organizing committee and had the chance to travel to Japan attending this influential symposium on thrombosis and hemostasis.

I still clearly remembered how excited I was when I read the email about my abstract being selected for presenting at the APSTH/JSTH. My supervisor Prof. Hou Ming was happy for me and told me that is the annual symposium of JSTH, an international congress. He said he had many friends in the field of thrombosis and hemostasis and knew many outstanding scholars in Japan that would be attending this meeting. When I connected with Prof. Satoshi Fujii and his work teams through e-mail, they impressed me a lot. Professor Satoshi Fujii always answered me in a timely way and was quite kind. They arranged the schedules and meetings very carefully. Of course, the travel agency who was responsible for our transportation and accommodation was also very professional and did the best to met my needs.



The trip from Jinan took nearly one day, I arrived at Kansai airport in the late afternoon the day before the conference and was amazed by the airport and helped onto a bus headed for Nara. After arriving at the hotel, Prof. Satoshi Fujii came to pick me up to go to the restaurant for the welcome party. I met other young scientists and scholars there. Prof. Yukio Ozaki was very nice and knew my supervisor well. It was my first time met Prof. TetsumeiUrano and other scientists. And I also had a good talk with Professors Shogo Tamura, Xiaowei Wang, Hui-ju Tsai.



On the first day of the symposium, a pre-symposium meeting was hosted by Professor Satoshi Fujii and Professor TetsumeiUrano right before our presentations. He highlighted some special English lectures and encouraged us to present our research to these world famous scientists. I was glad to meet the other four young scientists who also presented their research. They were KazuyoYamaji-Kegan from USA, Xiaowei Wang from Australia, Jaewoo Song from Korea and Hui-ju Tsai from Taiwan. We exchanged contact details, research interests, as well as culture from our respective countries.

The joint Symposium was an opportunity to share our team research. Our team lead by Professor Hou Ming at Qilu Hospital, Shandong University, has a strong interest in platelet research, especially in the common bleeding disease immune thrombocytopenia (ITP). As one of the selected presenters, I was keen to travel to Nara to meet colleagues and friends with similar interests and diverse expertise in the field of thrombosis and haemostasis. My presentation for this symposium was entitled "GSK-3 inhibitor promotes megakaryocytes apoptosis and platelets formation in immune thrombocytopenia". GSK-3 inhibitors increases megakaryocytes apoptosis and platelets release in the present of ITP plasma and also enhances TRAIL expression. Through questions asked by professors and feedback from this presentation, I found that there is much work for me to proceed with.

That night, I was invited to take part in the closed welcome party at Nara Hotel. It was really a wonderful banquet; there I met many other kind and warm researchers, We had interesting talks. They shared their research experiences as well as Japanese culture with us. On top of that, I was able to



taste graceful and delicious cuisine. Moreover, the conversations with the young researchers shortened the distance and we soon became familiar with each other. We talked about not only research, but also the lives, food, school, culture and many other aspects in our countries which let us know more about other Asian-Pacific countries and areas.

For the next two days of symposium, I was given an opportunity to learn about the new discoveries in thrombosis and hemostasis. Professor Bjorn Dahlback presented "Novel Insights into the Role of Factor V as Regulator of Blood Coagulation." Professor Andrew Selvaggi whose speech was entitled "The Benefits of Exercise for Joint Health and Living Healthy in Hemophilia Patients" impressed me a lot. And I think his speech would also encourage many people who suffered from hemophilia. The last English session in this congress was given by Professor David Lillicrap, who was invited to give this speech as a special guest and the topic was "Advances of basic and clinical aspects of hemophilia". He really did a lot of work in hemophilia and headed the progress of this disease in this area.

Like the first and second day, a great banquet was held at night. Many outstanding professors and young scholars from Japan and other countries participated in the feast. We talked and communicated further. I also had the chance to enjoy a wonderful Japanese performance. The music and

dance deeply affected me. What's more, it was my pleasure to taste the delicate Japanese food in Nara.

All in all, I would like to give a big thank you to the organising committee of the 38th APSTH/JSTH joint symposium for providing young researchers with this international opportunity and I would like to show my gratitude to the president of the JSTH Professor Yukio Ozaki, as well as the chairman of the APSTH joint symposium, Professor Fujii and all my Japanese friends I met in Nara for making us feel so welcome. Nara is an old city with a long history and culture. I was happy that I had the chance to stay there, taste delicious food, feed lovely deers, take pictures of beautiful scenery and meet kindly Japanese and make friends with other young researchers, that all of these brought me memorable, wonderful, and fruitful experiences.



