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## Message from the Chairman



Dear APSTH members,

This is the time of the year when we reflect on the happenings of the closing year and plan with anticipation the activities for the coming year.

We were well pleased with the success of our 10th Congress of APSTH held at Hokkaido in the month of June, in conjunction with the 40th Congress of the Japanese Society on Thrombosis and Hemostasis. APSTH on her own, received 450 participants from 22 countries. Thanks to Prof. Sathoshi Fuji and his organizing team, participants had enjoyed the meeting with vibrant with lively discussions and abundant learning opportunities. Many will have special memories of the delicious Hokkaido deserts, puddings and cakes that was specially brought in to sweeten the meeting.

In the coming year, we look forward to our country members holding education symposiums with financial assistance from the ISTH "Reach the World" funds. APSTH will support our members in pedagogy, course curriculum and identifying regional speakers and teachers for such education forums.

APSTH has been a great supporter of the World Thrombosis Day (WTD) to increase global awareness and to decrease disease burden of thrombotic diseases. Across the Asia Pacific countries, events such as press releases, public forums and professional education symposiums were held to support this worthy cause.

As we look forward to another good year for APSTH, I take this opportunity to wish all APSTH members a very happy new year filled with joy and good health.

**Lee Lai Heng**  
*Chairman of APSTH*

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## From the Editor



Dear Colleagues and friends

We hope you all to have a great New Year to come. If you have any comments, suggestions and/or any news you would like to disseminate among the Thrombosis and Hemostasis in Asia-Pacific region, please do not hesitate to contact me via email.

In this issue, Dr. Yang Zhang, one of the Travel Grant awardees, described her great experience of an oral presentation in the 10th APSTH meeting in Sapporo. This is followed by a brief article on the ISTH 2019 meeting in Melbourne, Australia. It is our great pleasure to have ISTH meeting in our region this year. The next section is the research news by Dr. Yoshitaka Miyakawa. He is working on a second generation thrombopoietin receptor agonist (TPO-RA) that is not affected by food and ion. Therefore, it would be much more convenient for patients.

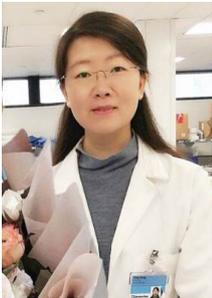
Andrew Masten highlights the world thrombosis day (WTD) activities in Asia-Pacific countries. I also add the WTD activity in Thailand.

Lastly, the upcoming meetings are listed. The notable one is the APSTH/JSTH joint symposium during the annual meeting of the Japanese Society of Thrombosis and Hemostasis (JSTH). The symposium invites 4 to 6 outstanding young scientists from the Asian-Pacific region to give their presentations in the 41st JSTH annual meeting (June 20-22, 2019 in Tsu, Japan). The travelling expense and hotel accommodations are covered and the registration fee is waived. The awardees are also invited to attend the Conference Welcome Party. For more information, please contact Prof. Satoshi Fujii, the chairman of the APSTH/JSTH joint symposium, via Email: sfujii@asahikawa-med.ac.jp

### **Ponlapat Rojnuckarin**

Officer of Public Relations and Communications APSTH

# APSTH Joint Symposium Experience



## Yang Zhang

*Center of Laboratory Medicine,  
National Center for Cardiovascular Diseases & Fuwai  
Hospital, China.*

First of all, I would like to express my gratitude to the organizing committee of the APSTH 2018 Joint Symposium for granting me this travel award to give my first oral presentation at an international congress. I could not forget the delight when I received the email from Prof. Satoshi Fujii informing me that my abstract was selected to be presented at the APSTH 2018 Joint Symposium.

I also want to give my thanks to Professor Fujii for his hospitable invitation to me to attend an unofficial casual party on the evening (around 7pm) of June 27 Wednesday. This is a gathering of travel award winners and the purpose of this party is to promote the exchange of young basic and clinical investigators at early career stage in Asia-Pacific. I have met many outstanding young scientists and learned their achievements and research fields through this party.



