



# APSTH

Asian - Pacific Society on Thrombosis and Hemostasis

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

January 2013 Volume 3 No. 1

## Inside

Message from the Chairman	1
From the Editor	2
APSTH Congress: a Memorable Meeting in Melbourne	3
Platelet Workshop	6
Asia-Pacific Haemophilia KIC-Start Meeting	7
Research News	8
Upcoming Meetings	10
2nd TSH International Symposium on Thrombosis and Hemostasis	11

## APSTH Officers

### Honorary Chairmen

Akikazu Takada  
Yasuo Ikeda  
Hatem Salem

### Chairman

Lai Heng Lee

### Secretary General

Yukio Ozaki

### Public Relations and Communications

Pantep Angchaisuksiri

## Contact Us

### Secretary General Office

**Yukio Ozaki**  
Department of Laboratory Medicine  
Faculty of Medicine  
University of Yamanashi  
1110 Shimokato  
Chuo Yamanashi 409-3898  
Japan  
E-mail: [yozaki@yamanashi.ac.jp](mailto:yozaki@yamanashi.ac.jp)  
Tel: 81-55-273-6770  
Fax: 81-55-273-6924

### Editor Office

**Pantep Angchaisuksiri**  
Division of Hematology  
Department of Medicine  
Ramathibodi Hospital  
Mahidol University  
Bangkok 10400  
Thailand  
E-mail: [pantep.ang@mahidol.ac.th](mailto:pantep.ang@mahidol.ac.th)  
Tel: 662-201-1796  
Fax: 662-201-1796

## Message from the Chairman

Fourteen years have whizzed by since I first met the founding members of APSTH in August 1999 at the China-Japanese Symposium on Coagulation, Fibrinolysis and Platelets, held at Hamamatsu (浜松市), a city located in western Shizuoka Prefecture, Japan. I was grateful to Professor Akikazu Takada for inviting doctors and scientists from the Asia-Pacific region to this meeting. That was an awesome experience for me, meeting so many experts and seeing how much good work they have done. It was in this setting where Asian researchers and doctors interested in thrombosis and haemostasis met and how APSTH was formed. Our inauguration meeting or the 1st Asia Pacific Congress of Thrombosis and Hemostasis (APCTH) was held in Taipei the following year in 2000. I look back with fond memories of these initial meetings where learning took place and friendships were forged.

Since then we have grown from strength to strength with increasing country members and swelling attendances at our bi-annual meetings. We have now representatives from Australia, Cambodia, China, India, Indonesia, Japan, Korea, Malaysia, Mongolia, New Zealand, Philippines, Singapore, Sri Lanka, Thailand, Taiwan and Vietnam. From about 50 attendees at our first meeting in Taipei, we have grown more than 10 fold to more than 500 delegates at our most recent APSTH congress held in Melbourne in October 2012. Congratulations and compliments to Professor Christopher Ward for putting up such an excellent programme! We have also seen interest groups sprouting out from this organization such as the group researching Thrombotic Thrombocytopenic Purpura led by Professor Ross Baker. Indeed, APSTH is our



**Lai Heng Lee**

platform for scientific collaboration and conduct of multi-centre clinical trials.

Even as we grow, we continue our ties with the Japanese Society of Thrombosis and Haemostasis with the APSTH-JSTH joint symposiums and are appreciative of the travel grants and education support that JSTH provides for our young scientists and investigators. Beyond the Asia-Pacific region, we make our presence felt at the International Society on Thrombosis and Haemostasis on the platform of ISTH-APSTH joint symposiums. We are also grateful for the support and financial assistance rendered by ISTH towards our educational programmes. With Professor Claire McLintock from New Zealand and Professor Yukio Ozaki from Japan, we currently have 2 members of the ISTH council coming from the Asia Pacific region and we thank them for securing the support of ISTH towards APSTH.

As I witness the growth and progress of our society APSTH, I am indeed grateful and humbled by your support for me as Chairman for this society. It is indeed my privilege to serve and I look forward to working with you to further the cause of APSTH. I also take this opportunity to urge every one of us to continue to support our APSTH

## Members of APSTH Council

### Australia

Ross Baker  
Beng Chong  
Chris Ward

### Cambodia

Robyn Devenish  
Chean Sophal

### China

Ming Hou  
Changgeng Ruan  
Yongqiang Zhao

### India

Alok Srivastava

### Indonesia

Aru Wisaksono Sudoyo  
Karmel Tambunan

### Japan

Satoshi Fujii  
Yukio Ozaki  
Koji Suzuki  
Tetsumei Urano

### Korea

Hynsook Chi  
Kwang-Hoe Chung  
Doyeun Oh  
Seonyang Park

### Malaysia

Faraizah Abdul Karim  
Jameela Sathar

### Mongolia

Otgonbat Altangerel  
Nergui Dagvadorj

### New Zealand

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  
Saenguree Jootar  
Wichai Prayoonwiwat  
Artit Ungkanont

### Vietnam

Bach Quoc Khanh  
Nguyen Anh Tri

newsletter as the portal of communication and dissemination of information. As a group and together, we can do much to enhance clinical care, propagate education and further scientific research in Thrombosis and Haemostasis to benefit over four billion people in the Asia-Pacific region. Please join me here to express our heartfelt thanks to our immediate past Chairman, Professor Hatem Salem

for all his contributions towards APSTH during his tenure and our appreciation to the continued efforts of Professor Yukio Ozaki our Secretary General and Professor Pantep Angchaisuksiri our Public Relations and Communications officer and the editor of the newsletter.

