CURRICULUM VITAE

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Education:

Apr, 2011-Mar, 2014	Graduate School of Pharmaceutical Sciences, Tohoku University, Sendai, Japan (Ph.D.)
Apr, 2009-Mar, 2011	Graduate School of Pharmaceutical Sciences, Showa University, Tokyo, Japan (Master)
Apr, 2005-Mar, 2009	Showa University, Tokyo, Japan

Professional Experience:

Jul, 2023-present	Assistant Professor, Laboratory of Molecular Toxicology, School of Pharmaceutical Sciences, University of Shizuoka.
Apr, 2017-Jun, 2023	Research Assistant Professor, Laboratory of Molecular Toxicology, School of Pharmaceutical Sciences, University of Shizuoka.
Apr, 2014-Mar, 2017	Visiting Fellow, Pharmacogenetics group, Reproductive & Developmental Biology Laboratory Branch, National Institute of environmental Sciences, NIH, Research Triangle Park, NC, USA

Research Interests: Toxicology, Nuclear receptors, Co-activator, transcription factor, Gene transcription, Protein interaction, Liver carcinogenesis, Liver hypertrophy,

Qualification and skills:

March, 2014	Ph. D (Pharm.D., Tohoku University)
May, 2009	Japanese pharmacist

Publications:

1. **Shizu R**, Otsuka Y, Ishii C, Ezaki K, Yoshinari K, PPARα induces the expression of CAR that works as a negative regulator of PPARα functions in mouse livers, ***Int J Mol Sci***, 24, 3953, 2023

2. Watanabe M, Kosaka H, Sugawara M, Maemoto M, Ono Y, Uemori T, **Shizu R**, Yoshinari K, Screening for DAX1/EWS-FLI1 functional inhibitors identified dihydroorotate dehydrogenase as a therapeutic target for Ewing's sarcoma, ***Cancer Med***, 12, 9802-9814, 2023

3. Murase W, Kubota A, Ikeda-Araki M, Terasaki K Nakagawa K, **Shizu R**, Yoshinari K, Kojima H, Effects of perfluorooctanoic acid (PFOA) on gene expression profiles via nuclear receptors in HepaRG cells: Comparative study with in vitro transactivation assays, ***Toxicology***, 153577, 2023

4. Sato T, **Shizu R**, Miura Y, Hosaka T, Kanno Y, Sasaki T, Yoshinari K, Development of a strategy to identify and evaluate direct and indirect activators of constitutive androstane receptor in rats. ***Food Chem Toxicol***, 170, 113510, 2022

5. Kanno Y, Saito N, Yamashita N, Ota K, **Shizu R**, Hosaka T, Nemoto K, Yoshinari K, Possible involvement of the upregulation of ΔNp63 expression mediated by HER2-activated aryl hydrocarbon receptor in mammosphere maintenance. ***Int J Mol Sci***, 23, 12095, 2022

6. Kanno Y, Saito N, Saito R, Kosuge T, Shizu R, Yatsu T, Hosaka T, Nemoto K, Kato K, Yoshinari K, Differential DNA-binding and cofactor recruitment are possible determinants of the synthetic steroid YK11-dependent gene expression by androgen receptor in breast cancer MDA-MB 453 cells. ***Exp Cell Res***, 419, 113333, 2022
7.
8. **Shizu R**, Nishiguchi H, Tashiro S, Sato T, Sugawara A, Kanno Y, Hosaka T, Sasaki T, Yoshinari K, Structural characterization of constitutive transcriptional activity of the nuclear receptor pregnane X receptor (PXR) to generate ligand-sensitive PXR mutants for chemical screening. ***J Biol Chem***, 297, 100978, 2021

9. **Shizu R**, Ishimura M, Nobusawa S, Hosaka T, Sasaki T, Kakizaki S, Yoshinari K, The influence of the long-term chemical activation of the nuclear receptor pregnane X receptor (PXR) on liver carcinogenesis in mice. ***Arch Toxicol***, 95, 1089-1102, 2021

10. **Shizu R**, Ezaki K, Sato T, Sugawara A, Hosaka T, Sasaki T, Yoshinari K, PXR suppresses PPARα-dependent *HMGCS2* gene transcription through inhibiting the interaction between PPARα and PGC1α. ***Cells***, 10, 3550, 2021

11. Lee SJ, **Shizu R**, Negishi M, Glucocorticoid receptor dimerization in the cytoplasm might

be essential for nuclear localization. ***Biochem Biophys Res Commun***, 553, 154-159, 2021

12. Shimizu Y, Sasaki T, Takeshita J, Watanabe M, **Shizu R**, Hosaka T, Yoshinari K, Average molecular weight as a useful chemical descriptor to discriminate liver injury-inducing drugs. ***PLoS One***, 16, e0253855, 2021

13. Shimizu Y, Sasaki T, Yonekawa E, Yamazaki H, Ogura R, Watanabe M, Hosaka T, **Shizu R**, Takeshita J, Yoshinari K, Association of CYP1A1 and CYP1B1 inhibition with drug-induced liver injury. ***J Toxicol Sci***, 46, 167-176, 2021

14. Asai T, Takeshita J, Shimizu Y, Tochikubo Y, **Shizu R**, Hosaka T, Kanno Y, Yoshinari K,Chemical characterization of anemia-inducing aniline-related substances and their application to the construction of a decision tree-based anemia prediction model, ***Food Chem Toxicol***, 157, 12548, 2021

