Meeting report

From DNA Mutation to RNA —Aberrant RNA and Quality Control of RNA— “Symposium 1” at the JEMS Annual Meeting 2010

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As is well known to JEMS members, various endogenous and environmental factors cause mutations in DNA. Transcription of mutated genes then produces aberrant RNA molecules. However, cells have quality control systems for RNA, which degrade these aberrant RNA molecules. Recent studies have begun to elucidate the molecular mechanisms of this RNA surveillance system. At the 39th annual meeting of the Japanese Environmental Mutagen Society (JEMS) held in Tsukuba city on November 16 and 17, 2010, the author organized a symposium that focused on the fate of mutations in the flow of genetic information from genes to proteins through RNA. At the symposium, four young scientists presented their studies on transcriptional mutagenesis, the quality control systems for rRNA and mRNA and template-independent RNA polymerization.

Key words: transcription, RNA surveillance, rRNA, mRNA, template-independent RNA polymerase, tRNA

The 39th annual meeting of the Japanese Environmental Mutagen Society (JEMS) was held at the Tsukuba International Congress Center (Epochal Tsukuba) in Tsukuba city on November 16 and 17, 2010. At this meeting, the author organized a symposium entitled “From DNA mutation to RNA —aberrant RNA and quality control of RNA—”. As is well known to every JEMS member, various endogenous and environmental factors cause mutations. Although twenty to thirty percent of mutations observed in genetic disorders and cancer cells are nonsense mutations (1), the formation of truncated proteins scarcely occurs in these cells (2). Cells have an mRNA surveillance system that causes the degradation of aberrant mRNA molecules. For example, a nonsense mutation in the β -globin gene causes β -thalassemia (3). However, thalassemic β -globin mRNA is barely detectable in the patient cells (4). The absence of thalassemic β -globin mRNA results from the rapid degradation of such mRNA in the cells (5). Recent studies have begun to elucidate the molecular mechanisms of this quality control system for mRNA. Therefore, the

author organized a symposium that focused on the fate of mutations in the flow of genetic information from genes to proteins through RNA.

In the symposium, the author first presented a brief introduction of environmental mutagenesis; Mutations caused by DNA lesions, especially DNA bulky adducts (6), that results in aberrant RNA molecules. Four researchers then gave lectures on the scientific topics listed below:

“Molecular mechanism of transcriptional mutagenesis induced by DNA lesions” by Dr. Isao Kuraoka (Osaka University)

“A role for ubiquitin in the clearance of nonfunctional ribosomal RNAs” by Dr. Makoto Kitabatake (Kyoto University)

“mRNA surveillance: Quality control of mRNA” by Dr. Akio Yamashita (Yokohama City University)

“Mechanisms for template-independent RNA polymerization” by Dr. Kozo Tomita (National Institute of Advanced Industrial Science and Technology)

Drs. Kuraoka and Kitabatake guided the audience from the field of DNA including damage and repair, with which JEMS members are familiar, to that of RNA. Dr. Kuraoka presented the effects of DNA lesions on transcription elongation and proposed the molecular mechanism of transcriptional mutagenesis induced by DNA lesions. Dr. Kitabatake explained the quality control mechanisms of rRNA, especially the nonfunctional rRNA decay (NRD) system that removes nonfunctional mutant rRNAs. He showed the connection between the NRD system and DNA repair system through components of ubiquitin E3 ligase. Dr. Yamashita introduced nonsense-mediated mRNA decay (NMD), which is the mRNA quality control system that removes aberrant mRNAs with premature termination codons. He also

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presented control mechanisms of NMD with RuvBL proteins. Dr. Tomita gave an account of a template-independent RNA polymerase that adds an invariant triribonucleotide 5'-CCA sequence at the 3'-end of tRNA without nucleic acid templates. He explained the molecular mechanism of the template-independent CCA synthesis based on his structural and biochemical studies.

These four young researchers have already accomplished prominent scientific achievements. Therefore, the symposium not only offered scientifically exciting information to the audience but also encouraged young researchers in JEMS. The knowledge obtained in these RNA studies will fill a gap between mutation and phenotypic alteration. The author believes that the knowledge contributes to better understanding of carcinogenesis as well.

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