



# APSTH

Asian - Pacific Society on Thrombosis and Hemostasis

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

July 2019 Volume 9 No.1

## Inside

Message from the Chairman	1
From the Editor	2
WFH 2020 World Congress coming to Kuala Lumpur	3
Report from Highlights of ASH (HOA) in Asia-Pacific 2019	4
Research News	5
World Thrombosis Day 2019 Campaign	8
Upcoming Meetings	12

## APSTH Officers

### Honorary Chairmen

*Akikazu Takada  
Yasuo Ikeda  
Hatem Salem*

### Chairman

*Lai Heng Lee*

### Secretary General

*Satoshi Fujii*

### Public Relations and Communications

*Ponlapat Rojnuckarin*

### Treasurer

*Yukio Ozaki*

## Contact Us

### Secretary General Office

**Satoshi Fujii**

*Department of Laboratory Medicine  
Asahikawa Medical University  
Midorigaoka-higashi 2-1-1-1  
Asahikawa, Japan 078-8510  
Email: [sfujii@asahikawa-med.ac.jp](mailto:sfujii@asahikawa-med.ac.jp)  
Tel: 0166-65-2111  
Fax: 0166-65-2744*

### Editor Office

*Ponlapat Rojnuckarin  
Division of Hematology  
Department of Medicine  
Faculty of Medicine  
Chulalongkorn University  
Bangkok 10330, Thailand  
E-mail: [Ponlapat.R@Chula.ac.th](mailto:Ponlapat.R@Chula.ac.th)  
[rojnuckarinp@gmail.com](mailto:rojnuckarinp@gmail.com)  
Tel: 662-256-4000 EXT 80252  
Fax: 662-256-4564*

## Message from the Chairman



Dear APSTH members,

Mid-year greetings and well wishes to all my friends and colleagues.

**Lee Lai Heng**

We look forward to meeting each other again at ISTH Melbourne very soon in July. Riding on this opportunity where many APSTH members will be present, we have planned our APSTH annual council meeting during this conference. We are looking forward to exciting updates on our future APSTH congresses in South Korea (2020) and China (2022).

In the latter part of this year, on 20th Sept 2019, the Myanmar Society of Hematology with members from APSTH had organised an educational workshop on Thrombosis and Hemostasis supported by an education grant from International Society on Thrombosis and Haemostasis (ISTH) on in Yangon. We are grateful to ISTH for providing the education grant and happy that APSTH's support towards the teaching faculty and program organization. I am sure this symposium will benefit many of our members and I urge you to support this effort.

Further down the calendar comes World Thrombosis Day which falls on 13th October. APSTH has been an ardent supporter of the World Thrombosis Day (WTD) to increase global awareness and to decrease disease burden of thrombotic diseases. We look forward to many activities by APSTH member countries across the Asia Pacific to support this worthy cause.

Best Wishes,  
Lee Lai Heng

## Members of APSTH Council

### Australia

Ross Baker  
Beng Chong  
Chris Ward

### Cambodia

Robyn Devenish  
Chean Sopha

### China

Ming Hou  
Changgeng Ruan  
Yongqiang Zhao

### Hong Kong (China)

Raymond Wong

### India

Alok Srivastava

### Indonesia

Djumhana Atmakusuma  
Aru Wisaksono Sudoyo  
Lugyanti Sukrisman  
Karmel Tambunan

### Japan

Satoshi Fujii  
Yukio Ozaki  
Koji Suzuki  
Tetsumei Urano

### Korea

Soo-Mee Bang  
Kwang-Hoe Chung  
Doyeun Oh  
Seonyang Park

### Malaysia

Faraizah Abdul Karim  
Jameela Sathar

### Mongolia

Otgonbat Altangerel  
Nergui Dagvadorj

### New Zealand

Claire McLintock  
Mark Smith

### Philippines

Maria Teresa B. Abola

### Singapore

Manjunatha Kini  
Lai Heng Lee  
Sim Leng Tien

### Sri Lanka

H.M. Sduharma Vidyatilake

### Taiwan

Hui-Chi Hsu  
Ching-Tien Peng  
Ming-Ching Shen

### Thailand

Pantep Angchaisuksiri  
Yingyong Chinthammitr  
Wichai Prayoonwiwat  
Ponlapat Rojnuckarin