## Research News



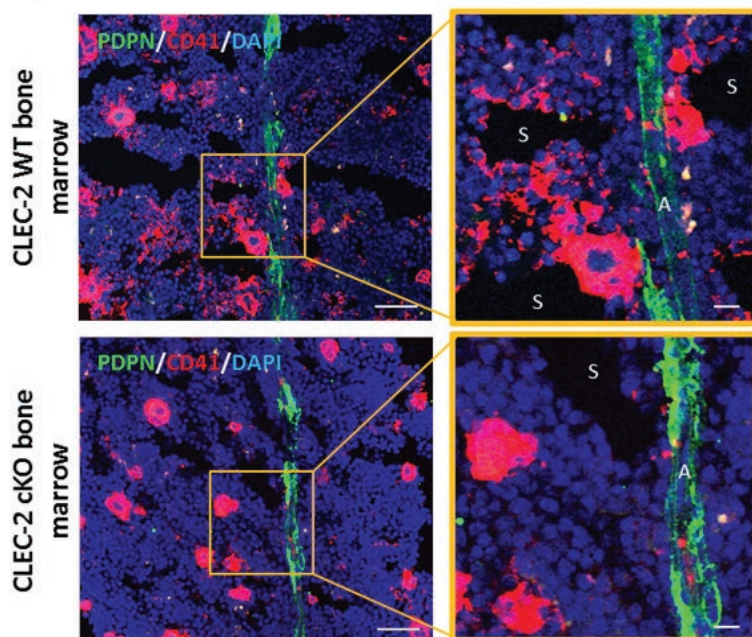
### A novel megakaryopoietic microenvironment in the bone marrow: Podoplanin-positive peri-arteriolar stromal cells regulate megakaryocyte proliferation and proplatelet formation via CLEC-2 binding

Shogo Tamura

Department of Pathophysiological Laboratory Sciences, Nagoya University Graduate School of Medicine

Megakaryopoiesis is the hierarchical differentiation of hematopoietic stem cells into megakaryocytes. Differentiating megakaryocytes undergo maturation characterized by extended cytoplasm with polyploidic nucleus. Fully matured megakaryocytes can produce numerous platelets through the elaboration of proplatelet formation (PPF). C-type lectin-like receptor 2 (CLEC-2) is a multifaceted platelet receptor that plays a role in lymph node (LN) homeostasis, maintenance of vasculature integrity, and thrombus formation (Suzuki-Inoue K et al. *Blood*. 2006. 107(7): 542-549, Suzuki-Inoue K et al. *J Biol Chem*. 2007. 282(36): 25993-26001). The endogenous ligand of CLEC-2,

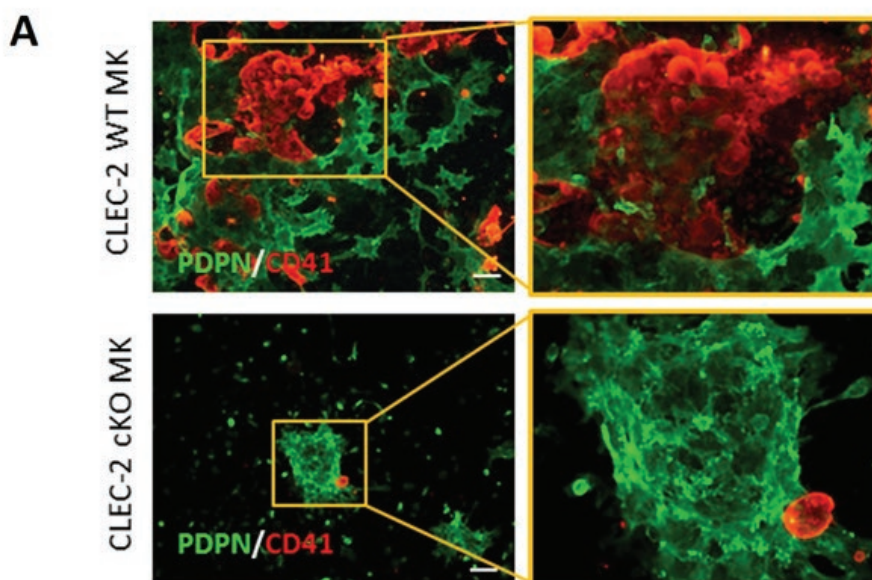
podoplanin (PDPN; also known as Aggrus or gp38), is highly expressed in lymphatic endothelial cells (LECs) and LN fibroblastic reticular cells (FRCs). Deletion of platelet/megakaryocyte CLEC-2 causes thrombocytopenia in mice; however, its contribution to megakaryopoiesis remains unknown. Recently, we showed that megakaryopoiesis was promoted through the CLEC-2/PDPN interaction in the vicinity of arterioles in the bone marrow (BM) (Tamura S, Suzuki-Inoue K et al. *Blood*. 2016. 127(13): 1701-1710). We also identified novel PDPN-expressing BM arteriolar stromal cells, termed as BM fibroblastic reticular cell (FRC)-like cells.