I wish everyone at APSTH a very happy and fulfilling New Year.

## From the Editor



Welcome to a new issue of the newsletter, a new APSTH Chairman - Dr. Lai Heng Lee of Singapore, and a new year. In this newsletter, we have summarized some recent events. We start with a very memorable meeting in Melbourne. Dr. Chris Ward, the 2012 APSTH Congress President, reports that the combined (with three Australian and New Zealand societies) meeting had close to 1,500 delegates from 33 countries. A large number of international coagulation speakers formed the basis of the meeting. In this newsletter, we have included

a detailed report on the Platelet Workshop held prior to the APSTH Congress. Next, we have Dr. Mark Smith's review of the Asia-Pacific Hemophilia KIC-Start meeting held in December in New Zealand. This meeting was targeted at young doctors starting out in their Hematology careers, and aimed to engage participants in areas relevant to good and comprehensive hemophilia management. Interestingly, this 5-day meeting was divided between two cities, Auckland and Christchurch. Next, Dr. Tetsumei Urano of the Hamamatsu University School of Medicine, Japan gives us some information on his group's latest research. They have studied how fibrinolytic activity is expressed both in plasma and on vascular endothelial cells under physiological and pathological conditions.

Last but not least, there is a meeting May 24-26, 2013 in Bangkok, Thailand, that you won't want to miss. It is the 2nd Thai Society of Hematology International Symposium on Hemostasis & Thrombosis. We have detailed information about this symposium on the last page of this newsletter and on the website, [www.tsh.or.th/tsh-is](http://www.tsh.or.th/tsh-is). A side benefit of attending is that Bangkok is one of the world's top tourist destination cities.

Pantep Angchaisuksiri, Editor  
Officer of Public Relations and Communications APSTH







## APSTH Congress: a Memorable Meeting in Melbourne

**Chris Ward**

*APSTH Congress President, Melbourne 2012*



The 7th Congress of our Society was held recently in Melbourne, Australia, in conjunction with the national scientific meeting of the Australian Haematology Societies (HAA). Located at the expansive new convention centre on the Yarra River, the combined meeting attracted close to 1500 delegates. There was strong interest from throughout the region, with attendees from 33 countries. By combining the Congress with the regular HAA sessions, we were able to expand the scientific programme, which ran over 5 days in total, from 27-31 October. The three Australian and New Zealand societies (the Haematology Society of Australia and New Zealand - HSAANZ, the Australian & New Zealand Society of Blood Transfusion - ANZSBT, and the Australian Society of Thrombosis and Haemostasis - ASTH) hosted the Congress programme this year, providing the financial and organisational structure for the combined meeting. The organising committee acknowledged the importance of fostering links across the region, through societies such as APSTH, and generously invited a large number of international coagulation speakers to form the basis of our programme. The Australian Society of Thrombosis and Haemostasis (ASTH) provided additional support for APSTH members to attend the meeting and several awards listed below.

Two "stand-alone" Workshops were held prior to the meeting proper – a Platelet Workshop over two days and the

(ASTH) diagnostic workshop on coagulation testing on Saturday 27th. This workshop is designed for laboratory scientists and deals with new assays and instrumentation. Featured topics this year included FXIII assays, teaching haemostasis to students, prothrombotic changes in cancer and the role of the laboratory in managing novel oral anticoagulants (NOACs). The Platelet Workshop programme was compiled by platelet experts from Australia, Japan and the UK. Speakers covered new advances in basic research, platelet function testing and the role of platelets in a range of disease states. A detailed report on the Platelet Workshop can be found elsewhere in this newsletter.



Our organising committee wanted to attract many of the delegates to hear our top coagulation speakers and to foster interaction between the societies. With this in mind, we planned a large number of combined symposia, which were well attended. A symposium on current and future platelet function testing was held with delegates from both the Platelet and ASTH Workshops. Combined plenaries in the main conference programme dealt with platelet disorders and platelet transfusion, atypical thrombotic syndromes and managing patients on NOACs. These were a great success and prompted questions and discussion from a wide range of delegates. The NOAC sessions were very popular with standing room only during a couple of sessions.

