2nd Annual Meeting of Asian Pediatric Hematology and Oncology Group (APHOG) 2023

Joint meeting with the 15th SIOP Asia 2023

May 21st Sunday, 2023

(Third day of the SIOP Asia Congress 2023)

9:00-12:15 (Armenia time; UTC+4)

Register here:

https://us06web.zoom.us/webinar/register/WN_OVisnX_0SKaGuIGGCdszpQ

Yerevan, Armenia; Hybrid (On site+On line)

Supported by the 15th SIOP Asia Congress 2023 and

NGO Magokoro Organization for Childhood Cancer (MOCC)

2nd APHOG Annual Meeting 2023

Symposium: "Fight Against Neuroblastoma in Asia"

Date: May 21st SUN, 2023 9:00-12:15 (Armenia time; UTC+4)
Venue: Yerevan, Armenia Hybrid (On site+On line)

Register here:
https://us06web.zoom.us/webinar/register/WN_OVisnX_0SKaGuIGGCdszpQ

Opening Remarks: **Akira Nakagawara** Chairperson, APHOG
Guillermo Chantada President, SIOP

Moderators: **Rashmi Dalvi** (India), **Muhammad Saghir Khan** (Pakistan),

Session 1: (9:05-10:35; 30min talk with discussion for each speaker)

1. **Leonid S. Metelitsa** Baylor College of Medicine, Texas Children's Hospital, USA
   "Anti-GD2 CAR-NKT cells are safe and produce antitumor responses in patients with relapsed/resistant neuroblastoma"
2. **Susan L. Cohn** The University of Chicago, USA
   "Advancing Research with the International Neuroblastoma Risk Group Data Commons"
3. **Alice L. Yu** Chang Gung Memorial Hospital & Academia Sinica, Taiwan
   "Advances in anti-GD2 immunotherapy of high risk neuroblastoma"

<Intermission>

Session 2: (10:45-12:15; 30min talk with discussion for each speaker)

1. **Kimikazu Matsumoto** National Center for Child Health and Development, Japan
   "Japanese trials for high-risk neuroblastoma"
2. **Hiroyuki Shimada** Stanford University School of Medicine, USA
   "Molecular pathology of high-risk neuroblastoma"
3. **Godfrey C. Chan** Hong Kong Children's Hospital, HK, China
   "Potential APHOG trials for neuroblastoma in Asia"

Closing remark: **Hiroki Hori** President, SIOP Asia

==========

13:00-14:00 **"APHOG General Assembly 2023 Spring"**

==========

==========

APHOG Annual General Meeting (AGM) 2023

APHOG Annual General Meeting 2023

Date: **May 21st SUN, 2023** **13:00-14:00 (Armenia time; UTC+4)**
Venue: **Yerevan, Armenia** **Hybrid (On site+On line)**

Register here:
https://us06web.zoom.us/webinar/register/WN_LRogdz4TSum74la_4jZuiw

1.	Opening message (3 min)	Akira Nakagawara
2.	APHOG Annual Report 2022 (10 min)	Godfrey C. Chan
3.	Collaboration between APHOG and SIOP Asia (5 min)	Hiroki Hori
4.	Action Plan 2023 (5 min)	Rashmi Dalvi
5.	Manuscripts in preparation (5 min)	Chi-Kong Li
6.	Result of the Questionnaire Survey of APHOG (10 min)	Muhammad Saghir Khan
7.	By-laws and APHOG Structure (5 min)	Godfrey Chan
8.	Global Collaborative Network (5 min)	Purna Kurkure
9.	Closing message (3 min)	Bharat Agarwal