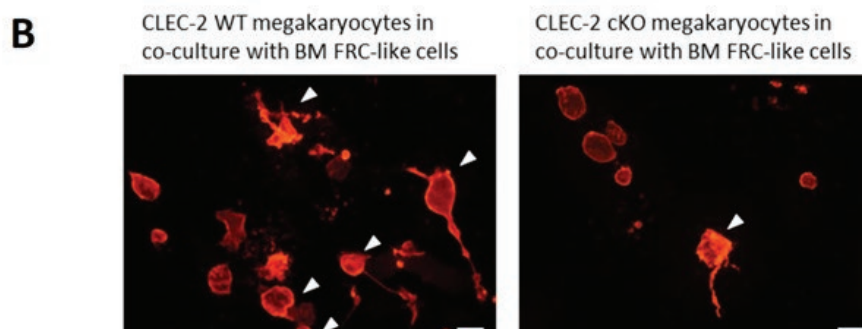
**Figure 1.** Representative IHC images of the CLEC-2 WT and CLEC-2 cKO BM staining with CD41 (red), PDPN (green), and DAPI (blue). In CLEC-2 WT BM, CD41+ megakaryocyte clusters located adjacent to BM FRC-like cells at periaarteriolar sites in the BM. Scale bars in unmagnified and magnified images indicate 100  $\mu$ m and 10  $\mu$ m, respectively. A, arteriole; B, bone; CV, central vein; S, sinusoid.

Platelet/megakaryocyte-specific CLEC-2 conditional knockout (cKO) mice showed a decrease in the number of immature megakaryocytes. In vitro experiments revealed that recombinant PDPN augmented megakaryocytic clonal expansion via binding to CLEC-2. In vivo, we found that megakaryocytic colonies developed in the vicinity of arterioles by associating with BM FRC-like cells (Figure 1). Mature large megakaryocytes and immature megakaryocytic colonies (CD41+ clusters) were adjacent to BM FRC-like cells in the WT BM (Figure 1, upper panel). In contrast, in the CLEC-2 cKO BM, megakaryocytes or immature megakaryocytic colonies were rarely detected in the periaarteriolar space (Figure 1, lower panel). These observations suggest that BM FRC-like cells contribute to megakaryopoiesis within the periaarteriolar space. To mimic in vivo conditions where megakaryocyte lineages form expanded colonies at periaarteriolar sites that associate with BM FRC-like cells, we co-cultured megakaryocyte progenitors on a heterogeneous BM stromal cell layer with

BM FRC-like cells. In co-culture of megakaryocytes with BM FRC-like cells, we found that CLEC-2 WT megakaryocyte colonies, but not CLEC-2 cKO megakaryocytes, associated with the BM FRC-like cells (Figure 2A). These results indicated that BM FRC-like cells augmented megakaryocyte expansion in a manner that depended on CLEC-2/PDPN interactions. With regard to megakaryocyte maturation, we also found that a number of CLEC-2 WT megakaryocytes displayed proplatelet-like morphologies, with enlarged cytoplasm and a protrusion of pseudopods in co-cultures with BM FRC-like cells, but not with CLEC-2 cKO megakaryocytes (Figure 2B). The autonomous PPF ratio between CLEC-2 WT and cKO megakaryocytes was not significantly different, and recombinant PDPN stimulation also failed to facilitate PPF in either the CLEC-2 WT or cKO megakaryocytes. We finally found that the binding of megakaryocyte CLEC-2 to PDPN present on BM FRC-like cells results in CCL5 secretion from BM FRC-like cells, which then potentiates PPF in megakaryocytes.