My presentation for this symposium was entitled "Monitoring of Anticoagulation for Adults Undergoing Cardiopulmonary Bypass in Cardiac Surgery." The purpose of this study was to investigate the heparin activity and AT activity in adults undergoing CPB.

I had a fruitful discussion and acquired new knowledge after my presentation from Ross Baker and Steven Kitchen.



On the last day, I also participated in the global movement to celebrate the 5th anniversary of the world thrombosis day. The purpose of this campaign is to tell us to stop blood clots and save lives from healthy walking.



It was my great honor to attend the APSTH 2018 Joint Symposium and I really enjoyed the valuable and wonderful experiences in Sapporo. Not only did this conference serve as a platform for me to meet and network with researchers, it also gave me the opportunity to learn about the frontiers study of thrombosis in the Asia Pacific region.

Therefore, I would like to extend a heartfelt “thank you” to the organizing committee for the warm hospitality before and during the symposium. I would also like to extend my gratitude to Prof Satoshi Fujii who made my trip to Japan smooth. This experience will be an unforgettable memory in my life.

# The ISTH Congress Returns to the Asia-Pacific Region in 2019

## Plan to Join the Global Leaders in Melbourne

# REGISTER & RESERVE HOTELS NOW



The International Society on Thrombosis and Haemostasis (ISTH) invites you to join thousands of the world's leading experts in thrombotic and bleeding disorders at the 27th ISTH Congress and 65th Annual Scientific and Standardization Committee (SSC) Meeting in Melbourne, Australia from **July 6-10, 2019**.

## Join us at ISTH 2019!

**[isth2019.org](http://isth2019.org) | [#ISTH2019](https://twitter.com/ISTH2019)**

*Abstracts Submission Period: Dec 3 - Feb 4*

**Curious about travel costs?**

Visit [isth2019.org/affordability](http://isth2019.org/affordability) for a cost analysis.



Registration and abstract submission is now open for the ISTH 2019 Congress, the XXVII Congress of the International Society on Thrombosis and Haemostasis (ISTH), scheduled for July 6-10 in Melbourne, Australia. This will be the first time the ISTH Congress will be located in the Asia-Pacific region since Kyoto, Japan, hosted the event in 2011.

Don't miss this opportunity to participate in the ISTH Congress in the Asia-Pacific region as this premier global event is the most impactful meeting in the field of thrombosis and hemostasis, featuring an international exchange of the most recent and important scientific advances.

View the program at [www.isth2019.org](http://www.isth2019.org) to see the latest science to be presented. Then, book your hotel and register. Don't wait to book your hotel as most preferred locations will fill up fast. To secure the discounted early registration rate, be sure to register for the meeting before April 17.

Researchers should also consider submitting your abstracts for global recognition at ISTH 2019. Thousands of experts will share their data at the event and present the newest findings. Abstract submission closes on February 4, 2019.

ISTH 2019 will bring together thousands of the world's leading experts in thrombosis, hemostasis and vascular biology to present the most recent advances, exchange the latest *science and discuss the newest clinical applications designed to improve patient care*.

For additional information about this meeting, please visit [www.isth2019.org](http://www.isth2019.org). If you have questions or comments, please email [meetings@isth.org](mailto:meetings@isth.org).

## Research News

### From Asian Bench to FDA Approval of the Second Generation TPO Receptor Agonist

**Yoshitaka Miyakawa, MD.**

Professor, Division of Hematology, Department of General Internal Medicine. Head, Thrombosis and Hemostasis Center, Saitama Medical University Hospital, Saitama, JAPAN

On July 2018, the Food and Drug Administration (FDA) approved lustrombopag (Mulpleta™, Shionogi Inc., Japan) for treatment of thrombocytopenia in adults with chronic liver disease, who are scheduled to undergo a medical or dental procedure (1). Lustrombopag is the 2nd generation of a small molecule thrombopoietin receptor agonist (TPO-RA). Its approval was based on two randomized, double blind, placebo-controlled trials (L-PLUS 1 and L-PLUS 2) involving 312 patients with chronic liver disorders and whose platelet counts were under  $50 \times 10^9/L$ . Patients were randomized 1:1 to orally intake 3 mg lustrombopag or placebo once a day for 7 days (1). In both studies, lustrombopag successfully reduced the need for platelet transfusion before invasive procedures compared with the placebo (1-3).

