The 40th Sysmex Scientific Seminar Introduction

June 3rd (Sat.)

Planning board

Theme: Making Further Advancements in the Treatment of Hematologic Diseases - Frontline therapies and future prospects -

Professor Yutaka YATOMI , M.D., Ph.D.,
The Department of Clinical Laboratory Medicine,
The University of Tokyo, Graduate School of Medicine

【Summary】

The second half of the 20th century has seen explosive developments in life sciences and molecular biology. The fruits of research in these fields have always been adopted as ground breaking medical technologies for both diagnosis and treatment of hematologic diseases earlier than in other areas. Such application is obvious, for instance, in genetic diagnosis, molecular targeted drugs, antibody drugs and stem cell transplantation. This positioning of medical care for hematologic diseases would probably remain unchanged in the coming years.

In this memorable 40th Sysmex Scientific Seminar, we will be discussing the rapidly advancing medical care for hematologic diseases. In particular, the speakers will introduce some cutting-edge technologies used for paroxysmal nocturnal hemoglobinuria, myeloproliferative neoplasms, genomic analysis-based diagnosis of hematopoietic tumors, thrombosis as an example of thrombotic and hemostatic diseases, and hemophilia. We also hope that this seminar would give us a glimpse of advanced medical care scenarios of the future.

The 40th Sysmex Scientific Seminar
Introduction ①

June 3rd (Sat.)

1st Lecture

TOKYO 10:10 ▶

Frontline medical care for paroxysmal nocturnal hemoglobinuria

Professor Yuzuru KANAKURA , M.D., Ph.D.,
The Department of Hematology and Oncology,
Osaka University Graduate School of Medicine

【Summary】

Paroxysmal nocturnal hemoglobinuria (PNH) is a clonal disease of hematopoietic stem cells with the three major symptoms of complement-mediated intravascular hemolysis, thrombosis, and bone marrow failure. Acquired Pig-A gene mutations lead to deficiency of GPI-anchored proteins such as the complement regulating factors CD59 and DAF (CD55) which in turn results in intravascular hemolysis. This hemolysis causes reduction of nitrogen monoxide in the blood and other conditions, and the patient shows various symptoms like abdominal pain, dysphagia and fatigue. The humanized monoclonal antibody drug eculizumab has been developed against the complement factor C5, which plays a key role in complement-mediated hemolysis, in order to improve the symptoms arising from anemia and intravascular hemolysis in PNH. Eculizumab is now regarded as a groundbreaking drug because of its marked hemolysis inhibiting effect, ability to alleviate various symptoms arising from the hemolysis, antithrombotic effect and kidney disease improving action. On the other hand, it has come to light that some cases in Japan do not respond to this drug and that a polymorphism of the C5 gene, which is unique to Japan (and some other parts of Asia), is responsible for this. The development of various types of new therapies is currently underway. We will examine their prospects as well, along with the latest findings on PNH.

sysmex

The 40th Sysmex Scientific Seminar
Introduction ②

June 3rd (Sat.)

2nd Lecture

KOBE 11:10 ▶

Myeloproliferative neoplasms in the context of gene mutations

Professor Norio KOMATSU , M.D., Ph.D.,
Department of Hematology,
Juntendo University School of Medicine

【Summary】

A gene mutation common to three myeloproliferative neoplasm (MPN) diseases, namely, polycythemia vera (PV), essential thrombocythemia (ET) and primary myelofibrosis (PMF), was discovered in 2005. This was the constitutively active JAK2V617F mutation. Since then mutations of JAK2exon12, MPL and CALR were also discovered. The fourth edition of the WHO Classification of 2008 adopted the JAK2V617F mutation as an essential diagnostic marker for MPN. In the revised WHO Classification of 2016, the MPL and CALR mutations were also adopted as essential criteria in addition to the JAK2 mutation. We developed our own method of detecting these mutations and analyzed their prevalence in the Japanese population. The results showed that their prevalence in PV, ET and PMF patients was about the same as in Western countries. In the meantime it came to light that there were a large number of cases for which a definitive diagnosis could not be made for reasons like inability to differentiate whether a patient had ET or PMF because the bone marrow test was not done despite the patient having one of these gene mutations, and chronic myelogenous leukemia could not be ruled out because the Philadelphia chromosome analysis/bcr-ab1 fusion gene analysis was not done. In the first half of this lecture, I shall discuss about the current status of medical care for MPN in Japan and in the second half the results of our studies on the molecular mechanism of how the CALR mutation leads to onset of ET or PMF.

sysmex

The 40th Sysmex Scientific Seminar
Introduction ③

June 3rd (Sat.)

3rd Lecture

KOBE 13:15 ▶

hematopoietic tumor

Professor Seishi OGAWA , M.D., Ph.D.,
Department of ,
Faculty of Medicine, Kyoto University

The 40th Sysmex Scientific Seminar
Introduction ④

June 3rd (Sat.)

4th Lecture

TOKYO 14:25 ►

Antithrombin resistance: A new inherited thrombophilia

Professor Tetsuhito KOJIKMA , M.D., Ph.D.,
Department of Pathophysiological Laboratory Sciences,
Nagoya University Graduate School of Medicine

【Summary】

Venous thromboembolism is a multifactorial disease that develops from the interaction of various congenital and acquired risks. In the past, it was said that this disease was more prevalent among Westerners than Japanese. However, the use of improved diagnostic technology has made it clear that the current prevalence of this disease is not in any way less among Japanese, because of westernization of the Japanese diet and other reasons. Genetic abnormalities of various coagulation-related factors have been identified as causes of inherited thrombophilia. There still are some types of inherited thrombophilias with unknown causes. Usually abnormality of prothrombin causes hemorrhagic symptoms. However, we discovered a gene mutation that caused a type of prothrombin abnormality that was a cause of thrombosis in a family that had inherited venous thrombophilia the reason for which was unknown for long. A detailed analysis showed that this mutant thrombin had a moderately low coagulation activity but because of its resistance to inactivation by antithrombin (AT), it retained its activity for a longer time and caused thrombosis. We reported this as a new AT resistant (ATR) thrombophilia. An overview of this new inherited ATR thrombophilia will be presented here along with the latest findings.

The 40th Sysmex Scientific Seminar
Introduction ⑤

June 3rd (Sat.)

5th Lecture

KOBE 15:40 ►

Progress and prospects of hemophilia treatment

Professor Midori SHIMA , M.D., Ph.D.,
Department of Pediatrics,
Nara Medical University

【Summary】

There has been improvement in the QOL of hemophilia patients in recent years due to the sharp reduction in bleeding incidents as regular prophylactic treatments have become widely available. Nevertheless, treatment of hemophilia still has some major issues. The first of these is the need for frequent intravenous administration of a clotting factor to suppress the bleeding. This causes significant physical and psychological burden on the patients, especially pediatric patients and their parents. The second problem is the development of inhibitors. Recently, a novel subcutaneously injectable therapeutic agent that is effective irrespective of the presence of inhibitors has been developed. We have developed an anti-FIXa/FX bispecific antibody and showed that it had FVIII-mimetic activity (Kitazawa K et al. Nature Med 2012). This antibody is a fully humanized recombinant therapeutic agent. We then conducted a Phase I study and an extension study using an improved form of the antibody ACE910 (emicizumab). Weekly subcutaneous administration of this drug sharply reduced the hemorrhagic symptoms, unaffected by the presence of inhibitors (Shima M et al. NEJM 2016). Furthermore, clinical studies on gene therapy are also advancing and a therapeutic level of gene expression is becoming possible.