### International Keynote Speakers

<b>Walter Ageno (Italy)</b>	Atypical thrombosis and risk factors for venous thromboembolism
<b>Jing-Fei Dong (USA)</b>	von Willebrand factor physiology and thrombotic microangiopathies
<b>Terry Gernsheimer (USA)</b>	ITP and platelet transfusion
<b>Peter Gross (Canada)</b>	Microparticles and thrombosis in cancer
<b>Paul Harrison (UK)</b>	Platelet disorders and platelet function tests
<b>Jong-Wook Lee (Korea)</b>	Paroxysmal nocturnal hemoglobinuria and aplastic syndromes
<b>Bernhard Nieswandt (Germany)</b>	Coagulation factors in stroke
<b>Yukio Ozaki (Japan)</b>	Platelet physiology and antiplatelet agents. Prof Ozaki had the honour of delivering the Barry Firkin Oration, the scientific highlight of the ASTH programme, to the combined meeting. His intriguing address on "Novel platelet functions beyond haemostasis" detailed a personal journey into exciting new aspects of biology with important therapeutic implications.
<b>Herbert Schoechl (Austria)</b>	Managing bleeding in trauma
<b>Alok Srivastava (India)</b>	Haemophilia
<b>Raymond Wong (Hong Kong)</b>	New anticoagulants and ITP



*Professor Yukio Ozaki (right) received the Barry Firkin Oration Award from Dr. Huyen Tran (left), the President of the ASTH.*

The success of the Congress owes much to the generous contributions from our international keynote speakers, listed below in alphabetical order. Their state-of-the-art summaries of coagulation disorders, and clear presentations of new research were accessible and informative. Together, their lectures covered a wide range of topics in coagulation science, thrombosis and haemostasis. Several of our speakers also presented Masterclasses where a small group of delegates could discuss clinical and diagnostic challenges in an informal setting.

With this outstanding faculty, delegates could choose from a wide range of clinical and basic science topics in coagulation. It was fascinating to hear how new perspectives on thrombus formation, and the growing links between coagulation and inflammation, are relevant to our clinical practice and have the potential to markedly change our therapeutic approaches.

Other invited speakers from APSTH included Maria Abola (Philippines), Lai Heng Lee (Singapore), Satoshi Nishimura (Japan), Doyeun Oh (Korea), Changeng Ruan (China), Jameela Sathar (Malaysia) and Tetsumei Urano (Japan). We were also grateful to the many APSTH Council members who participated as chairpersons during the Congress. Australian invited speakers included clinical experts from a variety of disciplines, including cardiology, neurology and trauma and several leading research scientists.

Another key aim of the Congress organisers was to encourage participation by young clinicians and scientists from all parts of the region. We were delighted to see over 150 submitted abstracts to the Congress, covering an enormous range of topics. Many of these papers were presented at a poster session on the Monday afternoon, with posters available for viewing throughout the meeting. Free communication sessions highlighted the best of these abstracts, with themes including coagulation science, bleeding disorders, laboratory methods and clinical thrombosis. A special session featured speakers selected for the ASTH Emerging and Young Investigator awards; their names and presentations are listed below:



## Young Investigator Awards

<b>Hideo Matsui</b> (Nara, Japan)	Endothelial progenitor cell-based therapy for hemophilia A
<b>Junko Fujita</b> (Nagoya, Japan)	A possible mechanism for inv22-related F8 large deletions in severe haemophilia A patients with high responding factor VIII inhibitors
<b>Miao Jiang</b> (Suzhou, China)	Mapping the amino-acid site of interaction between vWF A1 domain and A3 domain
<b>Yu Hu</b> (Shandong, China)	Decreased TIM-3 and its correlation with Th1 in patients with immune thrombocytopenia
<b>Colin Evans</b> (Cambridge, UK)	HIF signalling mediates cancer-associated thrombosis
<b>Xuan Lu</b> (Wuhan, China)	A novel association between a PROC variant and ischemic stroke in a Chinese Han population

The high standard of their work showed the growing prominence of coagulation research in the Asia-Pacific region, mentored by many of the founders of our Society.

Every year, the ASTH Medal is awarded for the best presentation by a young investigator and society member. In 2012, the Medal was won by Zane Kaplan (Monash University) for his paper "Directed intravascular leukocyte migration: a distinct leukocyte guidance mechanism mediated by platelet thrombi". Runners up were Ashley Ng (University of Melbourne) "Elucidation of lineage potential of murine progenitor populations: identification of thrombopoietin responsive bipotential progenitors" and Minh Hua (University of NSW) "Cell death imager-1 ligands in apoptotic platelets". The inaugural Werfen ASTH travel award was won by Yusra Harasheh "Determination and characterisation of anti-ADAMTS13 antibodies". ASTH awarded two prizes for the best posters: the laboratory prize went to Yasunori Matsunari (Nara Medical University, Japan): "Evaluation of soluble or surface-immobilized tissue factor in intra-thrombus fibrin generation under whole blood flow conditions" and the clinical prize to Moon Ju Jang (CHA University, Korea): "Seasonal variation in the occurrence of venous thromboembolism: a report from the Korean Venous Thromboembolism Working Party".

Congratulations are due to all the award winners for their outstanding efforts, and we look forward to hearing more from them as their careers develop.