### Vietnam

Bach Quoc Khanh  
Nguyen Anh Tri

## From the Editor



Dear Colleagues and friends

In this issue, Dr. Jameela Sathar kindly sent me the great news of World federation of Hemophilia (WFH) Congress 2020 that will be held in Malaysia next year. Hopefully, we will meet again in Kuala Lumpur in this largest meeting on hereditary bleeding disorders. Then, I reported the Highlights of ASH (HOA) in Asia-Pacific Meeting which took place in Bangkok during 23- 24 February 2019. Several up-to-date data on thrombosis and hemostasis were presented and discussed in this excellent educational event.

In the Research News section, Dr. Nagaharu Tsukiji described the fascinating work on the discovery of a novel platelet function on pulmonary development in mouse fetuses. The research project was published in Blood 2018; 132, 1167-1179.

The ISTH, again, presented the promotional World Thrombosis Day (WTD) campaign for this 13 October 2019. I would like to implore all of you to organize the activities for WTD in order to promote the public awareness that will lead to effective prevention of this deadly disease. For the last, but not least, section, the upcoming meetings are listed. You can see that a number of interesting conferences on Thrombosis and Hemostasis are coming to our region in 2020. Please mark your calendar and plan your trips for these forums.

If you have any comments and/or suggestions on this bulletin, as well as any news or information you would like to spread among the Asia-Pacific Thrombosis and Hemostasis community, please do not hesitate to contact me via email.

Ponlapat Rojnuckarin, Editor

Officer of Public Relations and Communications APSTH

## WFH 2020 World Congress coming to Kuala Lumpur

The World Federation of Hemophilia (WFH) 2020 World Congress will take place at the Kuala Lumpur Convention Centre (KLCC), in Kuala Lumpur from June 14 to 17, 2020.

The WFH World Congress is a unique event in the bleeding disorders community because it is multidisciplinary, and focuses on how extended teams care for patients.

As a vibrant metropolis well-located in Asia, Kuala Lumpur is a superb host city for a WFH World Congress. The city has an excellent infrastructure and a wide range of cultural experiences ready and waiting for visitors. The Malaysian bleeding disorders community has shown great enthusiasm for the WFH 2020 World Congress—enthusiasm which will surely help make the event a successful and impactful one.

- Gene therapy and hemophilia (including new country initiatives)
- Acquired bleeding disorders
- The critical need for harmonized post marketing surveillance in gene therapy
- Invasive procedures
- Thinking differently about inhibitors
- Management of comorbidities in bleeding disorders
- Substitution therapy
- Women with hemophilia
- von Willebrand disease (VWD)
- Rare bleeding disorders and platelet disorders
- Redefining prophylaxis in the modern era

To find out more about the WFH 2020 World Congress, visit [www.wfh.org/congress](http://www.wfh.org/congress).





## Report from Highlights of ASH (HOA) in Asia-Pacific 2019

It is the great honor of Thai Society of Hematology (TSH) to be a co-host with American Society of Hematology (ASH) to organize the 2019 Highlights of ASH in Asia-Pacific. This fascinating event took place at Bangkok Convention Center, Thailand, during February 22-24, 2019. This was the second HOA in Bangkok as TSH and ASH used to collaborate for HOA in 2015.

The scientific program was arranged by the Scientific Co-chairs who were representatives from both ASH (Dr. Mark Crowther and Dr. Marc J. Kahn) and TSH (Dr. Suradej Hongeng and Dr. Ponlapat Rojnuckarin) with the purpose of conveying the most ground-breaking scientific and clinical advances from the ASH annual meeting in December 2018 to the Asia-Pacific region.

More than 800 delegates from 26 countries attended this meeting. This is a great opportunity to communicate, collaborate and build network among multinational hematologists. Additionally, the presidents of hematological societies from various countries were invited for the meeting with ASH representatives discussing for the future partner activities.