#### L-PLUS 1 trial: Proportion of patients not requiring platelet transfusion prior to invasive procedure and proportion of responders

Endpoint	Proportion (n/N) Exact 95% confidence interval		Treatment difference (95% confidence interval), p value
	Mulpleta (N=49)	Placebo (N=48)	
Not requiring platelet transfusion prior to invasive procedure	78% (38/49) (63, 88)	13% (6/48) (4.7, 25)	64 (49, 79) <0.0001
Responder during study*	76% (37/49) (61, 87)	6% (3/48) (1.3, 17)	68 (54, 82) <0.0001

\*Platelet count reached at least  $50 \times 10^9/L$  and increased at  $20 \times 10^9/L$  from baseline.

#### L-PLUS 2 trial: Proportion of patients not requiring platelet transfusion prior to invasive procedure or rescue therapy for bleeding through 7 days after invasive procedure and proportion of responders

Endpoint	Proportion (n/N) Exact 95% confidence interval		Treatment difference (95% confidence interval), p value
	Mulpleta (N=49)	Placebo (N=48)	
Not requiring platelet transfusion prior to invasive procedure	78% (38/49) (63, 88)	13% (6/48) (4.7, 25)	64 (49, 79) <0.0001
Responder during study*	76% (37/49) (61, 87)	6% (3/48) (1.3, 17)	68 (54, 82) <0.0001

\*Platelet count reached at least  $50 \times 10^9/L$  and increased at  $20 \times 10^9/L$  from baseline.

In Japan, lustrombopag was approved for the same indication in 2015 (4). In contrast to eltrombopag, the absorption of lustrombopag is unaffected by food and bivalent cations such as Ca, Mg, and Fe (1,4). Therefore, patients can take lustrombopag at any time, which improves QOL and the platelet response.

Similar to other small molecule TPO-RAs such as eltrombopag, avatrombopag, and NIP-004, lustrombopag is effective only in humans and chimpanzees (1). Because chimpanzees are highly restricted for preclinical drug development, we established a humanized mouse model that produces human platelets in vivo. The Central Institute for Experimental Animals (CIEA), Shionogi, Nissan Chemical Corporation, and Keio University in Japan formed a collaborative team. Because human megakaryocytes and platelets cannot be produced in nude and NOD/SCID mice, we chose NOG mice bred by crossing NOD/SCID and IL-2R knockout mice by the brilliant veterinarian Dr. Ito at CIEA. Drs. Nakahata and Ito originally discovered a small amount of circulating platelets in NOG mice after transplantation of human hematopoietic progenitor cells.

After we optimized the irradiation dose and donor source of human CD34-positive cells for xenotransplantation, we finally found that half of megakaryocytes in murine bone marrow are replaced by human blood cells (5). This model mouse consistently produces human platelets in peripheral circulation (5).

Originally, Dr. Takemoto and his colleagues at Shionogi Inc. screened 53,000 chemical compounds to find compounds that stimulate proliferation of the Ba/F3-human Mpl cell line dependent on human TPO. Using a combinatorial chemistry technique to improve biological activity and bioavailability, they developed butyzamide as the lead compound.

We analyzed the pharmacokinetics and pharmacodynamics of butyzamide using our newly established humanized NOG mice. We found that oral intake of butyzamide at doses of 10 and 50 mg/kg for 20 days increased human platelet counts by 6.2- and 22.9-fold, respectively (5). In vitro, similar to TPO, we confirmed that butyzamide activates JAK-Stat and MAPK pathways in human platelets and cell lines. Interestingly, butyzamide did not accelerate ADP- and collagen-induced platelet aggregation in vitro (5).