Our Congress organisers are also grateful for the generous support from our corporate sponsors, including keynote speakers (Gernsheimer - Amgen, Schoechl - CSL). Three sponsored satellite symposia were held on the Monday and

attracted great interest from our delegates. These were the 3rd Asia Pacific Haemostasis forum on heparin-induced thrombocytopenia (Simon Davidson, UK), antiphospholipid antibodies (Pantep Angchaisuksiri, Thailand) and innovations in testing (Werfen - Instrumentation Laboratories), a symposium on practical management of NOACs (Bayer) and another on haemostasis in mothers and children (Stago). Many other companies also supported the meeting through trade displays in the large exhibition space.

Last, but not least, the Congress provided ample opportunity for delegates from across the region to meet, discuss their work and challenges, making new friends and collaborations in the process. A Welcome function in the conference foyer introduced our delegates to some of Australia's fascinating reptiles, including some baby crocodiles! Between sessions, our delegates could take advantage of the Convention Centre's proximity to Melbourne's entertainment district, with restaurants, museums and many of the city's highlight a short walk or tram-ride away. The Melbourne weather lived up to its reputation with cold rainy periods followed immediately by hot sun. The locals are known to say "if you don't like the weather, just wait for half an hour". Those who could stay until the Conference party on the Tuesday evening were treated to a lively racing themed event, with some very unusual entrants in our "best dressed" and "best hat" competition, a dinner with fellow delegates and enthusiastic dancing until late.

Our organising committee was delighted to see such a strong programme, well-supported and enjoyed by so many attendees from Australia and Asia-Pacific countries. We feel the "experiment" of combining the APSTH Congress with a well-established local meeting achieved its aim of producing an expansive scientific programme, which could attract many of the delegates to our coagulation sessions. Certainly the large faculty of world-class speakers and the many submitted abstracts from our Society members did us proud. Thank you to all of the APSTH members who gave their time and effort to make this meeting so memorable.

Initial feedback from colleagues was very positive, but we'd also like to hear about your suggestions for future Congress meetings via the APSTH Secretariat (email address: yozaki@yamanashi.ac.jp). It was an honour and a pleasure for our Australian colleagues to host the APSTH in 2012 and we look forward to renewing old and new friendships at the next Congress in Hanoi, Vietnam in two years time.



# Platelet Workshop

**Robert K. Andrews**  
Melbourne, Australia

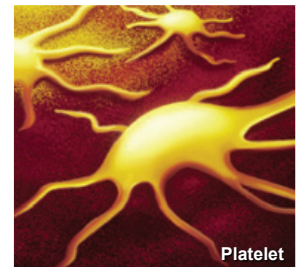
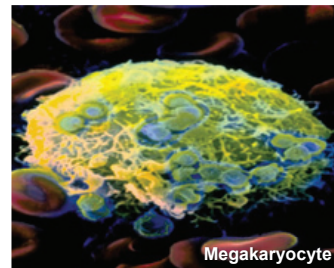
*The miraculous birth, roller-coaster life and all too rapid death of the platelet was on full display at the recent Platelet Workshop held at the Melbourne Exhibition and Convention Centre over the weekend of October 27th – 28th, 2012.*

There is no more fascinating topic than platelets. This experimental-clinical meeting, the Platelet Workshop, held in conjunction with the Haematology Society of Australia and New Zealand (HSANZ), the Australian & New Zealand Society of Blood Transfusion (ANZSBT), the Australasian Society of Thrombosis and Haemostasis (ASTH) and the Asian-Pacific Society of Thrombosis and Haemostasis (APSTH) joint conference (October 28-31), highlighted many new facets of platelet biology. The simultaneity with the HAA/APSTH meetings ensured notable international platelet experts including Yukio Ozaki (Japan), Satoshi Nishimura (Japan), Bernhard Nieswandt (Germany), Peter Gross (Canada), and Paul Harrison (UK), together with over 20 local speakers convened over two days for this special workshop. On the programme were 6 oral sessions, with 3 major symposia in each session and free communications featuring the highest-ranked abstracts. There was a stand-alone poster session, and plentiful social and networking opportunities, all in the heart of Melbourne's docklands entertainment precinct.

Workshop sessions were broadly arranged to cover megakaryopoiesis and platelet production, platelet function ex vivo and in vivo, and platelet death and clearance. These presentations featured state-of-the-art imaging, new experimental models of thrombosis or inflammation, biochemical analysis of platelet receptors and activation pathways, and the clinical importance of platelet function in human disease. Haematological systems involving platelets far exceed haemostasis and thrombosis, and platelets are increasingly studied in the context of inflammation, infectious diseases, metabolic diseases and cancer, a point brought home throughout the workshop. Research presented also highlighted how past and current investigations in basic science and molecular mechanisms can be translated to improve understanding,



**Elizabeth Gardiner (Melbourne) and Bernhard Nieswandt (Germany) – Invited speakers at the Platelet Workshop, 2012**



diagnosis or therapeutic approaches in clinical disease. One notable highlight on Saturday afternoon was a combined Platelet/ASTH/APSTH session on platelet functional analysis. Paul Harrison (UK) covered the status of current platelet tests used clinically – based in large part on his international experience with standardization of the relevant methods. He was followed by Elizabeth Gardiner and Warwick Nesbitt from Melbourne presenting innovative translational research on some of the newer experimental or future approaches, respectively, to platelet analysis, particularly taking into account quantitative measures of platelet-specific receptor expression and thrombus formation in the context of rheological shear stress.

