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「生体分子コバレント修飾の革新的解析拠点形成」プロジェクト研究成果

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【原著】

- Shimada T, Takenaka S, Murayama N, Kramlinger V M, Kim J-H, Kim D, Foroozesh M K, Yamazaki H, Guengerich F P, and Komori M. Oxidation of pyrene, 1-hydroxypyrene, 1-nitropyrene, and 1-acetylpyrene by human cytochrome P450 2A13. *Xenobiotica*, 46, 211-224, 2016. [\[PubMed\]](#)
- Uehara S, Inoue T, Utoh M, Toda A, Shimizu M, Uno Y, Sasaki E, and Yamazaki H. Simultaneous pharmacokinetics evaluation of human cytochrome P450 probes, caffeine, warfarin, omeprazole, metoprolol, and midazolam, in common marmosets (*Callithrix jacchus*). *Xenobiotica*, 46, 163-168, 2016. [\[PubMed\]](#)
- Uno Y, Yamazaki H. Development of a genotyping tool for a functionally relevant CYP2C19 allele (Phe100Asn, Ala103Val, Ile112Leu) in cynomolgus macaques, *J.Vet.Med.Sci.*, 78, 147-148, 2016. [\[Link\]](#)
- Sekiguchi K, Kanazu T, Murayama N, Yamazaki H, and Yamaguchi T. *In vitro* inhibition and enhancement of liver microsomal S-777469 metabolism by long-chain fatty acids and serum albumin: insight into *in vitro* and *in vivo* discrepancy of metabolite formation in humans. *Xenobiotica*, 46, 495-502, 2016. [\[PubMed\]](#)
- Uehara S, Uno Y, Inoue T, Suzuki T, Utoh M, Sasaki E, and Yamazaki H. Caffeine 7-*N*-demethylation and *C*8-oxidation mediated by liver microsomal cytochrome P450 enzymes in common marmosets. *Xenobiotica*, 46, 573-578, 2016. [\[PubMed\]](#)
- Uehara S, Uno Y, Inoue T, Sasaki E, and Yamazaki H. Molecular cloning, tissue distribution, and functional characterization of marmoset cytochrome P450 1A1, 1A2, and 1B1. *Drug Metab. Dispos.*, 44, 8-15, 2016. [\[PubMed\]](#)
- Okubo M, Narita M, Murayama N, Akimoto Y, Goto A, and Yamazaki H. Individual differences in *in vitro* and *in vivo* metabolic clearances of the antipsychotic drug olanzapine from non-smoking and smoking Japanese subjects genotyped for *cytochrome P450 2D6* and *flavin-containing monooxygenase 3*. *Hum.Psychopharmacol.Clin.Exp.*, 31, 83-92, 2016. [\[PubMed\]](#)
- Okubo M, Morita S, Murayama N, Akimoto Y, Goto A, and Yamazaki H. Individual differences in *in vitro* and *in vivo* metabolic clearances of antipsychotic risperidone from Japanese subjects genotyped for *cytochrome P450 2D6* and *3A5*. *Hum.Psychopharmacol.Clin.Exp.*, 31, 93-102, 2016. [\[PubMed\]](#)