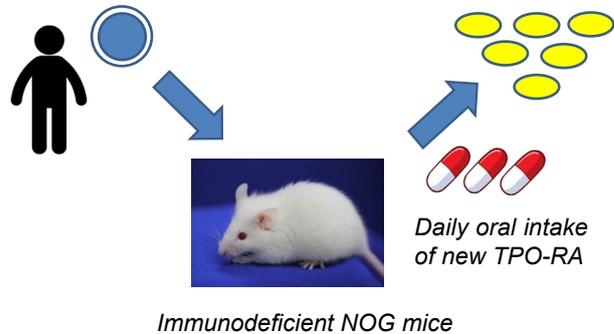
In conclusion, we are pleased to announce that our preclinical study contributed to launching the 2nd generation TPO-RA lustrombopag from the Asian bench to FDA approval. We expect that the EMA will approve lustrombopag for the same indication in 2019. We also speculate that lustrombopag has some potential for clinical application to ITP, aplastic anemia, MDS, and chemotherapy-induced thrombocytopenia.

## References

1. Package insert for Mulpleta (lustrombopag tablets) in US.
2. Afdhal N, et al. Platelet response to lustrombopag, a thrombopoietin receptor agonist, in patients with chronic liver disease and thrombocytopenia undergoing non-emergency invasive procedures: results from a phase 3 randomized, double-blind, placebo-controlled study. Annual Meeting of American Society of Hematology 2017, Blood 130 supplement, 291, 2017 abstract
3. Hidaka H, et al. Lustrombopag reduces need for platelet transfusion in patients with thrombocytopenia undergoing invasive procedures. Clin Gastroenterol Hepatol. S1542, 31324-31327, 2018 (Epub ahead of print)
4. Kim ES. Lustrombopag: First global approval. Drugs 76, 155-158, 2016
5. Nogami W, et al. The effect of a novel, small non-peptidyl molecule butyzamide on human thrombopoietin receptor and megakaryopoiesis. Haematologica 93, 1495-1502, 2018

## Development of new TPO receptor agonists using humanized NOG mice producing human platelets

Human CD34-positive cells      Increase of human platelets



Rights for original picture of NOG mice belongs to CIEA (Japan).

# World Thrombosis Day 2018 Has Influential Impact Across Asia-Pacific for Campaign's Fifth Anniversary

## **Andrew Masten**

International Society on Thrombosis and Haemostasis (ISTH)

World Thrombosis Day (WTD) 2018 was a landmark year for the campaign as it celebrated its fifth anniversary and experienced powerful influence and impact across the globe. In just five years, WTD has become the leading global awareness campaign on blood clotting disorders.

Together with more than 1,500 partners from 100+ countries, WTD 2018 included more than 10,000 activities and reached more than 3 billion impressions worldwide—an 11 percent increase from 2017. Learn more about the 2018 campaign by downloading the official WTD 2018 Impact Report.

In the Asia-Pacific region, WTD reached a record number of people furthering its mission to spread awareness about deadly blood clots. Nearly 250 partners across the Asia-Pacific region, as well as the leadership from three regional WTD steering committee members, worked tirelessly to organize events and activities that educated and inspired communities, media and healthcare professionals.

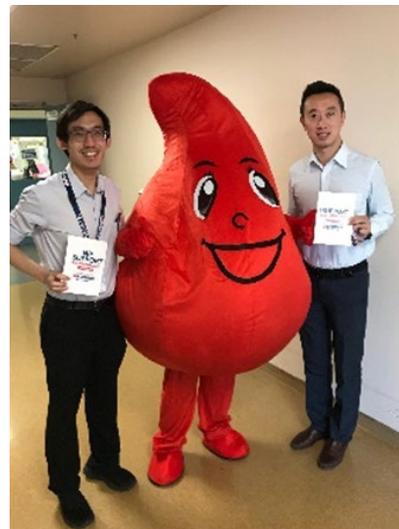
This year the campaign focused on expanding global media coverage about thrombosis and launched media market offices across Asia-Pacific, including in India (NEW!), Singapore, Thailand, and Australia. Another key focus area was to increase educational opportunities for healthcare professionals. As such, the WTD campaign developed two e-education modules on hospital associated venous thromboembolism (VTE) in partnership with Medscape Education.