==========

Akira Nakagawara, MD, PhD

Dr. Akira Nakagawara graduated from Kyushu University School of Medicine in 1972. During his medical student days, he decided his life work as to elucidate the molecular and genetic mechanism of spontaneous regression of neuroblastoma. He worked as a pediatric surgeon for 14 years before moving to the genetic and genomic research of neuroblastoma. He was trained and learned at the Rockefeller University, NY, the Washington University, St. Louis, and the University of Pennsylvania, USA. He was appointed to be the Director of Chiba Cancer Center Research Institute in 2004, President of Chiba Cancer Center in 2009, CEO of Saga Medical Center KOSEIKAN in 2014, and CEO of Saga HIMAT Foundation in 2015. He has successfully elucidated molecular and genetic mechanism of neuroblastoma, especially of spontaneous regression of the tumor. He also worked as the president of the Advances in Neuroblastoma Research Association (ANRA; 2003-2006), Continental President of Asia, SIOP (2010-2015), President of Japan Neuroblastoma Study Group (JNBSG; 2012-2016), and a founding member of Japan Children's Cancer Group (JCCG; 2014~). He is the first Chairman, Executive Council of the Asian Pediatric Hematology and Oncology Group (APHOG; 2021~) and is also the Vice-president of the Japanese Society for Quantum Medical Science (JSQMS; 2021~). He held many congresses as the president/chairman, which include the 21st Congress of Japan Society of Pediatric Oncology (JSPO2005), the 8th Meeting of Advances in Neuroblastoma Research (ANR2008, Chiba), the 2nd Japan-China Cancer Research Symposium (2012), the 6th International p63p73 Workshop (2013), and the 50th Congress of International Society of Paediatric Oncology (SIOP2018 Kyoto)

Opening Message

Akira Nakagawara, M.D., Ph.D.
Chairperson, Executive Council, Asian Pediatric Hematology and Oncology Group (APHOG)

Asian Pediatric Hematology and Oncology Group (APHOG) was formally founded in March, 2021, after a long struggle for about 10 years. The structure of APHOG is still under construction, but it is steadily going on. We had the 1st APHOG Annual Meeting in 2022 under the serious condition of COVID-19 pandemic through online. But now it is a great pleasure and honor for us to be able to have the 2nd APHOG Annual Meeting 2023 in Yerevan, Armenia, together with the SIOP Asia Congress 2023. We would very much appreciate Prof. Guillermo Chantada, President of SIOP, and Prof. Hiroki Hori, Continental President of SIOP Asia, for a great support and collaboration, Prof. Armen Muradyan, Rector of Yerevan State Medical University after Mkhitar Heratsi, Prof. Samvel Danielyan, Director of Hematology Center after Prof. R. H. Yeolyan, and Dr. Gevorg Tamamyan, Chair of the Local Organising Committee, SIOP Asia 2023, for providing us such a wonderful opportunity to have the 2nd APHOG Annual Meeting together with the SIOP Asia conference 2023 in Yerevan.

The theme of the symposium was set up to be the “Neuroblastoma” which is still a disastrous childhood cancer in Asia and whole world. The internationally well-known speakers will give us exciting presentations that should be so helpful to conquer neuroblastoma and lead the sick children to better cure as well as better care in the near future.

Guillermo L. Chantada, MD, PhD

Graduated as MD at the University of Buenos Aires, Argentina in 1988 where he obtained his PhD in 2014, he completed his postgraduate training in Clinical Pediatrics and Pediatric Hematology- Oncology at the Hospital JP Garrahan at Buenos Aires where worked as staff until 2020. From 2006 he is a contractor at the St Jude Children's Research Hospital as Editor in Chief of Oncopedia at the Cure4kids.org resource. In 2013, he joined the Hemato-oncology Service of the Hospital Sant Joan de Déu Hospital, Barcelona, Spain where he is the Head of the Pediatric Cancer Center Barcelona Outreach Program. In 2016, he was appointed as Principal Researcher of the National Council of Research (CONICET) in Argentina at the Institute of Translational Medicine at the Austral University. In 2020 he was appointed as Scientific Director of the Hematology-oncology service at the Fundacion Perez Scremini at the Hospital Pereira Rossell in Montevideo, Uruguay. He was president of SLAOP (Latin American Society of Pediatric Oncology), he was co-chair of GALOP (Latin American Group of Pediatric Oncology) and is currently SIOP (International Society of Pediatric Oncology) President. His areas of research are mainly devoted to retinoblastoma, where he was published extensively, new therapies in neuroblastoma and lymphomas.

Opening Message

Guillermo L. Chantada, MD, PhD
President, International Society of Paediatric Oncology (SIOP)

It is a big honor for me to represent SIOP in the opening of the APHOG Annual Meeting 2023 whose main topic is the “Fight Against Neuroblastoma in Asia” in the beautiful city of Yerevan. SIOP is proud to support the activities of APHOG that is generating essential data for the management of pediatric tumors in Asia which will influence the whole world. SIOP has launched the Program for Advancing Research Capacity (PARC) in low and middle income countries and welcomes APHOG as part of the PARC family of cooperative groups world wide. In this meeting, world experts in neuroblastoma will discuss the many challenges and new opportunities for the management of this tumor in Asia. I personally wish you a great meeting and encourage you to keep up with the great work APHOG is doing.