The next HOA in Asia-Pacific will be in Hanoi, Vietnam during March 13-14, 2020. Hopefully, we will meet you there for this remarkable forum.

Ponlapat Rojnuckarin  
Scientific Co-chair HOA 2019



Dr. Wichai Prayoonwiwat, the president of Thai Society of Hematology and a council member of APSTH, is giving a welcome speech to the delegates of 2019 Highlights of ASH

The format was designed for the most interactions between delegates and the speakers.

There were options to ask questions online, attend the Lunches with Experts and present Challenging cases in Hematology. There were a lot of exciting data on thrombosis and hemostasis including the roles of direct oral anticoagulants (DOACs) in cancer-associated thrombosis, perioperative management of anticoagulants, a novel long-acting factor VIII product and more information on Emicizumab in hemophilia without inhibitor and Caplacizumab in thrombotic microangiopathy among others. Furthermore, hematology trainees from Asian countries were supported by ASH, as well as by their country societies, to come for a research workshop in order to promote hematological researches in this area.

## Research News

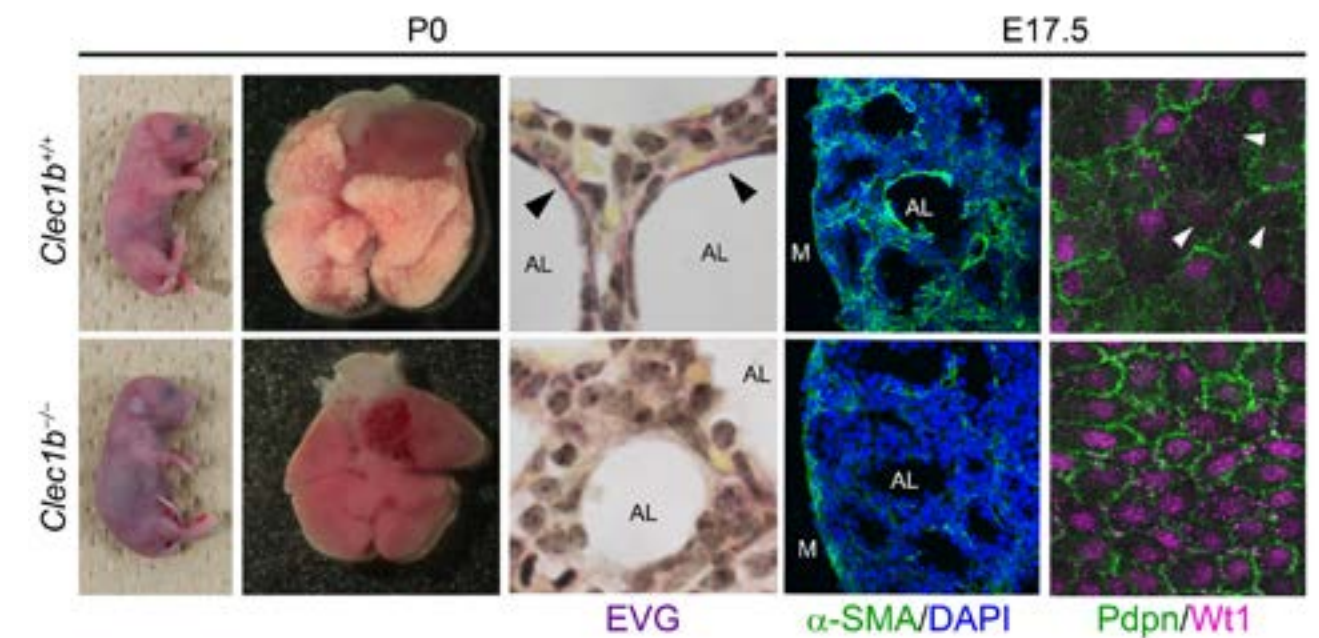
**Platelet function beyond thrombosis and hemostasis:** fetal lung development by platelet activation receptor CLEC-2 and its ligand podoplanin

Nagaharu Tsukiji, Ph. D.

