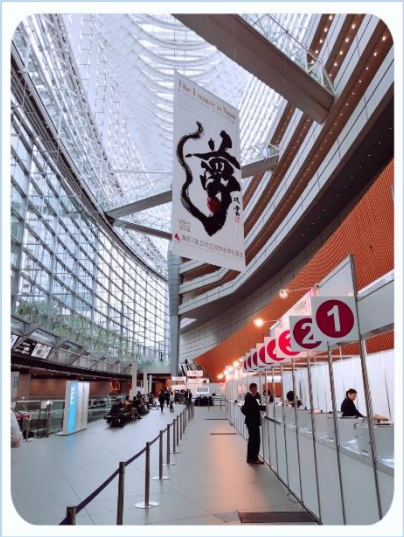
The 81st Annual Meeting of the Japanese Society of Hematology,

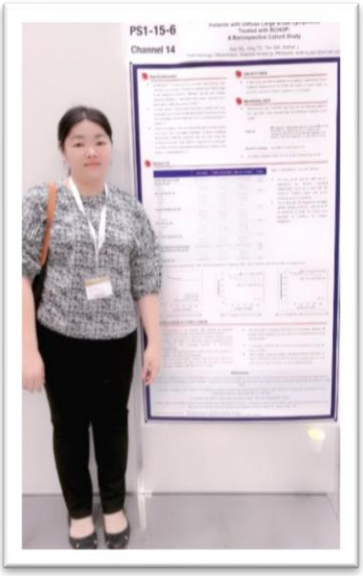
October 11-13, 2019 TOKYO JAPAN

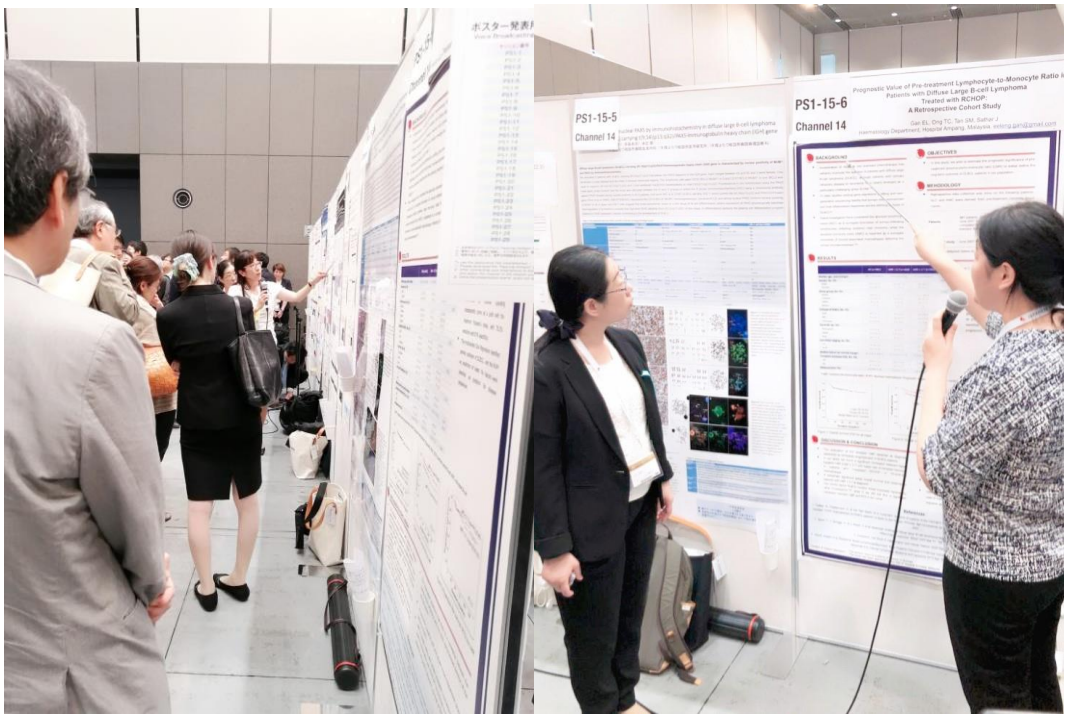
A report by Gan Ee Leng, Haematology trainee, Hospital Seremban / Hospital Ampang