Other scientific sessions examined high-resolution in vivo imaging, with the dual potential for both studying mechanisms of arterial or venous thrombosis, and, with the development of suitable new agents, for eventual diagnostic use in humans – key speakers were Satoshi Nishimura (Japan), Eric Westein (The Netherlands), and Christoph Hagemeyer (Melbourne). One of the spectacular motion pictures shown by Dr. Nishimura showed the generation of a new platelet from a megakaryocyte in vivo. Presenters in the following session (Emma Josefsson and Warren Alexander from Melbourne) provided fascinating insights into genetics and molecular pathways underlying thrombopoiesis and megakaryopoiesis, regulatory feedback loops that control normal platelet generation or sites where aberration can cause disease. Yukako Ono (free communication) also reported gene regulatory networks involved in inducible megakaryocyte generation from human fibroblasts, as monitored by microRNA profiling.

Later at the meeting, presentations by Bernhard Nieswandt (Germany) and Chris Sobey (Melbourne) described sophisticated experimental models of ischaemic stroke used to examine distinct molecular targets for potential therapeutic approaches, while Peter Gross (Canada) used an in vivo laser injury model and high-speed two-color confocal microscopy to monitor spatio-temporal platelet activation in arterioles of



mice, with future applications for analysing antiplatelet agents in particular. Other unique mouse models presented by Ben Kile and Ross Dickens (Melbourne) indicated mechanisms of controlling platelet number, while Jessica Mountford (free communication) in the same session reported a selective platelet defect in mice deficient in a functional signalling enzyme, PI3K. Additional experimental studies in mice examined aspects of dynamic platelet-leukocyte interplay in inflammation (Zane Kaplan and Yuping Yuan, Melbourne), and how platelets regulate leukocyte trafficking in the unusual vascular beds of the glomerulus (Michael Hickey, Melbourne). Other speakers presented studies of human platelets, covering effects of coronary artery stenosis (Len Kritharides, NSW), dietary agents (Murray Adams, TAS), membrane lipids (Adam Munday, USA) or bacterial toxins (Yukio Ozaki, Japan) on

platelet activation, aggregation, receptor expression or other pathology. Apologies to other excellent speakers not specifically mentioned here.

Overall, the Platelet Workshop provided an outstanding learning and networking opportunity for all, in particular for student attendees. Thanks are due to the other organizing committee members (Chris Ward and Simone Schoenwaelder), event organizers, major sponsors (Amgen and Leica Microsystems, who also sponsored the social event), and the ASTH and APSTH, all major factors in the success of the Platelet Workshop. Session chairs contributed superbly throughout. It is to be hoped that all stakeholders will support future platelet workshops at future conferences.

## Asia-Pacific Haemophilia KIC-Start Meeting



**Mark Smith**  
Christchurch, New Zealand



**Asia-Pacific Haemophilia KIC-Start Meeting**  
New Zealand, 2012

The Asia-Pacific Haemophilia KIC-Start meeting, was held for the second consecutive year in December 2012 in New Zealand. Participants included doctors from Taiwan, Korea, Malaysia, Australia and New Zealand. Designed with a theme of "Knowledge Inspires Confidence", the programme was targeted at young doctors starting out in their Haematology careers, and aimed to engage participants in areas relevant to good and comprehensive haemophilia management. The programme ran over five days; the first two days, convened in the North Island city of Auckland, followed a lecture format; the last three days comprised interactive, patient-oriented and laboratory-based workshops, and took place in the city of Christchurch, in New Zealand's South Island. The programme was designed by New Zealand haemophilia treating physicians Drs. Mark Smith, Julia Philips and Paul Harper. "We planned the programme to benefit young physicians with an interest in Coagulation Medicine" said Dr. Smith. "We were pleased that some experienced physicians also enrolled for the course, and they provided stimulating comment on management practices in their respective countries."

Dr. Tim Brighton from the Prince of Wales Hospital in Sydney introduced the meeting with an eloquent review of "Protein Structure Function". Subsequent topics addressed diagnostic challenges, paediatric and adult management issues. Separate discussions on the role of haemophilia-specific nurses and physiotherapists emphasised the importance of a team approach to haemophilia care. Dr. Helen Savoia, Haematologist from the Royal Women's and Children's Hospitals in Melbourne, spoke on "Practical plans for haemophilia carriers during pregnancy", complemented well by a review of "Preimplantation Genetic Diagnosis" by Dr. Smith. The lecture component of the programme finished with two challenging areas: inhibitor management and interpretation of biostatistics. Professor Philip Schluter from the University of Otago, New Zealand spoke on "A population health approach to haemophilia", where he introduced the basic tenets of population health, illustrating biostatistical concepts by analysing the NEJM publication on prophylactic FVIII treatment in paediatric patients.

A highlight of the practical component in Christchurch was a cultural evening that gave the participants a taste of a traditional Maori welcome, and also of hangi-cooked food (a traditional native technique of cooking food on hot stones, heated by fire-pits dug into the ground). "Thank you very much for the wonderful meeting in Auckland and Christchurch", said Dr. Pei-Chin Lin from Kaohsiung, Taiwan.