The campaign also proudly launched a new award, the WTD 2018 Thrombosis Ambassador of the Year, which was awarded to Christine Ashimwe from Rwanda. This prestigious recognition highlights Ashimwe's drive to achieve the mission of the WTD campaign and motivate others within thrombosis advocacy programs in Rwanda and around the world by exhibiting innovative approaches to raise awareness and accomplish advocacy goals.

To learn more about activities and outreach throughout the Asia-Pacific region, please see WTD 2018 highlights below listed in alphabetical order by country.

## **Australia**

Sydney, Australia, was designated as a key media market by WTD campaign headquarters, which provided significant media exposure.



The Sydney Morning Herald ran an article titled "Cool Runnings: The Life-Saving Surgery to Remove Blood Clots." The online publication Starts at 60 also published an article on, "The Signs, Symptoms, and Treatments of Thrombosis."

The John Curtin School of Medical Research at the Australian National University held a lunchtime event. The NSW Health Pathology team in Sydney celebrated WTD and the Northern Sydney Local Health District promoted WTD to its staff through posters and emails



### Bangladesh



Ibrahim Cardiac Hospital and Research Institute presented banners and held a seminar with scientific sessions focusing on the fatal effects and management of thrombosis. The event was broadcast through local media and via a Facebook LIVE video.

Partners in Bangladesh also created several informative videos for WTD 2018, including an in-terview with a patient and an interview with a physician.

### China

For WTD 2018, the China-Japan Friendship Hospital in Beijing focused on the prevention of hospital-associated VTE. It organized consultations for DVT/PE patients and shared social media posts to increase awareness.

### Georgia

The Georgian Society of Hypertension held meetings to help improve the management of the PE across the country.

### India

WTD launched a new media market office in India, which led to increased media coverage, including the inauguration of the Hemophilia and Thrombosis Centre at Sir JJ Hospital in Mumbai.



The Tribune in India published an article titled, "Blood Clots Create Potential Health Risks, Ex-perts Say" and Kalinga TV published an online article titled, "Frequent Traveling May Cause Blood Clot, Says Study. In addition, The Premier Hospital in India shared a blog post about WTD 2018.

There were many awareness activities across India. r<sup>2</sup> Diagnostics held a 5K run, shared informational brochures, and celebrated WTD through 50 different set-ups and activities across India in the Pathology Lab Chain Oncquest Laboratories.

Sanofi India held events spanning over 15 days in October, including an online pledge people for people to show their support of WTD. It also hosted two webinars featuring expert insights from doctors and educational graphics for nursing staff.

### Iran

The Iranian Hemophilia and Thrombophilia Association, MAHTA, along with the city of Tehran, set up billboards along highways and main streets in 14 different locations to raise awareness for WTD.



MAHTA also worked with the Abassabad District to light the Tabiat Bridge, the largest pedestrian bridge in Tehran red and blue in support of WTD.

Click [here](#) to watch a video of the bridge lighting in Iran. MAHTA also set up an educational booth at the entrance to Milad Tower, one of the tallest structures in the world, to help spread awareness for the dangers of thrombosis.

## Japan



The Japanese Thrombosis Society held a public lecture in Tokyo to help raise awareness, and a video of the lecture was later posted online.

The Asian-Pacific Society on Thrombosis and Hemostasis (APSTH) held a walk in Odori Park in Hokkaido, Japan during the APSTH 2018 Congress, which provided a fun and engaging opportunity to keep life flowing. There was also a WTD informational booth at the APSTH Congress.

The Japanese Society of Thrombosis and Haemostasis held two educational seminars, one on raising awareness and preventative measures, and another on the cancer-related risks of thrombosis.

## New Zealand

In honor of WTD 2018, OBEX offered free shipping on compression socks. There was also excellent media coverage in New Zealand, including a radio interview with expert Dr. Eileen Merriman, which can be listened to here.

## Philippines



In the Philippines, Asian Hospital and Medical Center held a forum discussing thrombosis, including a free consultation with vascular consultants.

Several regional experts and a thrombosis patient joined local TV Station Alagang Kapatid to talk about thrombosis and raise awareness about the campaign.

## Pakistan

Dr. Ziauddin Hospital held a panel to discuss the severity and importance of awareness for thrombosis. Topics included prophylaxis of VTE in surgical cases, VTE management, and the radiological aspect of VTE.