Research associate, Department of Clinical and Laboratory Medicine, Faculty of Medicine, University of Yamanashi, JAPAN

There is increasing evidence that platelets participate in a variety of pathophysiological situations other than thrombosis and hemostasis such as inflammation (sterile and unsterile), immunity, cancer metastasis and blood vessel integrity. C-type lectin-like receptor-2 (CLEC-2) is a platelet activation receptor that has been recently identified as a receptor for the snake venom, rhodocytin. According to a number of recent reports, interaction of CLEC-2 and its endogenous ligand podoplanin (PDPN) is considered to be an important molecular basis for the platelet function beyond thrombosis and hemostasis (1). CLEC-2-deficient (*Clec1b*<sup>-/-</sup>) mice have been known to show neonatal lethality without apparent bleeding (2), which is a unique phenotype that has not been reported in other platelet activation receptor-deficient mice. Since CLEC-2 is predominantly expressed in platelets and megakaryocytes, we hypothesized that loss of platelet CLEC-2 is associated with neonatal lethality (3).

Our phenotypic analysis showed lung developmental abnormalities in *Clec1b*<sup>-/-</sup> fetuses and neonates: lack of alveolar elastic fibers and alveolar duct myofibroblasts (adMYFs), and abnormal differentiation of lung mesothelial cells (luMCs), which is a major origin of adMYFs



**Figure 1. Respiratory failure and lung developmental abnormalities in *Clec1b*<sup>-/-</sup> mice.**

Representative images of body, lung, alveolar elastic fibers, adMYFs and luMCs of *Clec1b*<sup>+/+</sup> (wild type) and *Clec1b*<sup>-/-</sup> neonates at postnatal day 0 (P0) and embryonic day 17.5 (E17.5). Black arrow heads indicate alveolar elastic fibers stained dark purple. Regarding luMC differentiation, there are wilms' tumor 1 (*Wt1*, a mesothelial cell-specific transcription factor)-negative luMCs (white arrow heads) in wild type fetuses but not in *Clec1b*<sup>-/-</sup> fetuses. AL, alveolar space. M, lung mesothelium. EVG, elastica van gieson staining.  $\alpha$ -SMA,  $\alpha$ -smooth muscle actin (adMYF marker).

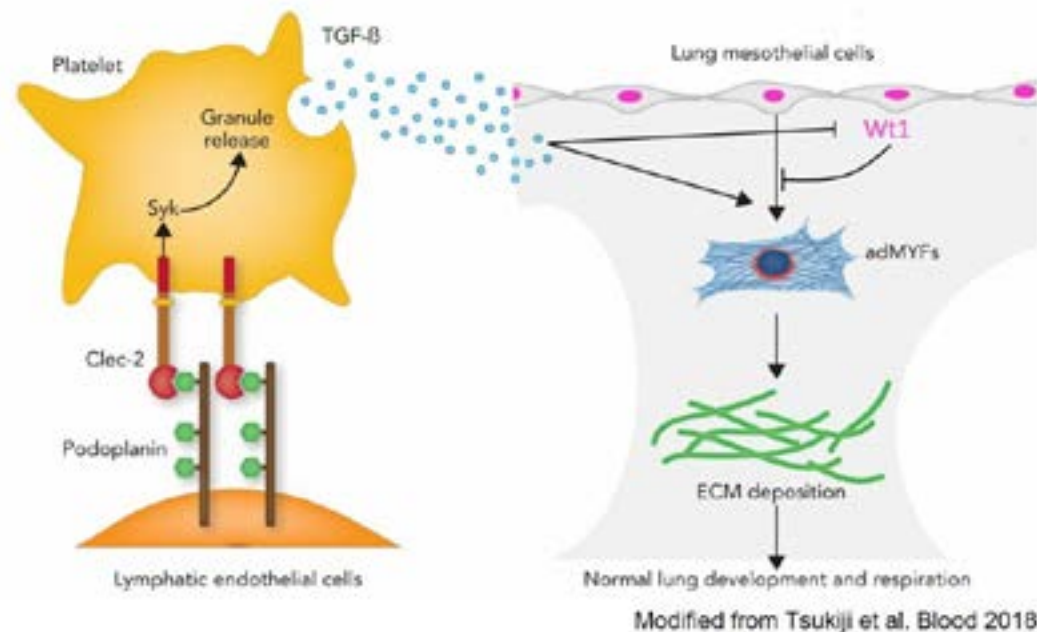
Previous reports suggested that platelet CLEC-2 was not involved in lung development and neonatal survival because platelet-specific CLEC-2-deficient mice (Pf4-Cre, Clec1b<sup>fl/fl</sup>, referred to as Clec1b<sup>ΔPLT</sup>) grew normally to adulthood (4).