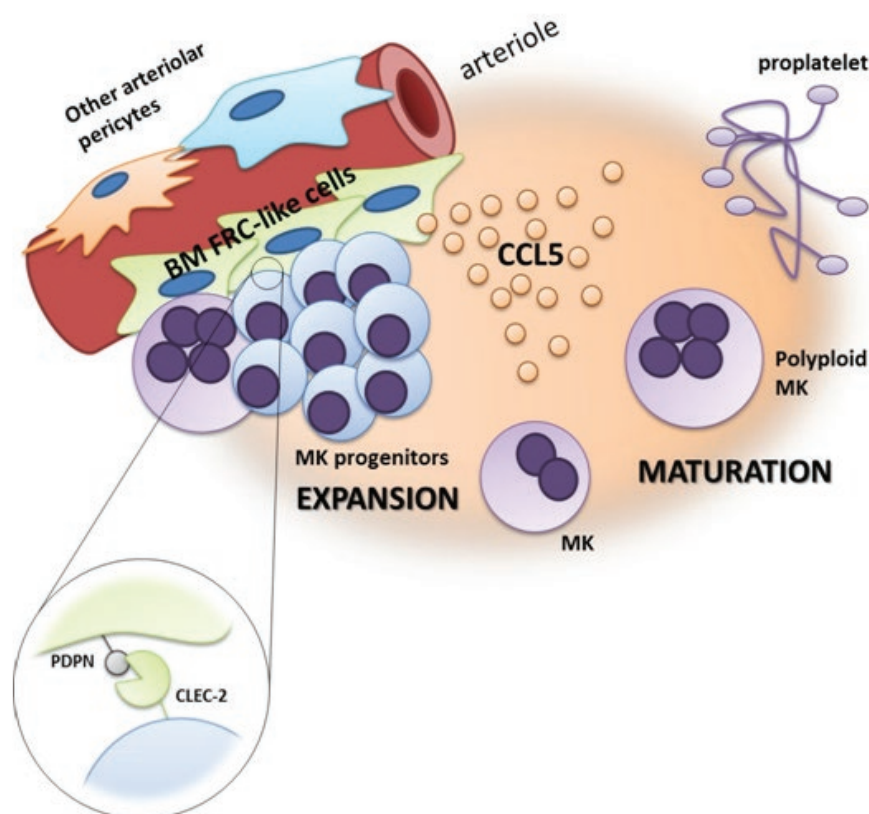


**Figure 2.** BM FRC-like cells positively regulate megakaryocyte expansion and proplatelet formation via the CLEC-2/PDPN interaction. (A) Representative ICC image of co-culture of CLEC-2WT megakaryocytes (top) or cKO megakaryocytes (bottom) with BM stromal cells. BM FRC-like cells were detected as PDPN1 cells (green). Megakaryocyte lineages were detected as CD41+ cells (red). Scale bars indicate 100  $\mu$ m. (B) Representative ICC images of proplatelet-forming megakaryocytes in co-culture with BM FRC-like cells. CLEC-2 WT megakaryocytes (left panel) and CLEC-2 cKO megakaryocytes (right panel) were co-cultured with BM FRC-like cells for 5 days. Megakaryocytes were stained with CD41 (red). Arrowheads indicate the proplatelet-forming megakaryocytes. Scale bars indicate 50  $\mu$ m.

From these observations, we propose a novel BM periarteriolar megakaryocytic niche that provides a proliferative and maturational microenvironment for megakaryocytes. A reciprocal interaction with between CLEC-2 on megakaryocytes and PDPN on BM FRC-like cells accelerates megakaryopoiesis, resulting from the direct promotion of megakaryocytic clonal expansion and indirect facilitation of megakaryocyte PPF (Figure 3). It is well documented and widely accepted that megakaryocyte progenitor expansion mainly occurs in proliferative endosteal niches and maturing megakaryocytes

migrate toward the sinusoidal vascular niches. In addition to this main stream, we consider that BM arteriolar megakaryopoietic microenvironment (arteriolar niche) should work as a side stream of megakaryopoietic pathway in the BM.

This study was picked up in the inside blood commentary (Fu J and Xia L. Blood. 2016. 127(13)1629-1630). Furthermore, the magnified upper panel of Figure 2A was selected as a cover image of the issue.