Hiroki Hori, M.D., Ph.D.

Prof. Hiroki Hori graduated from Mie University Faculty of Medicine, Japan in 1984 and earned his PhD degree from Mie University Graduate School of Medicine, Japan in 1990. He joined Department of Pediatrics, Mie University in 1984 and has continued clinical practice and research on pediatric cancer until now. He worked as a post-doctoral fellow at Department of Medicine, University of California at San Diego from 1994 to1996. He engaged in international medical cooperation by the Japanese government in Ghana and Tanzania. He promoted to Professor of Mie University Graduate School of Medicine in 2009 and is currently in the position of Dean, Mie University Graduate School of Medicine/Faculty of Medicine. He is a member of SIOP (Continental president-Asia) and Japanese Society of Pediatric Hematology/Oncology (Auditor). He has qualifications of Board Certified Pediatrician, Board Certified Hematologist and Board Certified Pediatric Hemato-oncologist in Japan. His major research interests include cancer chemotherapy, pharmacogenomics, psychosocial care for children with cancer and survivorship care.

Message

Hiroki Hori, M.D., Ph.D.
Continental President of Asia, International Society of Paediatric Oncology (SIOP) and Executive Council Member, Asian Pediatric Hematology and Oncology Group (APHOG)

I would like to extend my congratulation on APHOG annual meeting 2023. Since APHOG started it's academic activities, we have known each other through the screen because of the COVID-19 pandemic. This meeting is the first opportunity for APHOG members to have face-to- face discussions. I expect that medical professionals and scientists from Asian countries will share advanced knowledge and technology on childhood cancer care and enhance global and regional collaboration toward a goal "no child should die of cancer" through this hybrid meeting. I would express my deepest appreciation to Dr. Akira Nakagawara and all APHOG members for their efforts to this precious event.

Chairpersons:

RASHMI DALVI, MBBS, MD, DCH

Professor & Head, Dept of Pediatrics , Consultant Pediatric Hematologist Oncologist
Bombay Hospital Institute of Medical Sciences
Visiting Consultant, NH-SRCC Children's Hospital
Visiting Faculty PHO & BMT: LTMG Medical College & Hospital Mumbai, India

Immediate Past Continental President SIOP Asia (2018-2021)
APHOG : Steering committee member & SIOP/WHO-GICC liaison
Co-Chair, SIOP Membership Committee (2022)
Member, Steering Committee of SIOP-PARC program (Program for Advancing Research Capacity in Pediatric Oncology)
Member, SIOP Committee for Education & Training
Lead for SIOP Global Mapping Project for Asia
SIOP Asia liaison: Rare Cancers ESMO-Asia & Asian Society for Oncofertility Member Ethics Committee, Stem Cell Committee, King Edward Memorial Hospital, Mumbai
Board Member, Cherish Life India (Childhood Cancer NGO)
Founding Member InPOG (2010-15)
Member, Editorial Advisory Board, Pediatric Hematology Oncology Journal
Member, SIOP Governance Committee (2020-2021)
Chair, SIOP-PODC Committee on Training & Education (2010-2013)
SIOP-PODC Consultant (1994-2010)
Office Bearer SIOP Asia Board in various capacities: (2001-2013)
Past Chairperson, PHO Society, India* (2009-2012)
ICON* Ethics Committee Chairperson (2001-2003) & Member(2004-2016)

Muhammad Saghir Khan, Dr. (Pakistan)

- Co-Chair of SIOP Global Health Network (formerly known as SIOP PODC Committee; Pediatric Oncology Developing Country of International Society of Pediatric Oncology)
- Member of SIOP Board of Directors
- Chair, SIOP Education and Training Committee
- Member, SIOP Governance Committee
- Member, SIOP Membership Committee
- Member, SIOP Publication and Endorsement Committee
- Member, SIOP Scientific Program Advisory Committee (SPAC)
- Member, SIOP PARC Committee (Program for Advancing the Research Capacity for Pediatric Cancer Clinical Trials in Low-Income Countries and Middle-Income Countries)
- Member, Editorial Board Pediatric Blood & Cancer (PBC)
- Member, Executive Committee Asian Pediatric Hematology and Oncology Group (APHOG) Co-Chair, Taskforce for POEM group's 10th Anniversary Celebrations