- Kazuki Y, Akita M, Kobayashi K, Osaki M, Satoh D, Abe S, Takehara S, Kazuki K, Yamazaki H, Kamataki T, and Oshimura M. Thalidomide-induced limb abnormalities in a humanized CYP3A mouse model. *Sci.Rep.*, 6, 21419, 2016. [\[Link\]](#)
- Uehara, S., Uno, Y., Yuki, Y., Inoue, T., Sasaki, E., and Yamazaki, H. A new marmoset P450 4F12 enzyme expressed in small intestines and livers efficiently metabolizes an anti-histaminic drug ebastine. *Drug Metab. Dispos.*, 44, 833-841, 2016. [\[Link\]](#)
- Sawada G, Niida A, Uchi R, Hirata H, Shimamura T, Suzuki Y, Shiraishi Y, Chiba K, Imoto S, Takahashi Y, Iwaya T, Hayashi T, Takai H, Kawasaki Y, Matsukawa T, Eguchi H, Sugimachi K, Tanaka F, Suzuki H., Yamamoto K, Ishii H, Shimizu M, Yamazaki H, Yamazaki M, Tachimori Y, Kajiyama Y, Natsugoe S, Fujita H, Mafune K, Tanaka Y, Kelsell D P, Scott C A, Tsuji S, Yachida S, Shibata T, Sugano S, Doki Y, Akiyama T, Aburatani H, Ogawa S, Miyano S, Mori M, and Mimori K. Genomic landscape of esophageal squamous cell carcinoma in a Japanese population. *Gastroenterology*, 150,1171-1182,2016. [\[PubMed\]](#)
- Sakai C, Iwano S, Shimizu M, Onodera J, Uchida M, Sakurada E, Yamazaki Y, Asaoka Y, Imura N, Uno Y, Murayama N, Hayashi R, Yamazaki H, and Miyamoto Y. Analysis of gene expression for microminipig liver transcriptomes using parallel long-read technology and short-read sequencing. *Biopharm. Drug Dispos.*, 37, 220-232, 2016. [\[PubMed\]](#)
- Shida S and Yamazaki H. Human plasma concentrations of five cytochrome P450 probes extrapolated from pharmacokinetics in dogs and minipigs using physiologically based pharmacokinetic modeling. *Xenobiotica*, 46, 759-764, 2016. [\[PubMed\]](#)
- Sugiyama I, Murayama N, Kuroki A, Kota J, Iwano S, Yamazaki H, and Hirota T. Evaluation of cytochrome P450 inductions by anti-epileptic drug oxcarbazepine, 10-hydroxyoxcarbazepine, and carbamazepine using human hepatocytes and HepaRG cells. *Xenobiotica*, 46, 765-774, 2016. [\[PubMed\]](#)
- Shimada T, Takenaka S, Kakimoto K, Murayama N, Lim Y-R, Kim D, Foroozesh M, Yamazaki H, Guengerich F P, and Komori M. Structure-function studies of naphthalene, phenanthrene, biphenyl, and their alkynyl derivatives in interaction with and oxidation by cytochromes P450 2A13 and 2A6. *Chem. Res. Toxicol.*, 29, 1029-1040, 2016. [\[ACSL\]](#)
- Uehara S, Uno Y, Inoue T, Kawano M, Shimizu M, Toda A, Utoh M, Sasaki E and Yamazaki, H. Individual differences in metabolic clearance of *S*-warfarin

- efficiently mediated by polymorphic marmoset cytochrome P450 2C19 in livers. Drug Metab. Dispos., 44, 911-915, 2016. [\[PubMed\]](#)
- Uehara S, Uno Y, Inoue T, Okamoto E, Sasaki E, and Yamazaki H. Marmoset cytochrome P450 2J2 mainly expressed in small intestines and livers effectively metabolizes human P450 2J2 probe substrates, astemizole and terfenadine. Xenobiotica, 46,977-985,2016. [\[PubMed\]](#)
 - Hosaka S, Murayama N, Satsukawa M, Uehara S, Shimizu M, Iwasaki K, Iwano S, Uno Y, and Yamazaki H. Identification of putative substrates for cynomolgus monkey cytochrome P450 2C8 by substrate depletion assays with 22 human P450 substrates and inhibitors. Biopharm. Drug Dispos., 37, 310-313, 2016. [\[PubMed\]](#)
 - Higuchi Y, Kawai K, Kanai T, Yamazaki H, Chesne C, Guguen-Guilhouzo C, and Suemizu H. Functional polymer-dependent 3D culture accelerates the differentiation of HepaRG cells into mature hepatocytes. Hepatol.Res., 46,1045-1057, 2016. [\[PubMed\]](#)
 - Utoh M, Suemizu H, Mitsui M, Kawao M, Toda A, Uehara S, Uno Y, Shimizu M, Sasaki E, and Yamazaki H. Human plasma concentrations of cytochrome P450 probe cocktails extrapolated from pharmacokinetics in mice transplanted with human hepatocytes and from pharmacokinetics in common marmosets using physiologically based pharmacokinetic modeling. Xenobiotica, 46, 1049-1055, 2016. [\[PubMed\]](#)
 - Yonekura H, Murayama N, Yamazaki H, and Sobe K. A case of delayed emergence following propofol anesthesia: genetic analysis. Anesth.Analg.,7, 243-246, 2016. [\[PubMed\]](#)
 - Togashi K, Mutaguchi K, Kumuro S, Kataoka M, Yamazaki H, and Yamashita S. Systematic approach to optimize a pretreatment method for ultrasensitive LC/MS/MS analysis of multiple target compounds in biological samples. J.Sep.Sci., 39, 3212-3220, 2016. [\[Link\]](#)
 - Iwasaki K, Kitsugi Y, Ikeda K, Yoshikawa T, Hosaka S, Uehara S, Uno Y, Utoh M, and Yamazaki H. *In vivo* individual variations in pharmacokinetics of efavirenz in cynomolgus monkeys genotyped for cytochrome P450 2C9. Biopharm. Drug Dispos., 37, 379-383, 2016. [\[PubMed\]](#)
 - Yamazaki H, Suemizu H, Kazuki Y, Oofusa K, Kurabayashi S, Shimizu M, Ninomiya S, Horie T, Shibata N, and Guengerich F P. Assessment of protein binding of 5-hydroxythalidomide bioactivated in humanized mice with human P450 3A-chromosome or hepatocytes by two-dimensional electrophoresis/accelerator mass spectrometry. Chem. Res. Toxicol., 29, 1279-

