Current Topics**Recent Advances in the Understanding of Nuclear Receptors- and Drug-Metabolizing Enzymes-Mediated Inter-Individual Differences****Foreword**

Shuso Takeda

*Laboratory of Molecular Life Sciences, Faculty of Pharmacy and Pharmaceutical Sciences,
Fukuyama University; Sanzou 1, Gakuen-cho, Fukuyama, Hiroshima 729-0292, Japan.*

Colossal inter-individual differences existing in biological responses to endogenous and exogenous substances are attributable to minute biological interplays, including nuclear receptors' signaling and activities of drug-metabolizing enzymes. Nuclear receptors, such as estrogen receptor (ER), peroxisome proliferator-activated receptor β/δ (PPAR β/δ), and retinoic acid receptor-related orphan receptor α (ROR α), are basically ligand-inducible transcription factors. They are known to be robustly involved in the regulation of numerous physiological processes, such as metabolism, development, and reproduction *via* regulation of target genes, thus, rendering them as attractive drug targets. At the post-transcriptional level, some microRNAs are suggested to be directly/indirectly involved in the regulation of CYP3A protein expression. Furthermore, at the post-translational levels, it has been evidently shown that there are functional protein–protein interactions between different kinds of drug-metabolizing enzymes *i.e.*, P450 and uridine 5'-diphosphate (UDP)-glucuronosyltransferase, UGT, which results in modulation of the enzyme(s) activities.

In this *Current Topics* publication, 5 young promising scientists and their senior colleagues were invited to contribute papers for updating/improving our readers' appreciation of the nuclear receptors- and drug-metabolizing enzymes-mediated

inter-individual differences especially in the toxicological aspects. 1) Dr. Hirao-Suzuki highlights the significance of breast cancer malignancy stimulation by environmental chemicals, especially focusing on the interaction bisphenols and ER β subtype in the enhanced malignancy. 2) Dr. Koga and Dr. Peters review the critical roles of PPARs including PPAR β/δ in the pathogenesis of alcoholic liver disease. 3) Dr. Matsuoka and Dr. Michihara summarize the structure/function of ROR α and its potential utility as a therapeutic target for atherosclerosis. 4) Dr. Fujino, Dr. Sanoh, and Dr. Katsura evaluate the regulation of CYP3A expression in humans and rodents, coupled with individual differences in toxicological aspects, by focusing on the endo- and exogenous factors. 5) Dr. Miyauchi, Dr. Takechi, and Dr. Ishii recapitulate the functional protein–protein interactions between P450 and UGT, which imply a novel post-translational factor regulating inter-individual differences in drug metabolism.

I firmly believe that you, the reader, will essentially benefit and develop a better understanding of the nuclear receptors- and drug-metabolizing enzymes-driven inter-individual differences in toxicological aspects after reading this *Current Topics*.