However, CLEC-2 is exclusively expressed in platelets in the developing lung, and our detailed phenotypic analyses revealed that 23.1% of Clec1b<sup>ΔPLT</sup> neonates died on the day of birth and Clec1b<sup>ΔPLT</sup> fetuses showed a mild Clec1b<sup>-/-</sup>-like lung developmental abnormalities by insufficient Cre-mediated CLEC-2 deletion in platelets. Based on these findings, we next induced complete platelet CLEC-2 deletion (5) or thrombocytopenia in Clec1b<sup>ΔPLT</sup> fetuses by anti-Clec2 or anti-GPIb antibody treatment, which resulted in severe lung developmental abnormalities comparable with Clec1b<sup>-/-</sup> fetuses.

In addition, we newly found that one of the releasates from activated platelets, especially TGF-β<sub>1</sub>, mediated platelet CLEC-2-dependent lung development.

PDPN, a CLEC-2 ligand, is expressed in type I alveolar epithelial cells, luMCs and lymphatic endothelial cells of the developing lung. Systemic deletion of PDPN in mice (Pdpn<sup>-/-</sup>) has been known to lead to neonatal lethality by respiratory failure (6). We found that Pdpn<sup>-/-</sup> lung showed quite similar phenotypes to Clec1b<sup>-/-</sup> lung such as I of adMYFs and abnormal luMC differentiation. Furthermore, we utilized several tissue-specific PDPN-deleted mice and revealed that PDPN in lymphatic endothelial cells (LECs) is essential for PDPN-dependent lung development.

In conclusion, our study strongly suggests the novel mechanism of lung development; interaction between platelet CLEC-2 and LEC PDPN activates platelets and granule contents including TGF-β are released from activated platelets. TGF-β induced adMYF differentiation of luMCs and adMYFs secretes extracellular matrices (ECMs) in alveolar interstitium, which results in normal alveogenesis and neonatal respiration.



**Figure 2. Platelet CLEC-2/LEC PDPN-dependent lung development.**

Interaction of platelet CLEC-2 and LEC PDPN activates platelets, which results in the release of granule contents including TGF-β. TGF-β promotes adMYF differentiation of luMCs through the appropriate regulation of Wt1. Subsequently, sufficient deposition of ECMs (e.g. elastic fibers) from adMYFs contributes to normal alveogenesis and neonatal respiration.

In the platelet function beyond thrombosis and hemostasis, platelets are recently considered as a cargo of various bioactive substances, such as growth factors, small molecules, and lipid mediators. In this context, CLEC-2/PDPN signaling has a different characteristic from other signaling pathways of platelet activation, such as P2Y/ADP, PAR/thrombin and GPVI/collagen; PDPN is a membrane protein and is expressed in specific cell types in normal and pathological tissues, and direct contact between platelets (CLEC-2) and PDPN-expressing cells activate platelets and induce granule release from platelets. Therefore, CLEC-2/PDPN signaling induces the platelet granule release at different sites from that by soluble agonists or ECMs including collagen. Platelet activation at different sites due to the diverse pathways may underlie a multifaceted platelet function.