SOCIÉTÉ INTERNATIONALE D'ONCOLOGIE PÉDIATRIQUE
SIOP
INTERNATIONAL SOCIETY OF PAEDIATRIC ONCOLOGY

SIOP ASIA
the Asian Society for Paediatric Oncology

APHOG
Asian Pediatric Hematology and Oncology Group

Mogokoro Organization for Childhood Cancer
NPO法人 小児がん・まごころ機構

amazon

Abstracts
&
Speakers' profiles

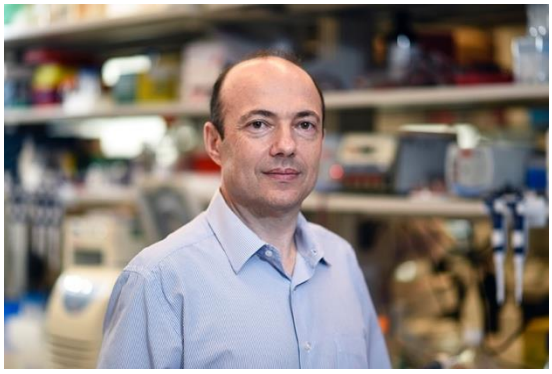
Session 1: (9:05-10:35; 30min talk with discussion for each speaker)

1. **Leonid S. Metelitsa** Baylor College of Medicine, Texas Children's Hospital, USA
   "Anti-GD2 CAR-NKT cells are safe and produce antitumor responses in patients with relapsed/resistant neuroblastoma"
2. **Susan L. Cohn** The University of Chicago, USA
   "Advancing Research with the International Neuroblastoma Risk Group Data Commons"
3. **Alice L. Yu** Chang Gung Memorial Hospital & Academia Sinica, Taiwan
   "Advances in anti-GD2 immunotherapy of high risk neuroblastoma"

Session 2: (10:45-12:15; 30min talk with discussion for each speaker)

4. **Kimikazu Matsumoto** National Center for Child Health and Development, Japan
   "Japanese trials for high-risk neuroblastoma"
5. **Hiroyuki Shimada** Stanford University School of Medicine, USA
   "Molecular pathology of high-risk neuroblastoma"
6. **Godfrey C. Chan** Hong Kong Children's Hospital, HK, China
   "Potential APHOG trials for neuroblastoma in Asia"

Leonid S. Metelitsa, M.D./Ph.D.



Dr. Leonid Metelitsa is an Endowed Chair in Cancer Immunotherapy at Texas Children's Hospital, Director of the Center for Advanced Innate Cell Therapy, and Professor of Pediatrics-Oncology at Baylor College of Medicine in Houston, Texas, USA.
Dr. Metelitsa earned his MD at Tver State Medical University in Tver, Russia and his PhD in Hematology/Oncology from the N.N. Blokhin Memorial Cancer Research Center of Russian Federation in Moscow, Russia. He completed his postdoctoral fellowship in Tumor Immunology at Children's Hospital Los Angeles/Keck School of Medicine at University of Southern California, where he remained as Assistant Professor in the Department of Pediatrics and Division of Hematology-Oncology. He then accepted an Associate Professor position at Baylor's Department of Pediatrics, where he remains today as a tenured Professor. After becoming an independent investigator in 2003, he has focused on understanding the mechanisms of natural killer T (NKT) cell localization to the tumor site and the function of these cells in the context of the tumor microenvironment. His lab was the first to describe the critical role that inflammation plays in the biology and clinical behavior of neuroblastoma. His research has been continuously supported by grants from the National Institutes of Health/National Cancer Institute, the US Department of Defense, the Cancer Prevention and Research Institute of Texas, Leukemia and Lymphoma Society, and other competitive sources. The technologies developed in his lab for human NKT-cell isolation, genetic modification, and expansion to clinical scale have led to the first-in-human clinical trials of CAR NKT cells (NCT03294954) and "off-the-shelf" allogeneic NKT cells (NCT03774654) with licensing to industry.