The course is an initiative of New Zealand Haemophilia treaters, supported by Bayer Healthcare. Discussions are underway to host the 2013 meeting at a location in Asia, to make the programme more accessible to doctors from Asian countries.



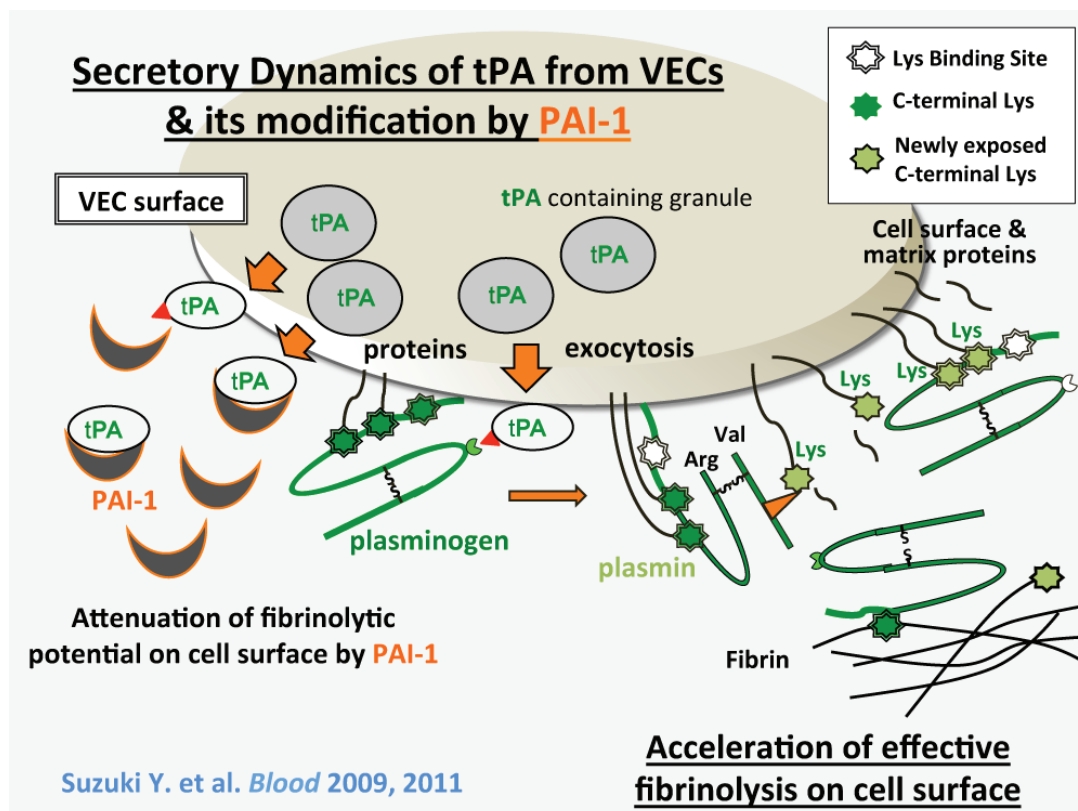
## Research News



**Tetsumei Urano**  
 Department of Medical Physiology, Hamamatsu  
 University School of Medicine, Japan

### Our Research Focus

We have studied how fibrinolytic activity is expressed both in plasma and on vascular endothelial cells (VECs) under physiological and pathological conditions. The activation of coagulation cascade and the resulted fibrin formation is an important trigger to express high fibrinolytic activity in plasma. Tri-molecular complex formation between tissue plasminogen activator (tPA) and Glu-plasminogen (Glu-plg) on fibrin surface, and the resulted conformational change of Glu-plg are the most important underlying mechanisms. We have also proposed that the activated coagulation factors enhance tPA activity by neutralizing the activity of plasminogen activator inhibitor type 1 (PAI-1) (Urano T et al, JTH 2003;1:2615-2620, Iwaki T et al, JTH 2011;9:1200-1206). We recently focused on how fibrinolytic potential is highly maintained and its activity is effectively expressed on the surface of VECs.