## References

1. Suzuki-Inoue K et al. Platelet CLEC-2: Roles Beyond Hemostasis. *Semin Thromb Hemost* 44 126-134, 2018.
2. Suzuki-Inoue K, et al. Essential in vivo roles of the C-type lectin receptor CLEC-2: embryonic/neonatal lethality of CLEC-2-deficient mice by blood/lymphatic misconnections and impaired thrombus formation of CLEC-2-deficient platelets. *J Biol Chem*. 285, 24494-24507, 2010.
3. Tsukiji N et al. Platelets play an essential role in murine lung development through CLEC-2/podoplanin interaction. *Blood* 132, 1167-1179, 2018.
4. Finney BA et al. CLEC-2 and Syk in the megakaryocytic/platelet lineage are essential for development. *Blood* 119, 1747-1756, 2012.
5. Shirai T et al. C-type lectin-like receptor 2 promotes hematogenous tumor metastasis and prothrombotic state in tumor-bearing mice. *J Thromb Haemost* 15, 513-525, 2017.
6. Ramirez MI et al. T1alpha, a lung type I cell differentiation gene, is required for normal lung cell proliferation and alveolus formation at birth. *Dev Biol* 256, 61-72, 2003.



## World Thrombosis Day 2019 Campaign Launches New Programs to Engage Healthcare Professionals and Highlight Patient Voices

*By the International Society on Thrombosis and Haemostasis (ISTH)*

The [World Thrombosis Day](#) (WTD) campaign is proud to recognize its sixth year of elevating awareness and education about the often overlooked condition of thrombosis. In 2019, the WTD campaign places a renewed emphasis on hospital-associated venous thromboembolism (VTE) awareness, as well as an additional focus on cancer-associated thrombosis and gender-specific thrombosis – both across the Asia-Pacific region and worldwide.

A campaign of the [International Society on Thrombosis and Haemostasis](#) (ISTH), led by a [global steering committee](#) of scientific experts, WTD mobilizes a global community of more than 1,600 partners across 100+ countries. Just last year, WTD partners organized more than 10,000 activities and secured 2.6 billion impressions in global media outlets.

The Asia-Pacific regional has been a prominent and longstanding supporter of WTD. Since the campaign's inception, the Asia-Pacific region has hosted thousands of awareness activities, media events, and educational conferences to provide education and awareness about VTE.

From Australia and New Zealand, to Thailand and Japan, explore a variety of exciting opportunities to participate in and support WTD 2019. The following is a list of five ways to get involved in WTD 2019:



### 1. Submit an Educational Flyer to the WTD Early Career Flyer Competition

Participate in the WTD campaign's inaugural flyer competition! Open to all early career professionals working in the area of thrombosis and/or hemostasis, participants are invited to create a one-page flyer to educate patients on the causes, risk factors and prevention of hospital-associated VTE.

The winner will receive a \$250 USD Visa gift card and his/her flyer will be featured on the WTD website for download. Entries are due no later than Friday, 21 June, at 5:00 p.m. US EST. [Click here](#) to learn more about competition eligibility and official guidelines.



### 2. Nominate the WTD 2019 Thrombosis Ambassador of the Year

Do you know an outstanding member of the thrombosis advocacy community who should be recognized for their efforts? Help select the second-annual WTD Thrombosis Ambassador of the Year by nominating someone for this prestigious award.

Eligible candidates include thrombosis advocates dedicated to building awareness about thrombosis in his/her community, region, country, and/or globally. Please note that healthcare professionals are not eligible to be nominated.



The WTD 2019 Thrombosis Ambassador of the Year will receive a complimentary full admission and travel expenses to the [ISTH 2020 Congress](#) in Milan, Italy, as well as the opportunity to serve as a panelist during the WTD educational session at the congress. The award winner will also receive a \$5,000 USD donation to a charity of choice.

Nominations are due no later than 1 August. [Click here](#) to learn more about the award and submit a nomination to recognize an outstanding awareness advocate in your community.