The meeting was held at the Tokyo International Forum on October 11 to 13, 2019. The annual meeting takes place when Tokyo is filled with ambience of high spirits and expectations in conjunction with Rugby World Cup 2019, and the enthronement ceremony of the Japanese Emperor which will be carried about 10 days after the meeting. The main theme of the annual meeting is "The Future is Now", which is a simple phrase, carries an important underlying message, "The future does not come to us simply, but is the result of what we do today." The word "dream" is translated as "夢" in Japanese and the word was written by a famous Japanese calligrapher, Souun Takeda, with the red ball in the middle of "夢" in the poster is meant to represent a red blood cell.

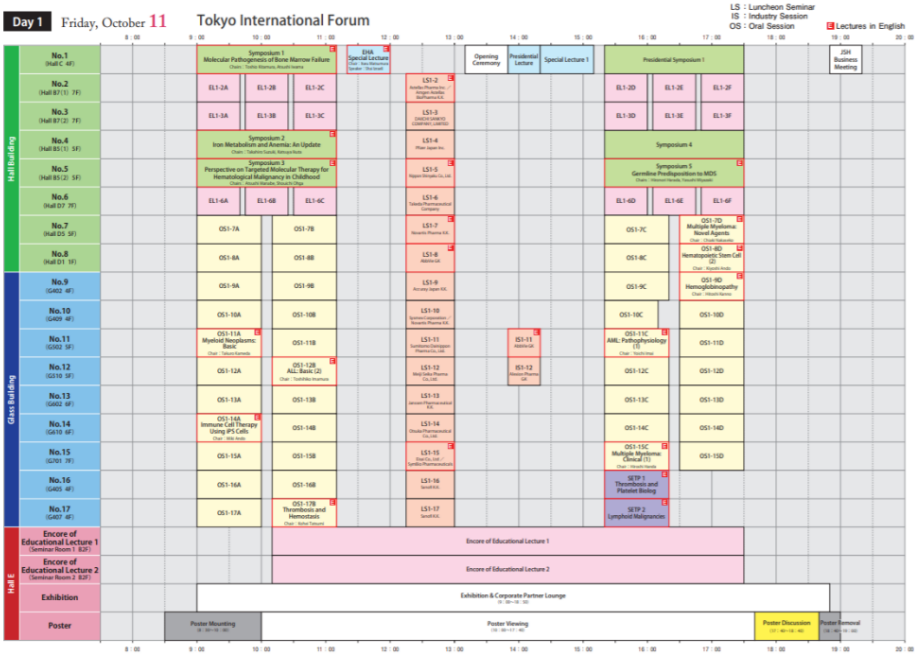
The opportunity to attend this workshop was invaluable and I was grateful to be able to share my poster presentation during the meeting. My topic of presentation is "Prognostic Value of Pre-treatment Lymphocyte-to-Monocyte Ratio in Patients with Diffuse Large B-cell Lymphoma Treated with RCHOP: A Retrospective Cohort Study". All participants need to prepare a 3 minutes oral presentation during the poster discussion session, followed by 2 minutes questions and answers. My poster presentation session was grouped under 'B cell lymphoma", and it was chaired by Professor Chisako Iriyama from Department Hematology, Fujita Health University, Toyoake, Japan. The best poster award was given to Dr Hanh Luong from Nagasaki University, presenting incidence of malignant lymphoma in Nagasaki Cancer registries, 1985-2012.