Anti-GD2 CAR-NKT cells are safe and produce antitumor responses in patients with relapsed/resistant neuroblastoma

Leonid S. Metelitsa, M.D./Ph.D.
Texas Children's Hospital and Baylor College of Medicine, Houston, TX, USA

Vα24-invariant natural killer T cells (NKTs) have antitumor properties that can be enhanced using chimeric antigen receptors (CARs). We have conducted a phase 1 clinical trial of autologous NKTs co-expressing a GD2-specific CAR with interleukin (IL)15 (GD2-CAR.15) in 12 children with relapsed and therapy-resistant neuroblastoma (NB) using standard 3+3 dose-escalation schema (NCT03294954). Primary objectives were safety and determination of maximum tolerated dose. The antitumor activity of GD2-CAR.15 NKTs was assessed as a secondary objective, and immune response was evaluated as an additional objective. No dose-limiting toxicities occurred, and one patient experienced grade 2 cytokine release syndrome resolved by tocilizumab. Antitumor responses were evaluated using International Neuroblastoma Response Criteria. The overall response rate was 25% (3/12) and disease control rate was 58% (7/12) including four patients with stable disease (SD), two partial responses (PR), and one complete response (CR) that lasted 12 months. The frequency of CD62L+ NKTs in products correlated with CAR-NKT expansion in patients and was higher in responders than non-responders (p=0.002). Thus, GD2-CAR.15 NKTs are safe and mediate objective responses in NB patients.

Susan L. Cohn, MD

I have devoted my career to caring for children with neuroblastoma and conducting clinical and translational research focused on understanding the biologic underpinnings of high-risk neuroblastoma to identify new therapeutic targets. I have also led efforts to develop risk classification algorithms in the International Neuroblastoma Risk Group (INRG) Task Force and the Children's Oncology Group (COG). Through my leadership positions in COG, I have worked with my colleagues to translate laboratory findings into clinical trials for children with neuroblastoma. I co-Chair the INRG Task Force with Drs. Andrew Pearson, Julie Park and Gudrun Schleiermacher. I am currently working closely with Dr. Mark Applebaum and Dr. Chuan He at the University of Chicago to investigate the epigenomic landscape of neuroblastoma and to develop liquid biopsy epigenomic biomarkers for response and survival. We are also conducting studies to determine the biological implications of the m^6A epitranscriptome and are testing the anti-neuroblastoma activity of inhibitors of METTL3, a writer that installs m^6A RNA modifications. I am also collaborating with Dr. Desai to investigate the prognostic value of the immunogenomic determinants of the tumor microenvironment in high-risk neuroblastoma and other biomarkers to optimize treatment strategies for children with high-risk neuroblastoma. I am also dedicated to training the next generation of leaders in pediatric cancer and academic pediatrics, and I have mentored undergraduate students, medical students, residents, fellows and junior faculty, many of whom have gone on to have successful academic careers. I am the Inaugural Director of Faculty Scholars Program in the Department of Pediatrics at the University of Chicago in 2020 and also serve as the Director for Faculty Development, University of Chicago's Comprehensive Cancer Center.

Advancing Research with the International Neuroblastoma Risk Group Data Commons

Susan L. Cohn, MD
The University of Chicago, Chicago Illinois, USA

There is a culture of international collaboration and data sharing within the pediatric neuroblastoma community as demonstrated by the development of the International Neuroblastoma Risk Group (INRG) Data Commons. This cloud-based ecosystem houses clinical information from patients enrolled clinical and cooperative group biology studies conducted around the world. Importantly, the resource is able to co-locate neuroblastoma-related data, analysis tools, and high-performance computational resources in a secure environmental. The INRG Data Commons currently includes information from more than 24,000 individual patients with neuroblastoma, the largest such neuroblastoma data repository in the world. The INRG data are available to the research community, and seminal studies, never possible with smaller patient cohorts, have been conducted (https://inrgdb.org/research/). Data from new patients and updated outcome data are uploaded as cooperative groups approve the data transfer. New data fields for ALK, segmental and numerical chromosomal, and patients with relapsed neuroblastoma are currently being developed. An INRG Strategy Development Committee, Mentorship Program, and Bootcamps have been established to assist young investigators interested in conducting INRG research projects. Future studies analyzing INRG data with enriched genomic annotation are likely to further advance our understanding of neuroblastoma biology and provide insight for novel treatment approaches.

Alice L. Yu, MD, PhD.

Alice L. Yu, MD, PhD, is an Academician of Academia Sinica, Taiwan. She is a Distinguished Chair Professor & Deputy Director of the Institute of Stem Cell & Translational Cancer Research at Chang Gung Memorial Hospital, and Professor Emeritus at the University of California in San Diego.