**Figure 3.** Illustration of the proposed periarteriolar megakaryopoietic micro-environment formed via the reciprocal CLEC-2/PDPN axis. BM FRC-like cells accelerate megakaryocyte progenitor expansion through the CLEC-2/PDPN axis, adjacent to BM arterioles. Moreover, the interaction of CLEC-2 and PDPN induces BM FRC-like cells to secrete CCL5 (RANTES), resulting in the promotion of PPF in matured megakaryocytes.



## Upcoming Meetings:

- 1 **World Federation of Hemophilia (WFH) 2016 World Congress**  
24-28 July 2016 – Orlando, USA  
[www.wfh.org/congress](http://www.wfh.org/congress)
- 2 **ESC Congress 2016**  
27-31 August 2016 – Rome, Italy  
<http://www.escardio.org/ESC2016>
- 3 **EHA Scientific Conference on Bleeding Disorders**  
14-17 September 2016– Barcelona, Spain  
<http://www.ehaweb.org>
- 4 **9<sup>th</sup> Congress of the Asian-Pacific Society on Thrombosis and Hemostasis**  
6-9 October 2016 – Taipei, Taiwan R.O.C  
<http://www.apsth2016.org>
- 5 **23<sup>rd</sup> International Congress on Fibrinolysis & Proteolysis and 26th International Workshop on Molecular and Cellular Biology of Plasminogen Activation**  
17-21 October 2016 – Shizuoka, Japan  
<http://www2.hama-med.ac.jp/w1a/phys2/isfppa-home.html>
- 6 **58<sup>th</sup> ASH Annual Meeting and Exposition**  
3-6 December 2016– San Diego, USA  
[www.hematology.org/Annual-Meeting](http://www.hematology.org/Annual-Meeting)
- 7 **Maastricht Consensus Conference on Thrombosis**  
21-24 February 2017 – Maastricht, Netherlands  
[www.mcct.eu](http://www.mcct.eu)





# The 1<sup>st</sup> Joint Meeting of ISFP and PA Workshop

XXIII<sup>rd</sup> International Congress on Fibrinolysis & Proteolysis  
and  
XVI<sup>th</sup> International Workshop on  
Molecular and Cellular Biology of Plasminogen Activation.

Oct. 17<sup>th</sup>-21<sup>st</sup> 2016



Venue: Nippondaira Hotel, Shizuoka, Japan

## President

Tetsumei Urano (Hamamatsu University School of Medicine)

## Local Organizing Committee

Yuko Suzuki, Takayuki Iwaki, Nobuo Nagai, Satoshi Fujii  
Hidetoshi Sano, Seiji Madolwa, Taiichirou Seki,  
Koji Yamamoto, Shigeru Ueshima, Hideo Wada

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Hamamatsu University  
School of Medicine

# Tentative Program

	Oct. 17th (Mon)	Oct. 18th (Tue)	Oct. 19th (Wed)	Oct. 20th (Thu)	Oct. 21st (Fri)
8:00					
9:00		PA system (Protein Structure & Function)	young investigator's award lecture	LOC-organized symposium (New Therapeutical Strategies)	sponsored lecture (Asahi- Kasei Pharma: Ikuro Maruyama)
10:00			Plenary Lecture 2 (ISFP Prize winner: Robert Medcalf)	coffee break	Infection, SEPSIS, DIC
		coffee break		State of the Art 4 (Scott Diamond)	coffee break
11:00		State of the Art 1 (Dudly Strickland)	coffee break		State of the Art 5 (Satoshi Gando)
12:00	registration	PA system (cell biology)	cell-associated modification of fibrinolysis	Tissue Remodeling 2	Trauma and Bleeding
13:00		lunch	lunch		lunch
14:00		State of the Art 2 (Katherine Hajjar)	State of the Art 3 (Manuel Yepes)	Tour (Including lunch)	State of the Art 6 (Robert Ariens)
15:00		Vascular Biology	PA system and CNS		the cutting edge research
16:00		coffee break	sponsered symposium		thrombolysis
17:00	opening ceremony & Plenary Lecture 1 (Francis J castellino)	Tissue Remodeling 1	poster manning		closing remarks
18:00		poster manning			
19:00		banquet	congress dinner		
20:00					
21:00					





# 2<sup>nd</sup> MCCT

21 - 24 February 2017

Maastricht, The Netherlands

SAVE  
THE  
DATE

## Maastricht Consensus Conference on Thrombosis

Theme: Atherothrombosis and thromboembolism  
(new experimental avenues and clinical challenges)

[www.mcct.eu](http://www.mcct.eu)