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Education

Ph. D., Pharmaceutical Sciences: **Tohoku University**, Graduate School of Pharmaceutical Sciences (April 1995-March 1998).
M.S., Pharmaceutical Sciences: **Tohoku University**, Graduate School of Pharmaceutical Sciences (April 1993-March 1995).
B.S. Pharmaceutical Sciences: **Tohoku University**, Faculty of Pharmaceutical Sciences. (April 1989-March 1993).

Employment

April 2014-present: **University of Shizuoka**, School of Pharmaceutical Sciences, Professor.
March 2007-March 2014: **Tohoku University**, Graduate School of Pharmaceutical Sciences, Associate Professor
April 2006-February 2007: **Tohoku University**, Graduate School of Pharmaceutical Sciences, Assistant Professor.
April 2002 – March 2006: **University of Shizuoka**, School of Pharmaceutical Sciences, Assistant Professor.
October 2001-Mrach 2002: **University of Shizuoka**, School of Pharmaceutical Sciences, Research Assistant Professor.
April 1998-September 2001: **National Institute of Environmental Health Sciences/National Institutes of Health**, Postdoctoral Fellow.

Research Interests

- Gene regulation of drug-metabolizing enzymes.
- Roles of xenobiotic-responsive nuclear receptors in liver function and toxicity.
- Chemical-induced liver toxicity: the identification of mechanisms and the development of prediction system.

Academic Honors

2018 The Pharmaceutical Society of Japan Award for Divisional Scientific Promotion
2017 Japanese Society of Toxicology/Japan Chemical Industry Association LRI Award
2011 International Society for the Study of Xenobiotics (ISSX), Asia Pacific New Investigator Award
2009 Japanese Society for the Study of Xenobiotics (JSSX), Award for Young Scientists.
2005 The Pharmaceutical Society of Japan, Tokai-region Award for Young Scientists.

List of Publication (Selected)

Books (English)

Receptor-mediated regulation of cytochromes P450. K. Yoshinari, E. Tien, M. Negishi and P. Honkakoski: in Cytochrome P450: Role in the Metabolism and Toxicity of Drugs and Other Xenobiotics (Issues in Toxicology). C. Ioannides (Edt.), Royal Society of Chemistry. pp. 417-448, 2008

Review articles

Nuclear receptor CAR-mediated liver cancer and its species differences. R. Shizu, K. Yoshinari: ***Expert Opin Drug Metab Toxicol***, 16: 343-351, 2020.

Role of nuclear receptors PXR and CAR in xenobiotic-induced hepatocyte proliferation and chemical carcinogenesis. K. Yoshinari: ***Biol Pharm Bull***, 42: 1243-1252, 2019.

Construction of a CYP2E1-template system for prediction of the metabolism on both site and preference order. Y. Yamazoe, K. Ito, K. Yoshinari: ***Drug Metab Rev***, 43: 409-439, 2011.

Roles of nuclear receptors in the gene expression of drug-metabolizing enzymes under various physiological conditions. K. Yoshinari: ***Yakugakuzasshi***, 126: 343-348, 2006.

Original articles

Association of CYP1A1 and CYP1B1 inhibition in in vitro assays with drug-induced liver injury. Y Shimizu, T Sasaki, E Yonekawa, H Yamazaki, R Ogura, M Watanabe, T Hosaka, R Shizu, J. Takeshita, K. Yoshinari: ***J Toxicol Sci***, 2021, in press.

The influence of the long-term chemical activation of the nuclear receptor pregnane X receptor (PXR) on liver carcinogenesis in mice. R. Shizu, M. Ishimura, S. Nobusawa, T. Hosaka, T. Sasaki, S. Kakizaki, K. Yoshinari: ***Arch Toxicol***, 95: 1089, 2021.

PXR functionally interacts with NF-κB and AP-1 to downregulate the inflammation-induced expression of chemokine CXCL2 in mice. M. Okamura, R. Shizu, T. Abe, S. Kodama, T. Hosaka, T. Sasaki, K. Yoshinari: ***Cells***, 9: 2296, 2020.

Antiepileptic drug-activated constitutive androstane receptor inhibits peroxisome proliferator-activated receptor α- and peroxisome proliferator-activated receptor γ coactivator 1α-dependent gene expression to increase blood triglyceride levels. R. Shizu, Y. Otsuka, K. Ezaki, C. Ishii, S. Arakawa, Y. Amaike, T. Abe, T. Hosaka, T. Sasaki, Y. Kanno, M. Miyata, Y. Yamazoe, K. Yoshinari: ***Mol Pharmacol***, 98: 634-647, 2020.