15. **Shizu R**, Otsuka Y, Ezaki K, Ishii C, Arakawa S, Amaike Y, Abe T, Hosaka T, Sasaki T, Kanno Y, Miyata M, Yamazoe Y, Yoshinari K, 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. ***Mol Pharmacol***, 98, 634-647, 2020

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

17. Hosaka T, Wakatsuki A, Sasaki T, **Shizu R**, Yoshinari K, Construction of a PPARα reporter assay system with drug-metabolizing capability. ***BPB Reports***, 3, 7-10, 2020

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

19. **Shizu R**, Yokobori K, Perera L, Pedersen L, Negishi M, Ligand induced dissociation of the AR homodimer precedes AR monomer translocation to the nucleus. ***Sci Rep***, 9, 16734, 2019

20. Abe T, **Shizu R**, Sasaki T, Shimizu Y, Hosaka T, Kodama S, Matsuzawa A, Yoshinari K, Functional interaction between PXR and YAP in xenobiotic-dependent liver hypertrophy and drug metabolism. ***J Pharmacol Exp Ther***, 371, 590-601, 2019

21. Okamura M, **Shizu R**, Hosaka T, Sasaki T, Yoshinari K, 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. ***Drug Metab Pharmacokinet***, 34, 272-279, 2019

22. **Shizu R**, Kano M, Abe T, Tsuchiya S, Shimizu Y, Watanabe M, Hosaka T, Sasaki T, Yoshinari K, Screening of industrial and agricultural chemicals for searching a mouse PXR activator using cell-based reporter gene assays. ***BPB Reports***, 1, 11-19, 2018.

23. Yoshimaru S, **Shizu R**, Tsuruta S, Amaike Y, Kano M, Hosaka T, Sasaki T, Yoshinari K, Acceleration of murine hepatocyte proliferation by imazalil through the activation of nuclear receptor PXR. ***J Toxicol Sci***, 43, 443-450, 2018.

24. Abe T, Amaike Y, **Shizu R**, Takahashi M, Kano M, Hosaka T, Sasaki T, Kodama S, Matsuzawa A, Yoshinari K, Role of YAP activation in nuclear receptor CAR-mediated proliferation of mouse hepatocytes. ***Toxicol Sci***, 165, 408-419, 2018

25. **Shizu R**, Min J, Sobhany M, Pedersen LC, Mutoh S, Negishi M, Interaction of the phosphorylated DNA-binding domain in nuclear receptor CAR with its ligand binding domain regulates CAR activation. ***J Biol Chem***, 293, 333-344, 2018.

26. **Shizu R**, Osabe M, Perera L, Moore R, Sueyoshi T, Negishi M, Phosphorylated nuclear receptor CAR forms a homodimer to repress its constitutive activity for ligand activation. ***Mol Cell Biol***, 37, e00649-16, 2017.

27. **Shizu R**, Abe T, Benoki S, Takahashi M, Kodama S, Miyata M, Matsuzawa A, Yoshinari K, PXR stimulates growth factor-mediated hepatocyte proliferation by cross-talk with FOXO transcription factor. ***Biochem J***, 473, 257-266, 2015.

28. **Shizu R**, Benoki S, Numakura Y, Kodama S, Miyata M, Yamazoe Y, Yoshinari K, 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. ***PLoS One***, 8, e6180, 2013.

29. **Shizu R**, Shindo S, Yoshida T, Numazawa S, Cross-talk between constitutive androstane receptor and hypoxia-inducible factor in the regulation of gene expression. ***Toxicology Letters***, 219, 143-150, 2013.

30. **Shizu R**, Shindo S, Yoshida T, Numazawa S, MicroRNA-122 down-regulation is involved in phenobarbital-mediated activation of the constitutive androstane receptor. ***PLoS One***, 7, e41291, 2012.

Reviews and book chapters:

1. Shindo S, Kakizaki S, Sakaki T, Kawasaki Y, Sakuma T, Negishi M, **Shizu R**, Phosphorylation of Nuclear Receptors: Novelty and Therapeutic Implications, ***Pharm Ther***, 248, 108477, 2023

2. **Shizu R**, Understanding the underlying mechanism of xenobiotic-sensing nuclear recepeptor activation. ***Yakugaku Zasshi***, in press, 2023.

3. Yoshinari K, **Shizu R**, Distinct roles of the sister nuclear receptors PXR and CAR in liver cancer development. ***Drug Metab Dispos***, 2022

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

5. **Shizu R**, Numazawa S, Yoshida T, Involvement of microRNA in the induction of drug-metabolizing enzymes. ***Yakugaku Zasshi***, 132, 311-318, 2012.

Honors:

1. **Young Scientist Award**, The Japanese Society of Toxicology, 2023

2. **Tanabe award**, The Japanese Society of Toxicology, 2023

3. **Young Scientist Award**, Tokai Branch, The Pharmaceutical Society of Japan, 2023

4. **Young Poster Award**, 80th Japanese Cancer Association Annual Meeting, 2021

5. **Postdoctoral poster award**, The 12th international ISSX meeting, Portland, OR, 2019

6. **Tanabe award**, The Japanese Society of Toxicology, 2019

7. **Best poster award**, The 21st International symposium on Microsomes and Drug Oxidations, Davis, CA, 2016

8. **Travel grant**, Gordon Research Conference (Drug Metabolism), Holderness, NH, 2015