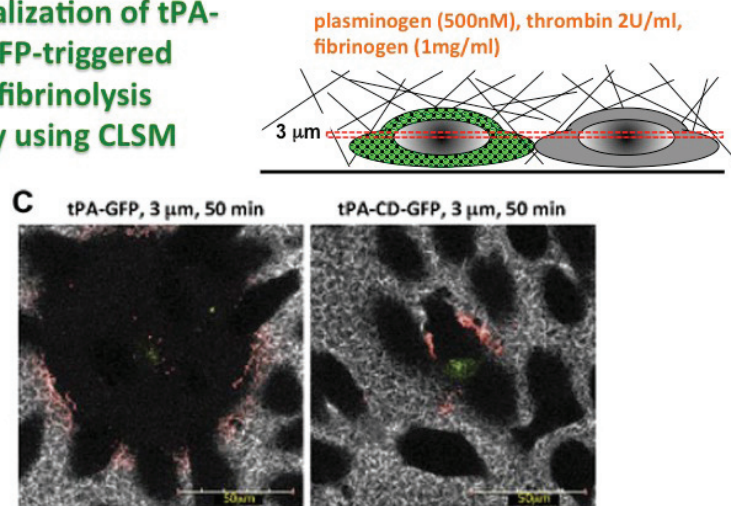


## Accelerated fibrinolysis and its propagation on vascular endothelial cells by secreted and retained tPA

tPA, the primary PA in the vasculature, is synthesized and released from VECs as an active form to initiate intravascular thrombolysis. We recently successfully visualized the secretory dynamics of tPA tagged by green fluorescent protein (tPA-GFP) from cultured VECs using total internal reflection fluorescence (TIRF) microscopy. tPA-GFP appeared to have unique secretory dynamics from VECs, showing that the release of tPA-GFP from the opened granule was very slow after the opening of its containing granule (Suzuki Y et al, Blood 2009;113:470-478). The retention of tPA on cell surfaces was heavy-chain dependent, and the release of tPA appeared to be facilitated by plasminogen activator inhibitor type 1 (PAI-1). The retained tPA on cell surface efficiently expressed its activity to generate plasmin, which then proteo-

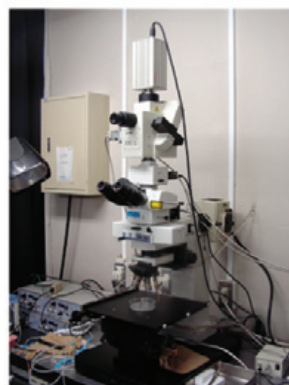
lytically cleaved surface-associated proteins to expose lysine residues at their C-termini. This was demonstrated by both progressive accumulation of Alexa568 labeled Glu-plasminogen on the surface of active tPA-GFP expressing cells in a lysine binding sites (LBS) dependent manner and effective digestion of fibrin network formed over the cells (Suzuki Y et al, Blood 2011;118:3182-3185). Thus prolonged retention of tPA appeared to play an important role in initiating and amplifying plasmin generation on VECs. LBS-dependent binding of plasminogen was also observed as a narrow band at the lytic front of the fibrin mesh formed on active tPA-GFP expressing cells, which expanded outward as the lytic area increased. This binding was not observed on inactive mutant tPA-GFP expressing cells or in the presence of aprotinin. The binding of plasminogen to partially digested fibrin was directly proved indispensable for spontaneous fibrinolysis as was speculated for long time.

### Visualization of tPA-GFP-triggered fibrinolysis by using CLSM

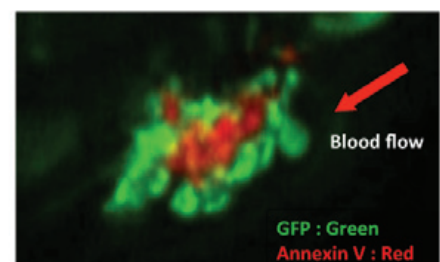
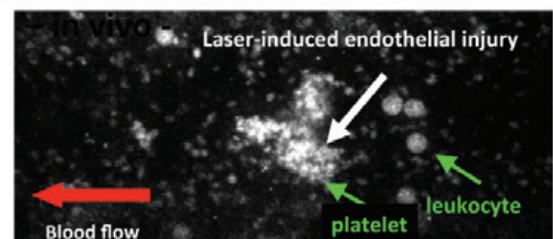


Progressive lysis of fibrin mesh (white) formed over tPA-GFP expressing cell is demonstrated (Lt). The binding of Glu-plasminogen (Red) to the lytic edge was always recognized. The lysis was substantially attenuated when heavy-chain lacking tPA-GFP (tPA-CD-GFP) was employed (Rt). Suzuki Y. et al. Blood 2011

## Real time imaging of laser-induced thrombus formation and platelets activation in GFP mouse



In vivo confocal fluorescent microscopy



PS exposure on platelet surface was detected by labeled annexin V in laser-induced thrombus