1281, 2016. [\[PubMed\]](#)

- Takahashi T, Ohtsuki Y, Uno Y, Utoh M, Yamazaki H, and Kume T. Pre-incubation with cyclosporine A potentiates its inhibitory effects on pitavastatin uptake mediated by recombinantly expressed cynomolgus monkey hepatic organic anion transporting polypeptide. *Biopharm. Drug Dispos.*, 37, 479-490, 2016. [\[PubMed\]](#)
- Mori K, Saito R, Nakamaru Y, Shimizu M, and Yamazaki H. Physiologically based pharmacokinetic-pharmacodynamic modeling to predict concentrations and actions of sodium-dependent glucose transporter 2 inhibitor canagliflozin in human intestines and renal tubules. *Biopharm. Drug Dispos.*, 37, 491–506, 2016. [\[PubMed\]](#)
- Shimada T, Kakimoto K, Takenaka S, Koga N, Uehara S, Murayama N, Yamazaki H, Kim D, Guengerich F P, and Komori M. Roles of human CYP2A6 and monkey CYP2A24 and 2A26 cytochrome P450 enzymes in the oxidation of 2,5,2',5'-tetrachlorobiphenyl. *Drug Metab. Dispos.*, 44, 1899-1909, 2016. [\[PubMed\]](#)
- Uehara S, Kawan M, Murayama N, Uno Y, Utoh M, Inoue T, Sasaki E, and Yamazaki H. Oxidation of R- and S-omeprazole stereoselectively mediated by liver microsomal cytochrome P450 2C19 enzymes from cynomolgus monkeys and common marmosets . *Biochem. Pharmacol.*, 120, 56-62, 2016. [\[PubMed\]](#)

【総説】

- Uno Y, Uehara S, and Yamazaki H. Utility of non-human primates in drug development: comparison of non-human primate and human drug-metabolizing cytochrome P450 enzymes. *Biochem. Pharmacol.*, 121, 1-7, 2016. [\[PubMed\]](#)
- Yamazaki H, Suemizu H, Mitsui M, Shimizu M, and Guengerich F P. Combining Chimeric mice with humanized liver, mass spectrometry, and physiologically-based pharmacokinetic modeling in toxicology. *Chem. Res. Toxicol.*, 29, 1903-1911, 2016. [\[PubMed\]](#)
- Autrup H N, Berry S C L, Cohen S M, Creppy E E, de Camargo J L, Dekant W, Dietrich D, Galli C L, Goodman J I, Gori G B, Greim H A, Klaunig J E, Lotti M, Marquardt H W, Wallace K B, and Yamazaki H. Whither the impending european regulation of presumed endocrine disruptors? *Regul. Toxicol. Pharmacol.*, 82, A1-A2, 2016. [\[PubMed\]](#)
- Aschner M, Autrup H N, Berry S C, Boobis A R, Cohen S M, Creppy E E, Dekant W, Doull J, alli C L, Goodman J I, Gori G B, Greim H A, Joudrier P, Kaminski N E, Klaassen C D, Klaunig J E, Lotti M, Marquardt H W J, Pelkonen O, Sipes I G,

Wallace K, and Yamazaki H. Upholding science in health, safety and environmental risk assessments and regulations. *Toxicology*, 371, 12-16, 2016.

[\[PubMed\]](#)

【著書】

- Yamazaki H, Chowdhury G and Guengerich F P. Activation of Thalidomide to Reactive Metabolites by Autoinduced Human Cytochrome P450 3A Enzymes, with Substrate Cooperativity, and Implications for Development of Analogs. In: *Advances in Medicine and Biology*, Vol. 93, Ed. L.V. Berhardt, pp. 23-30, Hauppauge, NY, USA: Nova Science Publishers, Inc, 2016.