Enhancement of acetaminophen-induced chronic hepatotoxicity in spontaneously diabetic torii (SDT) rats. K. Kondo, N. Yamada, Y. Suzuki, T. Hashimoto, K. Toyoda, T. Takahashi, A. Kobayashi, S. Sugai, K. Yoshinari: ***J Toxicol Sci***, 45: 245, 2020.

Construction of a PPARα reporter assay system with drug-metabolizing capability. T. Hosaka, A. Wakatsuki, T. Sasaki, R. Shizu, K. Yoshinari: ***BPB Reports***. 3: 7, 2020.

Application of cytochrome P450 reactivity on the characterization of chemical compounds and its association with repeated-dose toxicity. M. Watanabe, T. Sasaki, J. Takeshita, M. Kushida, Y. Shimizu, H. Oki, Y. Kitsunai, H. Nakayama, H. Saruhashi, R. Ogura, R. Shizu, T. Hosaka, K. Yoshinari: ***Toxicol Appl Pharmacol***, 388: 114854, 2020.

Functional interaction between pregnane X receptor and yes-associated protein in xenobiotic-dependent liver hypertrophy and drug metabolism. T. Abe, R. Shizu, T. Sasaki, Y. Shimizu, T. Hosaka, S. Kodama, A. Matsuzawa, K. Yoshinari: ***J Pharmacol Exp Ther***. 371: 590, 2019.

Possible involvement of the competition for the transcriptional coactivator glucocorticoid receptor-interacting protein 1 in the inflammatory signal-dependent suppression of PXR-mediated CYP3A induction in vitro. M. Okamura, R. Shizu, T. Hosaka, T. Sasaki, K. Yoshinari: ***Drug Metab Pharmacokinet***, 34: 272, 2019.

Chimeric mice with humanized livers demonstrate human-specific hepatotoxicity caused by a therapeutic antibody against TRAIL-receptor 2/death receptor 5. K. Nihira, K. Nan-ya, M. Kakuni, Y. Ono, Y. Yoshikawa, T. Ota, M. Hiura, K. Yoshinari: ***Toxicol Sci***, 167: 190, 2019.

Profiling of bisphenol A and eight its analogues on transcriptional activity via human nuclear receptors. H. Kojima, S. Takeuchi, S. Sanoh, K. Okuda, S. Kitamura, N. Uramaru, K. Sugihara, K. Yoshinari: ***Toxicology***, 413: 48, 2019.

Screening of industrial and agricultural chemicals for searching a mouse PXR activator using cell-based reporter gene assays. R. Shizu, M. Kano, T. Abe, S. Tsuchiy, Y. Shimizu, M. Watanabe, T. Hosaka, T. Sasaki, K. Yoshinari: ***BPB Reports***, 1, 11, 2018.

Role of YAP activation in nuclear receptor CAR-mediated proliferation of mouse hepatocytes. T. Abe, Y. Amaike, R. Shizu, M. Takahashi, M. Kano, T. Hosaka, T. Sasaki, S. Kodama, A. Matsuzawa, K. Yoshinari: ***Toxicol Sci***, 165: 408, 2018.

Acceleration of murine hepatocyte proliferation by imazalil through the activation of nuclear

receptor PXR. S. Yoshimaru, R. Shizu, S. Tsuruta, Y. Amaike, M. Kano, T. Hosaka, T. Sasaki, K. Yoshinari: ***J Toxicol Sci***, 43: 443, 2018.

Characterization of CYP2C induction in cryopreserved human hepatocytes and its application in the prediction of the clinical consequences of the induction. M. Nagai, T. Hosaka, M. Satsukawa, K. Yoshinari: ***J Pharm Sci***, 107: 2479, 2018.

Discriminative models using molecular descriptors for predicting increased serum ALT levels in repeated-dose toxicity studies of rats. J. Takeshita, H. Nakayama, Y. Kitsunai, M. Tanabe, H. Oki, T. Sasaki, K. Yoshinari: ***Comp Toxicol***, 6: 64, 2018.

Pregnenolone 16α-carbonitrile ameliorates concanavalin A-induced liver injury in mice independent of the nuclear receptor PXR activation. S. Kodama, T. Shimura, H. Kuribayashi, T. Abe, K. Yoshinari: ***Toxicol Lett***, 271: 58, 2017.

