Analysis of Toxicity Using Metallothionein Knockout Mice

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Two research groups produced metallothionein (MT) -I/II knockout mice with null mutation of *MT-I* and *MT-II* genes. In 1993, Dr. Choo *et al*. produced MT-I/II knockout mice with a mixed genetic background of 129 Ola and C57BL/6 strains. Dr. Palmiter *et al*. also produced MT-I/II knockout mice with a genetic background of 129/Sv strain in 1994. Subsequently, MT-I/II knockout mice have used to clarify the biological function and physiological role of MT in many research groups.

We were also provided MT-I/II knockout mice from Dr. Choo (Australia). F1 hybrid mice were mated with C57BL/6, and their offspring were back-crossed to C57BL/6 for six generations. MT-I/II knockout ($MT^{-/-}$) mice and wild-type ($MT^{+/+}$) mice were obtained by mating of those heterozygous ($MT^{+/-}$) mice. We have been investigating the susceptibility of MT-I/II knockout mice to toxicity of harmful factors and some diseases. Our present studies found that MT-I/II knockout mice have an increased sensitivity to harmful metals such as cadmium, mercury and arsenic, oxidative stress, chemical carcinogenesis, inflammatory diseases and neurodegenerative diseases. These results clearly indicate that MT plays an important role in defense of these toxicities.

In this Symposium, we present our findings and the recent reports with MT-I/II knockout mice concerning the role of MT as a biological protective factor.