

医工薬融合 GCOE Seminar Series*Center for Medical System Innovation
through Multidisciplinary Integration
The University of Tokyo***Diverse Enzymatic Mechanisms for Generating
Reactive Electrophiles
and Relevance to Drug Toxicity****Frederick Peter Guengerich****Harry Peason Broquist Professor of Biochemistry/
Interim Chairman of Department of Biochemistry
Vanderbilt University School of Medicine, USA****Date: Tuesday, July 10, 2012****Time: 18:00 -19:30****Venue: Tetsumon Memorial Hall, 14th Floor,****Faculty of Medicine Experimental Research Bldg., The University of Tokyo**

Activation of chemicals, including drugs, is an important process and is related to toxicity. Cytochrome P450 enzymes catalyze ~ 2/3 of the activations, using a basic chemical mechanism. Conjugating enzymes are not always involved in detoxications and can also activate chemicals. The relationship of bioactivation and other types of toxicity will be discussed in relationship to drug development, in that toxicity is a major reason for failure of candidates. Although bioactivation is critical as a first step in the toxicity of many drugs, there are multiple biological aspects as well. Accurately predicting the toxicity of drug candidates at an early stage is a major goal in the pharmaceutical industry today, and biomarkers may provide help.

Rendic, S. and Guengerich, F.P. (in press) Contributions of human enzymes in carcinogen metabolism. *Chem. Res. Toxicol.*, in press (PMID 22531028, Web access)

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