The Aga Khan University Hospital created special graphics for WTD 2018 to share on social media. Providing translated graphics is an excellent way to share resources across global regions.



## Russia

The Northern State Medical University Department of Clinical Pharmacology and Pharmacotherapy held a conference for doctors on the safety and efficacy of antithrombotic therapy. It also held a flash mob in the pool, emphasizing the importance of movement and active lifestyles to fight against thrombosis. The flash mob was attended by students, teachers, patients, and local media.



Partners in Russia created several awareness videos, including a video recap and media interview of local WTD activities and an expert interview.

### **Saudi Arabia**

Prince Nourah Bint Abdulrahman University, College of Medicine held a program titled, "Advance VTE Awareness, Prevention and Treatment for Healthcare Providers" aimed at addressing the prevention and management of thrombosis.

The Ministry of Health in Saudi Arabia created posters with guidelines and statistics about VTE to be posted in hospitals. The Saudi Gazette published an article titled, "The Trouble With Long Flights."

### **Singapore**

Singapore General Hospital hosted an educational forum on the management of cancer-associated thrombosis (CAT) and DVT. Additionally, in Singapore, stories were published in The New Paper and Channel News Asia Online written by Prof. Ng on a patient case looking at the effects of video games and binge watching television on cases of thrombosis.

### **Turkey**



The Turkish National Society of Vascular and Endovascular Surgery held a parade and field day with games, snacks and obstacle courses.

CardioOncology Division of Trakya University hosted a conference on "Cancer and its Treatment Related Thrombosis."

### **United Arab Emirates**



During Dubai Thrombosis 2018, WTD banners were placed by partners throughout the convention to share information about information about the campaign and its Know Thrombosis campaign.

For more information about the WTD campaign, visit [www.worldthrombosisday.org](http://www.worldthrombosisday.org). Join the conversation on social media by following the WTD campaign on your favorite social media channels.

# World Thrombosis Day 2018 Activity in Thailand

## Ponlapat Rojnuckarin, MD, PhD

The Thai Society of Hematology and The National Blood Centre (Thai Red Cross Society) organized the WTD event on 6 October 2018 at King Chulalongkorn Memorial Hospital.

The event includes the talks and discussions on the clinical significance, diagnosis, treatment and the modes of prevention of venous thromboembolism by doctors for general public. One of the patients with recurrent thrombosis volunteered to describe her catastrophic events to demonstrate the symptoms of venous thromboembolism. There were also information posters, personal health consultations and opportunities for questions from audiences. There were 190 participants who asking a lot of questions on thrombosis. The event was covered by Thairath, the most popular newspaper in Thailand.

### Participants are deeply interested in the info-graphics on thrombosis



### Doctors are consulted by patients



### (From left) Dr. Chatphatai Moonla, Dr. Theera Ruchutrakul and Dr. Bundarika Suwannawiboon are answering questions from audiences



### The column in a newspaper reporting on WTD 2018 in Bangkok: (From left) Dr. Chatphatai Moonla, Dr. Pitiphong Kijrattanakul, Dr. Noppacharn Uaprasert, Dr. Ponlapat Rojnuckarin, Dr. Darintr Sosothikul, Dr. Theera Ruchutrakul and Dr. Piti Techavichit



**Upcoming Meetings:**

- 1** **Highlights of ASH in Asia-Pacific**  
23-24 February 2019 – Bangkok, Thailand  
<http://www.hematology.org/Highlights/Asia.aspx>
  
- 2** **APSTH/JSTH joint symposium in 41st Japanese Society of Thrombosis and Hemostasis (JSTH) Annual Meeting**  
20-22 June 2019 - Tsu, Japan  
<http://www.c-linkage.co.jp/jsth2019/>
  
- 3** **International Society of Thrombosis and Haemostasis (ISTH) meeting**  
6-10 July 2019 – Melbourne, Australia  
<https://www.isth2019.org/>
  
- 4** **The 11th Congress of the Asian-Pacific Society on Thrombosis and Hemostasis (APSTH)**  
3-5 September 2020 – Gwangju, Korea