

## The 42<sup>nd</sup> Sysmex Scientific Seminar Introduction

June 1<sup>st</sup> (Sat.), 2019

# Cancer Genome Medicine Moving Forward

— Present Status and  
Future Perspectives —



### 1<sup>st</sup> Lecture

#### Origin of Esophageal Cancer

— Age-related Remodeling of Esophageal Epithelia by Mutated  
Cancer Drivers —



**Seishi Ogawa, M.D., Ph.D.**

*Department of Pathology and Tumor Biology,  
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**Key Words:** Clonal Expansion, *NOTCH1*, Alcohol, Smoking, Driver-mutated Clones, Aging

#### [Summary]

Clonal expansion in aged normal tissues has been implicated in the development of cancer. However, the chronology and risk dependence of the expansion are poorly understood. Here we intensively sequence 682 micro-scale esophageal samples and show, in physiologically normal esophageal epithelia, the progressive age-related expansion of clones that carry mutations in driver genes (predominantly *NOTCH1*), which is substantially accelerated by alcohol consumption and by smoking. Driver-mutated clones emerge multifocal from early

childhood and increase their number and size with ageing, and ultimately replace almost the entire esophageal epithelium in the extremely elderly. Compared with mutations in esophageal cancer, there is a marked overrepresentation of NOTCH1 and PPM1D mutations in physiologically normal esophageal epithelia; these mutations can be acquired before late adolescence (as early as early infancy) and significantly increase in number with heavy smoking and drinking. The remodeling of the esophageal epithelium by driver-mutated clones is an inevitable consequence of normal aging, which – depending on lifestyle risks – may affect cancer development.

## 2nd Lecture

### Clinical Implementation of Genomic Cancer Medicine in Japan and Strategic Approaches for Sharing its Benefits across Borders



**Hitoshi Nakagama, M.D., Ph.D.**

*President, National Cancer Center, Japan*

**Key Words :** Precision Cancer Medicine, Clinical Sequencing, Driver Gene, Clonal Revolution

#### [Summary]

Recent and revolutionary progress in DNA sequencing technology has enabled us to clarify the presence of hundreds to tens of thousands of genomic alterations in individual cancer cases. Furthermore, individual cancers have been revealed to possess specific and heterogeneous features in genomic profiles. This indicates that each cancer develops after exposure to various environmental factors and harbors genomic alterations induced consequently by those insults. Therefore, it is important and also ideal to deliver the most fitting and affordable treatment through understanding of the specific characters of individual cancer cases and by considering the patient-specific profiles of driver gene alterations. Non-small cell lung cancers (NSCLC) with the EGFR mutations, for example, respond quite nicely to EGFR inhibitors. However, cases without EGFR mutations do not respond to the inhibitors. NSCLS cases with ALK, RET or ROS1-fusion genes are in the same situation. Precision cancer medicine based on patient-specific genetic profiles is to be provided nationwide in Japan from Spring 2019 under universal health care insurance coverage. I would like to present here the clinical significance and current situation of genomic cancer medicine in

Japan, and also discuss several issues that require addressing in providing nation-wide precision cancer medicine and strategies for sharing the benefits across borders.

### 3rd Lecture

#### The Road to Exome Sequence for Next Stage of Cancer Precision Medicine



**Hiroshi Nishihara, M.D., Ph.D.**

*– Professor, Clinical and Transitional Research Center, Keio University School of Medicine*

*– Unit Manager, Genomics Unit, Keio Cancer Center, Keio University School of Medicine*

**Key Words:** Cancer Genomics, Next Generation Sequencer, Precision Medicine, Molecular Targeted Drug

**[Summary]**

Precision medicine means individualized medicine based on gene profile, environment and life style. Cancer Precision Medicine is one of the most successful strategies in clinical application of precision medicine, and now the multigene testing is performed as a routine laboratory examination. Here I would like to present the current situation and future direction of Cancer Precision Medicine in Japan.

### 4th Lecture

#### Quality Management of Molecular Methods in Cancer Genomic Medicine



**Masato Maekawa, M.D., Ph.D.**

*Department of Laboratory Medicine, Hamamatsu University School of Medicine*

**Key Words:** Quality Management, Analytical Validity, Internal Quality Control, External Quality Assessment, Cancer Genomic Medicine, Next-Generation Sequencing, Cancer Gene Panel

### **[Summary]**

Currently, cancer genome medicine has rapidly implemented to common practice in cancer treatment decision making. It is truly dependent on the development of molecular methods, especially next-generation sequencing (NGS) technologies. NGS and cancer gene panel could analyze multiple gene mutations simultaneously by efficient DNA sequencing, and lead to individualized treatment decision making and precision medicine.

Quality management of clinical laboratory testing, including molecular methods has been highlighted. It is based on the revised medical care act which started from December 1, 2018. Molecular genetic testing by use of NGS is very complexing because it consists of nucleic acid extraction, library preparation and sequencing chemistry, bioinformatics pipeline and so on, and NGS technologies and database are continuing evolving. Interpretation of NGS data remains challenging, therefore, optimization of the NGS process is needed to obtain correct results and adequate treatment.

Because we shall appeal the importance of analytic validity, we formed a working group named sub-committee for genomic testing in Japanese Promotion Council for Laboratory Testing, and we have drawn up the document“. Basic concept for quality management of cancer gene panel testing“. It is consisted of basic principles and examples of quality standards and quality assurance. Basic principles are focused on the quality management composed of analytic validity, internal quality control and external quality assessment on the all of the testing processes, e.g. preanalytic, analytic and postanalytic processes. Especially, we shall plan external quality assessment scheme to reveal the quality of cancer gene panel testing in Japan immediately.