Activation of nuclear receptor CAR by an environmental pollutant perfluorooctanoic acid. T. Abe, M. Takahashi, M. Kano, Y. Amaike, C. Ishii, K. Maeda, Y. Kudoh, T. Morishita, T. Hosaka, T. Sasaki, S. Kodama, A. Matsuzawa, H. Kojima, K. Yoshinari: ***Arch Toxicol***, 91: 2365, 2017.

Establishment of in silico prediction models for CYP3A4 and CYP2B6 induction in human hepatocytes by multiple regression analysis using azole compounds. M. Nagai, Y. Konno, M. Satsukawa, S Yamashita, K. Yoshinari: ***Drug Metab Dispos***, 44: 1390-8, 2016.

PXR stimulates growth factor-mediated hepatocyte proliferation by cross-talk with FOXO transcription factor. R. Shizu, T. Abe, S. Benoki, M. Takahashi, S. Kodama, M. Miyata, A. Matsuzawa, K. Yoshinari: ***Biochem J***, 473: 257, 2016.

Dual roles of nuclear receptor liver X receptor α (LXRα) in the CYP3A4 expression in human hepatocytes as a positive and negative regulator. K. Watanabe, K. Sakurai, Y. Tsuchiya, Y. Yamazoe, K. Yoshinari. ***Biochem Pharmacol***, 86: 428, 2013.

Novel cell-based reporter assay system using epitope-tagged protein for the identification of agonistic ligands of constitutive androstane receptor (CAR). J. Imai, Y. Yamazoe, K. Yoshinari. ***Drug Metab Pharmacokinet***, 28: 290, 2013.

Xenobiotic-induced hepatocyte proliferation associated with constitutive active/androstane receptor (CAR) or peroxisome proliferator- activated receptor α (PPARα) is enhanced by pregnane X receptor (PXR) activation in mice. R. Shizu, S. Benoki, Y. Numakura, S. Kodama, M. Miyata, Y. Yamazoe, K. Yoshinari. ***PLoS One***, 8: e61802, 2013.

Constitutive androstane receptor transactivates the hepatic expression of mouse Dhcr24 and human DHCR24 encoding a cholesterogenic enzyme 24-dehydrocholesterol reductase. K. Yoshinari, H. Ohno, S. Benoki, Y. Yamazoe. ***Toxicol Lett***, 208: 185, 2012.

Transactivation of *ABCG2* through a novel cis-element in the distal promoter by constitutive androstane receptor but not pregnane X receptor in human hepatocytes. S. Benoki, K. Yoshinari, T. Chikada, J. Imai, Y. Yamazoe: ***Arch Biochem Biophys***, 517: 123, 2012.

Liver X receptor alpha bidirectionally transactivates human CYP1A1 and CYP1A2 through two cis-elements common to both genes. K. Araki, K. Watanabe, Y. Yamazoe, K. Yoshinari: ***Toxicol Lett***, 215: 16, 2012.

Activated sterol regulatory element-binding protein-2 suppresses hepatocyte nuclear factor-4-mediated Cyp3a11 expression in mouse liver. S. Inoue, K. Yoshinari, M. Sugawara, Y. Yamazoe: ***Mol Pharmacol***, 79: 148, 2011.

Clioquinol is sulfated by human jejunum cytosol and SULT1A3, a human-specific dopamine sulfotransferase. K. Yoshinari, M. Sakamoto, L. Senggunprai, Y. Yamazoe: ***Toxicol Lett***, 206: 229, 2011.

Constitutive androstane receptor transcriptionally activates human CYP1A1 and CYP1A2 genes through a common regulatory element in the 5'-flanking region. K. Yoshinari, N. Yoda, T. Toriyabe and Y. Yamazoe: ***Biochem Pharmacol***, 79: 261-9, 2010.

Simultaneous expression of plural forms of human cytochrome P450 at desired ratios in HepG2 cells: adenovirus-mediated tool for cytochrome P450 reconstitution. K. Aoyama, K. Yoshinari, H. J. Kim, K. Nagata, Y. Yamazoe: ***Drug Metab Pharmacokinet***, 24: 209, 2009.

Inhibitory effects of kynurenic acid, a tryptophan metabolite, and its derivatives on cytosolic sulfotransferases.L. Senggunprai, K. Yoshinari, Y. Yamazoe: ***Biochem J***, 422: 455, 2009.

Selective role of sulfotransferase 2A1 (SULT2A1) in the N-sulfoconjugation of quinolone drugs in humans. L. Senggunprai, K. Yoshinari, Y. Yamazoe: ***Drug Metab Dispos***, 37: 1711, 2009.