“Poster discussion session “

The 3 days conference was packed with many lectures and symposium, including EHA/ASH special lectures, educational lectures, presidential lectures, special lectures as well as luncheon seminars and industry sessions being carried out concurrently in 17 lecture halls and 2 seminar rooms. I was only able to attend most of the English-speaking lectures on day 1 and day 3 of conference as day 2 conference was cancelled due to typhoon Hagibis. I would like to share some key point messages that I had learned from the meeting.



Day 1 program at a glance

Opening ceremony:
(L) Professor Norio Komatsu from Department of Hematology Juntendo University, the congress president giving speech on day 1 opening ceremony
(R) AI robots dancing for opening ceremony

Below are the few lectures that I find it interesting:
"Cellular recycling by autophagy – lessons from yeast"

By Professor Dr Yoshinori Ohsumi from Institute of Innovative Research, Tokyo Institute of Technology, Tokyo, Japan

Every cellular event is achieved through a balance between synthesis and degradation of protein. We now know that cellular degradation is highly regulated and is as equally important as synthesis. Taking advantage of yeast as a model system, Professor Dr Yoshinori and his team, successfully isolated many autophagy-defective mutants, revealing 18 ATG genes essential for autophagy. The encoded ATG proteins function in the sequestration of cytoplasmic constituents into a specialized membrane structure, the autophagosome. Those core ATG proteins fall into six functional groups, including two unique ubiquitin like conjugation systems and a PI3 kinase complex. Soon they found that most of the ATG genes are well conserved from yeast to mammals and plants, indicating that autophagy was acquired at an early stage in the evolution of eukaryotic cells. The identification of the ATG genes completely changed the landscape of autophagy research. Using the ATG genes as a starting point, studies of the physiological function and mechanism of autophagy are now under way in various organisms, cells, organs and individuals. Up to now a truly broad range of physiological functions of autophagy have been unveiled. Autophagy plays critical roles not only in nutrient recycling, but also intracellular clearance through the elimination of harmful proteins and organelles, which is relevant to many diseases. The membrane dynamics of autophagy, which occur via unique de novo membrane and compartment formation events, raises various interesting questions that remain to be answered. It is necessary to study carefully on the degradation process and also fate of the degradation products, and the

yeast model system provides a clear advantage in the biochemical analyses of these processes. They also found that autophagy plays important roles in cytoplasmic ion homeostasis. Moreover, they found that autophagy is involved not only in protein but also RNA turnover.

“High risk JAK STAT driven acute lymphoblastic leukemia lessons from Down syndrome”

By Professor Dr Shai Izraeli from Schneider Children's Medical Center of Israel, Division of Pediatric Hematology and Oncology, Israel

Somatic activation of JAK/STAT signalling in B cell precursor ALL is most commonly caused by aberrant expression of CRLF2 that by heterodimerization with interleukin 7 receptor alpha (IL7R) creates the receptor to Thymic Stromal Lymphopoietin (TSLP). This receptor signals through JAK1 and JAK2. Often additional activating mutations in JAK enzymes or CRLF2 or IL7R cause constitutive activation of this pathway. These aberrations characterize 50% of the ALLs in children with Down Syndrome and 5-10% of ALLs in children and young adults without Down Syndrome. The prognosis of these leukemia is poor. Importantly, the discovery of Ruxolitinib, the JAK1 and JAK2 inhibitor can act as a double edge sword. Low dose Ruxolitinib paradoxically enhances survival JAK driven B-ALL while high dose eliminates the leukemic cells. This observation may represent a general phenomenon of B-ALL cells that could complicate treatment with signalling inhibitors.