As a pioneer in cancer immunotherapy, Dr. Yu has taken an anti-GD2 monoclonal antibody (Dinutuximab) from preclinical to phase III clinical trial, culminating in its FDA approval for the treatment of high-risk neuroblastoma in 2015. This marks the first immunotherapeutic agent to target glycolipid worldwide. She has continued to improve the efficacy of anti-GD2 immunotherapy through international collaboration. She is also working on the most prevalent cancer-associated glycolipid, Globo H ceramide, and demonstrated the adverse impact of Globo H expression on the outcome of patients with hepatoma, cholangiocarcinoma and gallbladder cancer. Her group also uncovered the roles of Globo H in cancer as an immune checkpoint molecule and angiogenic factor, providing rationales for the ongoing development of Globo H-targeted immunotherapeutics. Recently, she have identified several novel markers for cancer stem cells and is developing CSC-targeted therapeutics.

She has received many awards, including the Pediatric Oncology Award by the American Society of Clinical Oncology (ASCO) in 2020, Excellence in Technology Transfer Award from Federal Laboratory Consortium, USA in 2016, The 55th Academic Award from the Ministry of Education, Taiwan, Year 2000 “Key to Life” Award, Leukemia & Lymphoma Society, USA, etc..

Advances in anti-GD2 immunotherapy of high risk neuroblastoma

Alice L. Yu, MD, PhD.

Chang Gung Memorial Hospital and Academia Sinica, Taiwan

The approval of Dinutuximab, an anti-GD2 antibody, for the treatment of high-risk neuroblastoma in 2015 marks the first new agent targeting a glycolipid molecule. In 2017, Dinutuximab-β produced in CHO cells received EMEA, based on SIOPEN study. A long term follow-up (median 9.97yrs) of the COG randomized cohort continued to show significant survival benefit of immunotherapy over standard therapy, however, the differences narrowed due to late relapses. The non-randomized cohort of 1183 patients showed five-year EFS and OS of 61% and 72%, respectively, confirming the benefit of GD2-targeted immunotherapy. To further improve the efficacy, Hu14.18k322a derived from humanized ch14.18, in combination with induction chemotherapy showed impressive 97% (60/62)) end-of-induction partial response or better. The 3-year EFS/OS were 73.7% and 86.0%, respectively. Naxitamab, another humanized anti-GD2 3F8, received FDA approval in 2020 for relapsed/refractory neuroblastoma. Other strategies to improve its efficacy by combination with anti-PD1, GD2-CAR cell therapy are under development.

Kimikazu Matsumoto, MD, PhD

Office Address: Children's Cancer Center,
National Center for Child Health and Development,
2-10-1 Okura, Setagaya-ku, Tokyo,
157-8535, JAPAN
Telephone number: +81-3-3416-0181 ext.7703
Fax number: +81-3-3416-2222
E-mail: matsumoto-kmk@ncchd.go.jp

Education:

1987	Graduated, Nagoya University School of Medicine

Professional Experience:

2013 - Present	Director, Children's Cancer Center, National Center for Child Health and Development
2002 – 2013	Medical staff at Japanese Red Cross Nagoya First Hospital, Department of Pediatrics
1998 – 2002	Medical staff at Toyota Memorial Hospital, Department of Pediatrics
1996 – 1998	Medical staff at Nagoya University School of Medicine, Department of Pediatrics
1994 – 1996	Post-doctoral fellow at Fred Hutchinson Cancer Research Center, USA (Dr. Claudio Anasetti)
1989 – 1994	Medical staff at Japanese Red Cross Nagoya First Hospital
1988– 1989	Trainee at Nagoya University School of Medicine, Department of Pediatrics
1987 – 1988	Trainee at Kakegawa City General Hospital

Japanese trials for high-risk neuroblastoma - 15 years experience

Kimikazu Matsumoto, MD, PhD
Children's Cancer Center, National Center for Child Health and Development, Tokyo, JAPAN

Japan Children's Cancer Group -Neuroblastoma Committee (JCCG-NB; JNBSG) has conducted nation-wide clinical trials for 15 years. JN-H-07 was the first trial which was a single-arm, late phase II trial for high-risk neuroblastoma treatment. The second JN-H-11 trial aimed to establish the feasibility of "delayed local treatment", in which tumor resection was performed after completing all chemotherapeutic courses including myeloablative high-dose chemotherapy. JN-H-15 was a phase II nation-wide clinical trial which included "delayed local treatment", ICE and Bu/Mel regimen. JN-H-15 protocol has improved the outcome of high-risk neuroblastoma especially in *MYCN* amplified tumor. JN-H-20 trial is a new protocol which include KIR-ligand mismatched allogeneic cord blood transplantation as a consolidation therapy. The structure and dosage of anti-tumor drugs of our Japanese trials would be compared with SIOPEN and COG studies.