Involvement of Vitamin D receptor in the intestinal induction of human ABCB1. S. Tachibana, K. Yoshinari, T. Chikada, T. Toriyabe, K. Nagata, Y. Yamazoe: ***Drug Metab Dispos***, 37: 1604, 2009.

Unveiling a new essential cis element for the transactivation of the CYP3A4 gene by xenobiotics. T. Toriyabe, K. Nagata, T. Takada, Y. Aratsu, T. Matsubara, K. Yoshinari, Y. Yamazoe: ***Mol Pharmacol***, 75: 677, 2009.

Omeprazole transactivates human *CYP1A1* and *CYP1A2* expression through the common regulatory region containing multiple xenobiotic-responsive elements. K. Yoshinari, R. Ueda, K. Kusano, T. Yoshimura, K. Nagata, Y. Yamazoe: ***Biochem Pharmacol***, 76: 139, 2008.

Involvement of ST1B subfamily of cytosolic sulfotransferase in kynurenine metabolism to form natriuretic xanthurenic acid sulfate. L. Senggunprai, K. Yoshinari, M. Shimada, Y. Yamazoe: ***J Pharmacol Exp Ther***, 327: 789, 2008.

Hepatic CYP3A expression is attenuated in obese mice fed a high-fat diet. K. Yoshinari, S. Takagi, T. Yoshimasa, J. Sugatani, M. Miwa: ***Pharm Res***, 23: 1188, 2006.

Changes in the expression of cytochromes P450 and nuclear receptors in the liver of genetically diabetic db/db mice. K. Yoshinari, S. Takagi, J. Sugatani, M. Miwa: ***Biol Pharm Bull***, 29: 1634, 2006.

Induction of detoxifying enzymes in rodent white adipose tissue by aryl hydrocarbon receptor agonists and antioxidants. K. Yoshinari, N. Okino, T. Sato, J. Sugatani, M. Miwa: ***Drug Metab Dispos***, 34: 1081, 2006.

Expression and induction of cytochromes P450 in rat white adipose tissue. K. Yoshinari, T. Sato, N. Okino, J. Sugatani and M. Miwa: ***J Pharmacol Exp Ther***, 311: 147-54, 2004.

Identification of the nuclear receptor CAR:HSP90 complex in mouse liver and recruitment of protein phosphatase 2A in response to phenobarbital. K. Yoshinari, K. Kobayashi, R. Moore, T. Kawamoto, M. Negishi: ***FEBS Lett***, 548: 17, 2003.

Role of constitutive androstane receptor in the in vivo induction of Mrp3 and CYP2B1/2 by phenobarbital. H. Xiong, K. Yoshinari, K.L. Brouwer, M. Negishi: ***Drug Metab Dispos***, 30: 918, 2002.

Nuclear receptor CAR as a regulatory factor for the sexually dimorphic induction of CYB2B1 gene by phenobarbital in rat livers. K. Yoshinari, T. Sueyoshi, R. Moore, M. Negishi: ***Mol Pharmacol***, 59: 278, 2001.

The phenobarbital response enhancer module in the human bilirubin UDP-glucuronosyl-transferase UGT1A1 gene and regulation by the nuclear receptor CAR. J. Sugatani, H. Kojima, A. Ueda, S. Kakizaki, K. Yoshinari, Q. H. Gong, I. S. Owens, M. Negishi, T. Sueyoshi: ***Hepatology***, 33: 1232, 2001.

Estrogen activation of the nuclear orphan receptor CAR (constitutive active receptor) in induction of the mouse Cyp2b10 gene. T. Kawamoto, S. Kakizaki, K. Yoshinari, M. Negishi: ***Mol Endocrinol***, 14: 1897, 2000.

Molecular cloning, expression, and enzymatic characterization of rabbit hydroxysteroid sulfotransferase AST-RB2 (ST2A8). K. Yoshinari, K. Nagata, T. Shiraga, K. Iwasaki, T. Hata, M. Ogino, R. Ueda, K. Fujita, M. Shimada, Y. Yamazoe: ***J Biochem***, 123: 740, 1998.

Molecular characterization of ST1C1-related human sulfotransferase. K. Yoshinari, K. Nagata, M. Shimada, Y. Yamazoe: ***Carcinogenesis***, 19: 951, 1998.

Molecular cloning and expression of an amine sulfotransferase cDNA: a new gene family of cytosolic sulfotransferases in mammals. K. Yoshinari, K. Nagata, M. Ogino, K. Fujita, T. Shiraga, K. Iwasaki, T. Hata, Y. Yamazoe: ***J Biochem***, 123: 479, 1998.