### 3. Support WTD Activities at ISTH 2019 in Melbourne

All are invited to attend WTD events and activities taking place at the [ISTH 2019 Congress](#) from 8-13 July in Melbourne, Australia. See below for a list of WTD activities to add to your itinerary at ISTH 2019:

- [ISTH Charity Run/Walk](#), 8 July, 6:00 local time. When registering, select "World Thrombosis Day Team" to join the campaign team.
- **WTD Session**, 8 July, 12:15-13:15 local time
- **Submit a Vote**: Visit the ISTH booth to vote for the winner of the WTD Early Career Flyer Competition. [Click here](#) for ISTH 2019 exhibition hours.

### 4. Participate in WTD Online Activities

Share your input by participating in the [ISTH Global Survey on VTE Risk Assessment Policy](#).

This short survey on hospital-associated VTE risk assessment policies at your facility to help inform the WTD campaign. Survey participants will be eligible to win a free WTD prize pack. [Click here](#) to complete the survey.

Since 13 October takes place on a Sunday this year, many WTD 2019 awareness events and activities will take place in the week leading up to WTD. As the campaign continues to expand, this is a great opportunity to celebrate WTD throughout the month of October and not only on one day.



Mark your calendar for several must-attend WTD digital activities taking place this year.

- **WTD 2019 Twitter Cat** (Wednesday, 9 October, 10:00 a.m. US EST): The Twitter Chat is one of WTD's most highly regarded global events and provides an opportunity to connect with thousands of WTD partners and supporters around the globe.
- **WTD 2019 Global Webinar** (Thursday, 10 October, 10:00 a.m. US EST): This free webinar is hosted in partnership with the Centers for Disease Control and Prevention (US) and will explore the topic of hospital-associated VTE with leading experts. Registration for the webinar will open in mid-July.

### 5. Plan a WTD Activity in Your Local Community

WTD partners and supporters are critical to the success of the campaign each year. Consider planning a WTD activity in your local community, healthcare facility, or other venue. To get started, [view the list of 100 WTD ideas](#) and gather colleagues, friends and family to help with planning and promotion.

[Post your event here](#) to be featured on the official WTD 2019 events listing for others to participate as well. To view activities and events taking place in the Asia-Pacific region, visit the [events page on the WTD website](#) for updates in your area.



### Thank You for Supporting WTD 2019

Make a difference and help save lives by getting involved in World Thrombosis Day 2019. Connect with the WTD campaign on social media for the latest news and to interact with the global community of WTD supporters.

Follow WTD on [Facebook](#), [Twitter](#), [LinkedIn](#), [Instagram](#), [YouTube](#) and [Pinterest](#). Please use the official campaign hashtags: #WTD19, #KnowThrombosis, #KnowAFib, and #KeepLifeFlowing. If you have questions or comments, please contact the WTD campaign team at [wtd@isth.org](mailto:wtd@isth.org). To learn more about WTD, visit [www.worldthrombosisday.org](http://www.worldthrombosisday.org).

## Upcoming Meetings:

- 1**    **The 27th International Society of Thrombosis and Haemostasis (ISTH) Congress with 65th SSC (Scientific and Standardization Committee) meeting**  
6-10 July 2019 – Melbourne, Australia  
<https://www.isth2019.org/>
- 2**    **ISTH Educational Workshop on Coagulation Disorders**  
8-9 May 2020 – Singapore General Hospital, Singapore  
<https://www.isth.org/page/workshop20>
- 3**    **World Federation of Hemophilia (WFH) World Congress**  
14-17 June 2020 – Kuala Lumpur, Malaysia  
<https://www.wfh.org/congress/en/>
- 4**    **The 28th International Society of Thrombosis and Haemostasis (ISTH) Congress with 66th SSC (Scientific and Standardization Committee) meeting**  
11-15 July 2020 – Milan, Italy  
<https://www.isth2020.org/>
- 5**    **The 11th Congress of the Asian-Pacific Society on Thrombosis and Hemostasis (APSTH)**  
3-5 September 2020 – Gwangju, Korea  
<http://www.apsth2020.org/>
- 6**    **The 38th World Congress of International Society of Hematology (ISH)**  
13-16 September – Bangkok, Thailand  
<https://www.isth2020.org/>