Hiroyuki Shimada, MD, PhD, FRCP (Hon)

Dr. Hiroyuki Shimada is Professor of Pathology and of Pediatrics at Stanford University School of Medicine in California. Born in Tokyo, Japan, Dr. Shimada completed MD (1973) and PhD (1982) at Yokohama City University School of Medicine, Yokohama, Japan. He went on to complete his pathology training at the Children's Hospital (now the Nationwide Children's Hospital) and Ohio State University, Columbus, Ohio, USA. Before moving to Stanford University in 2019, he was Professor of Pathology (Clinical Scholar) at University of Southern California Keck School of Medicine and working at Children's Hospital Los Angeles.

Dr. Shimada served as Chair of the International Neuroblastoma Pathology Committee (1999-2017) and is founder of the International Neuroblastoma Pathology Classification (INPC). As Director of the Children's Oncology Group (COG) Neuroblastoma Pathology Reference Laboratory since 2001, he has been actively reviewing pathology samples of ~700 neuroblastoma cases per year from United States, Canada, Australia, and New Zealand. Pathology review results according to the INPC have been providing critical information for patient stratification and protocol assignment in the COG international neuroblastoma clinical trials.

His contributions to the field have been recognized by numerous honors and awards, including The Lotte Straus Prize in 1989 and The Enid Gilbert-Barness Prize in 2018 - both from the Society for Pediatric Pathology, The Eleanor Humpherys Visiting Professorship at Department of Pathology, University of Chicago in 2005, an Honorary Fellowship from the Royal College of Pathologists of Australasia in 2012, and The Lawrence G. Crowley Endowed Lectureship in Pediatrics at Stanford University in 2018. Recently he was presented with The Fred W. Stewart Award from the Memorial Sloan Kettering Cancer Center in 2022 and The Presidential Distinguished Colleague Award from the Society for Pediatric Pathology in 2023.

Molecular Pathology of High-Risk Neuroblastoma

Hiroyuki Shimada, MD, PhD
Department of Pathology, Stanford University School of Medicine, USA

Based on the latest analyses of COG neuroblastoma cases, the International Neuroblastoma Pathology Classification significantly distinguished Favorable Histology (FH) Group (5-yr EFS: 88.1+/-0.9%; 5-yr OS: 96.4+/-0.5%) and Unfavorable Histology (UH) Group (EFS: 54+/-1.3%; OS: 65.6+/-1.3%) with very high hazard ratios (95% CI) [EFS: 4.41(3.86 to 5.03); OS: 10.50 (8.44 to 13.04)]. Survival-tree regression analysis demonstrated that High-risk neuroblastomas were found exclusively in the UH group with stage M disease. Further investigation of UH Group supports that High-risk neuroblastomas are composed of molecularly different subgroups:

1. MYC subgroup: This subgroup includes tumors overexpressing MYCN protein or MYC (c-MYC) protein. MYCN overexpression is observed in >90% of *MYCN*-amplified neuroblastomas, whereas MYC overexpression is rarely found with *MYC* amplification.
2. TERT subgroup: Long-range genomic rearrangements of *TERT* are responsible for the protein overexpression causing telomere abnormality in this subgroup.
3. ALT (Alternative Elongation of Telomeres) subgroup: Tumors in this subgroup also have telomere abnormality. Most of the ALT phenotype is associated with ATRX loss, and rare cases are seen with DAXX loss.
4. Null subgroup: There are still High-risk neuroblastoma cases without MYC-family protein overexpression, TERT overexpression, and ALT phenotype.

ALK protein overexpression by the gene mutation/rearrangement/amplification seems to be responsible to some neuroblastomas. However, in animal models, activated *ALK* efficiently induces neuroblastoma in combination with *MYCN* overexpression.

Godfrey Chi-Fung Chan

DMD(UE, Phil), MD(UE, Phil), MD(HKU), LMCHK, MSc(U Birmingham, UK), Dip Palliative Med(U Wales, UK), FHKAM, FHKCPaed, FRCP(Edin), FRCPCH(UK), FAAP(USA)

Prof. Chan graduated from Dentistry and Medicine respectively from University of the East, Philippines. He joined the Department of Pediatrics, HKU in 1989. Then he pursued fellowship training at the St. Jude Children's Research Hospital (1993-1996). He subsequently obtained Dip of Palliative Medicine (U Wales, 1997) and MSc (U Birmingham, 1999). He was promoted to Clinical Professor of HKU in 2009 and was awarded Tsao Yen-Chow Endowed Professorship of Pediatrics in 2013. He was the Head of the same Department from 2012 to 2022.