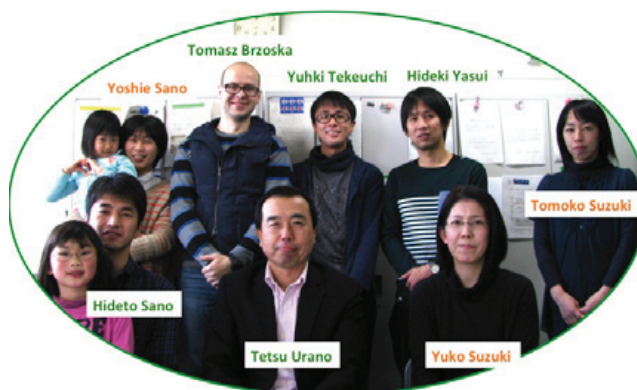
Hayashi T. et al. Eur J Physiol 2009

### Time- and space-dependent control of both thrombus formation and its lysis revealed in in-vivo system.

Since both thrombus formation and its lysis in vivo are finely regulated time- and space-dependently to repair vascular injury along with keeping vascular patency. Employing in-vivo real time confocal microscopy system, we have analyzed platelets activation, thrombus formation and its lysis in mesenteric vein in GFP expressing transgenic mice after laser-induced injury of vessel intima. Platelets adhesion and aggregation were clearly monitored and their activation was demonstrated by the specific binding of fluorescent-labeled annexin V to phosphatidylserine exposed on the outer leaflet of activated platelets. Surprisingly only platelets existing in the center of thrombus, in which sustained elevation of intracellular calcium ion concentration was observed, exposed PS, which was followed by fibrin formation (Hayashi T et al, Eur J Physiology 2008;456:1239-1251, Rybaltowski M et al, Pflugers Arch 2011;461:623-633, Kramkowski K et al, ATVB 2012;32:2149-2157). We also observed the accumulation of Glu-plasminogen in LBS-dependent manner at the later phase, and we are now analyzing those physiological function.

### Members of the laboratory

Tetsu Urano (Professor), Yuko Suzuki (Associate Professor), Hideto Sano (Assistant Professor), Hideki Yasui, Tomasz Brzoska, Tae Ito, Daisuke Takechi (Graduate students), Tomoko Suzuki and Yoshie Sano (Technicians).



### Collaboration with other laboratories

We are collaborating not only with the laboratories in Japan, but in other countries including Bialystok University in Poland and Notre Dame University in the U.S.A.

## Upcoming Meetings:

- 1 5th International Symposium on Women's Health Issues in Thrombosis and Haemostasis**  
1-3 February 2013 - Vienna, Austria  
[www.whith.org](http://www.whith.org)
- 2 Global Thrombosis Forum 2013**  
2-3 March 2013 - Prague, Czech Republic  
Contact your local Boehringer Ingelheim for further information
- 3 WFH 13th International Musculoskeletal Congress**  
18-21 April 2013 - Chicago, U.S.A.  
[www.wfh.org/msk2013](http://www.wfh.org/msk2013)
- 4 2nd Thai Society of Hematology International Symposium on Thrombosis and Hemostasis**  
24-26 May 2013 - Bangkok, Thailand  
[www.tsh.or.th/tsh-is](http://www.tsh.or.th/tsh-is)
- 5 18th Congress of the European Hematology Association**  
13-16 June 2013 - Stockholm, Sweden  
[www.ehaweb.org](http://www.ehaweb.org)
- 6 XXIV Congress of the International Society on Thrombosis and Haemostasis**  
29 June - 4 July 2013 - Amsterdam, Netherlands  
[www.isth2013.org](http://www.isth2013.org)



## The 2nd Thai Society of Hematology International Symposium on Hemostasis & Thrombosis

### Preliminary Scientific Program

**Date:** May 24-26, 2013

**Venue:** Centara Grand @ CentralWorld, Bangkok, Thailand

[www.tsh.or.th/tsh-is](http://www.tsh.or.th/tsh-is)

Date	Time	Topics	Speakers
Fri. May 24, 2013	08.30-10.00	Mechanisms of platelet activation	Michael Berndt (Ireland)
		Inherited platelet disorders and platelet function tests	Shinji Kunishima (Japan)
	10.00-10.30	Coffee Break	
	10.30-12.00	Consultative thrombocytopenia:	
		Immune thrombocytopenia	Ross Baker (Australia)
		Heparin-induced thrombocytopenia	Andreas Greinacher (Germany)
		Thrombotic microangiopathy	Ross Baker (Australia)
	12.00-13.30	Luncheon Symposium I	
	13.30-15.00	Von Willebrand disease	TBA
		Hemophilia	TBA
		Acquired hemophilia	Theera Ruchutrakool (Thailand)
	15.00-15.30	Coffee Break	
	15.30-17.00	Tropical hemostatic disorders:	
		Dengue hemorrhagic fever	Ampaiwan ChuanSumrit (Thailand)
		Coagulopathy in malaria	Pantep Angchaisuksiri (Thailand)
		Snake bite-induced coagulopathy	Ponlapat Rojnuckarin (Thailand)
Sat. May 25, 2013	08.30-10.00	Thrombophilia:	
		Hereditary thrombophilia	Paul Monagle (Australia)
		Antiphospholipid syndrome	Thomas Ortel (USA)
		Laboratory tests in thrombophilia	Harshal Nandurkar (Australia)
	10.00-10.30	Coffee Break	
	10.30-12.00	Current management on VTE:	
		Thrombosis in children	Paul Monagle (Australia)
		VTE in adult	Per Morten Sandset (Norway)
		Cancer-associated VTE	TBA
	12.00-13.30	Luncheon Symposium II	
	13.30-15.00	Novel antithrombotic therapy:	
		Antiplatelets	Per Morten Sandset (Norway)
		Anticoagulants	TBA
		Monitoring of new anticoagulants	Harshal Nandurkar (Australia)
	15.00-15.30	Coffee Break	
	15.30-17.00	Bleeding and thrombosis in pregnancy	TBA
		Perioperative anticoagulant	Thomas Ortel (USA)

**Sun. May 26, 2013** Coagulation Workshop