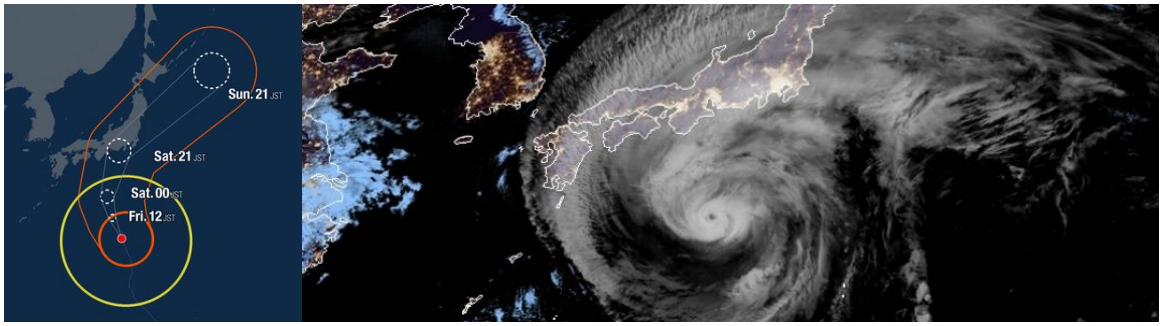
“Iron refractory iron deficiency anaemia: pathophysiology and clinical management”

By Professor Dr Dorine W. Swinkels from Laboratory Medicine, Radboud University Medical Center, Netherlands

Patients with Iron Refractory Iron Deficiency Anemia (IRIDA) often present in childhood with fatigue and iron deficiency anemia. IRIDA is a rare autosomal recessive anemia caused by mutations in the TMPRSS6 gene encoding Matriptase-2 (MT-2). MT-2 is a liver transmembrane serine protease that plays an essential role in down-regulating hepcidin, the key regulator of iron homeostasis. Hepcidin decreases blood iron concentrations by limiting dietary iron absorption and iron release from stores. To date, 78 different TMPRSS6 variants have been identified in 115 patients of 85 families worldwide, all spread along the MT-2 large ectodomain. Hallmarks of IRIDA are inappropriately high hepcidin levels that result in remarkably low transferrin iron saturation (TSAT) and low/normal serum ferritin and as a consequence, microcytic hypochromic anaemia. The majority of IRIDA patients are refractory to oral iron. Current

treatment therefore consists of parenteral iron administration, that leads to partial and incomplete correction of anaemia. In the absence of inflammation, a decreased TSAT/hepcidin ratio has been reported as promising diagnostic tool for IRIDA. However, implementation of this ratio in the clinic requires the definition of its gender and age specific clinical decision limits, preferably defined by a standardized hepcidin assay. Recently, a new digenic form of IRIDA due to a heterozygous mutation of TMPRSS6 combined with a variant in a BMP receptor involved in hepcidin regulation was reported, suggesting that variants in genes regulating hepcidin function or its plasma levels other than TMPRSS6 may underly the phenotype of patients with heterozygous TMPRSS6 variants. Further studies are required to elucidate the contribution of other genetic and environmental factors in the pathophysiology and clinical penetrance of TMPRSS6 variants and to determine the optimal treatment regime. However, in order to prevent misdiagnosis and unnecessary invasive diagnostic workup, the first challenge for clinicians remains the recognition of the disorder and its differentiation from other common causes of microcytic anaemia.

Unfortunately, day 2 conference was cancelled due to Hagibi's typhoon (12th October 2019)



The Japanese Meteorological Agency (JMA) called for the public to remain vigilant for rain and gusts of wind, after it issued an "Emergency Weather Warning (Level 5)." Evacuation advisories have been issued throughout much of the Tokyo region, affecting tens of millions of people. The Japanese capital is in lockdown, with usually busy streets abandoned amid torrential rain. The storm had weakened as it approached Japan but still remained highly dangerous, with maximum winds of up to 195 kilometers per hour, which is equivalent to a Category 3 Atlantic hurricane. All flights to and from Tokyo and nearby airports have been cancelled until at least Sunday morning. All bullet trains between Tokyo, Nagoya and Osaka are also cancelled, as are most non high-speed trains.

All in all, the above event was extremely fruitful and we managed to return to our country safely. I wish to record my thanks and appreciation to MSH for the kind sponsorship and hope to be able to attend similar events in the future.

Prepared by, Gan Ee Leng 20.10.2019