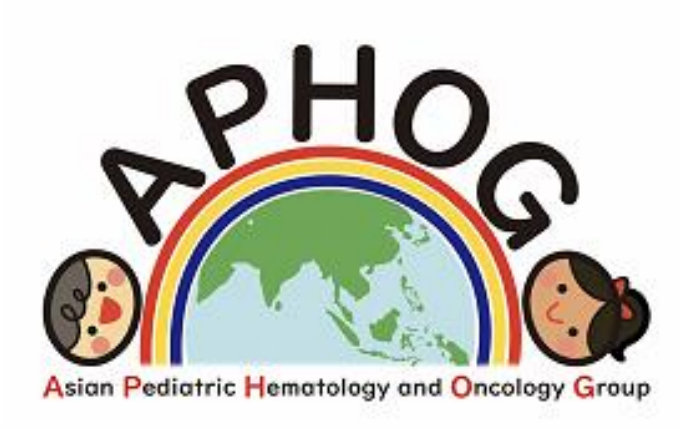
He served as the Chief of Service of Departments of Pediatrics & Adolescent Medicine, Queen Mary Hospital (2012-2018); Hong Kong Children's Hospital (2018-2022); Gleneagle Hospital (2015-2022); and HKU-Shenzhen Hospital (2012-now). He published >400 indexed papers and is the current Chief Editor of HK Journal of Paediatrics. He owned 8 patents on stem cells research (MSCs and iPSC). He received multiple international awards (ANR, SIOP, ASPR, Endeavor Executive Award-Australian Government, Outstanding Pediatrician-APPA) for his clinical and laboratory research works. He is currently the Continental Chairman of ANR, Secretary of APHOG, and Advisory Board Member of St Jude-VIVA Foundation.

His major research interests include immunotherapy for pediatric neurogenic tumors and the drug resistant mechanisms of cancer microenvironments.

Potential APHOG Trials for Neuroblastoma in Asia

Godfrey Chi-Fung Chan
Department of Paediatrics & Adolescent Medicine, The University of Hong Kong
& Department of Paediatrics, Hong Kong Children's Hospital

With the advances of therapies for high-risk neuroblastoma, we witness significant improvement in the survival. However, new treatments such as anti-GD2 are very expensive and many patients in Asia cannot afford. As an advocate for conducting our own clinical trials in Asia, APHOG should investigate what may be the best approaches for countries with different economic background. For those that can gain access to the anti-GD2 therapy, we can test whether adding it upfront with chemotherapy will yield better result. Another approach is to add HDAC inhibitor to MIBG/DOTA treatment. Adding GD2-CAR-T or GD2/GD3 tumor vaccine to the maintenance phase is another approach. But for those countries which cannot afford all these treatments, what may be the options? Use of KIR ligand mismatched haploidentical hematopoietic stem cell transplant (HSCT) rather than autologous HSCT as consolidation therapy may be one alternative. But the disease status should be monitored closely so donor lymphocytes infusion can circumvent the relapse. Prolonging or intensifying chemotherapy will not benefit neuroblastoma patients. Collaborative group should be formed under APHOG to facilitate treatment design that can match the actual situation of different countries. APHOG can also help to negotiate with drug companies to run sponsored trials in Asia.



APHOG Executive Council members

Dr. Akira Nakagawara	**Chairman, APHOG (2021~); President, SIOP Asia (2021~2015), Japan**
Dr. Godfrey C. Chan	**Secretary, APHOG (2021~); Hong Kong SAR, China**
Dr. Purna Kurkure	**Treasurer, APHOG (2021~); President, SIOP Asia (2007~2010), India**
Dr. Bharat Agarwal	**President, SIOP Asia (2001~2004) $ Gen. Secretary, SIOP (2005~2011), India**
Dr. Chi-Kong Li	**President, SIOP Asia (2015~2018), Hong Kong SAR, China**
Dr. Rashmi Dalvi	**President, SIOP Asia (2018~2021), India**
Dr. Hiroki Hori	**President-elect, SIOP Asia (2020~), Japan**
Dr. Saghir Khan	**Chair, PODC, SIOP (2019~), Pakistan**
Dr. Alice Yu	**COG, Pioneer of Cancer Immunotherapy, Taiwan**