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Academic career

1982	Department of Pharmaceutical Sciences,	BS in Pharmaceutical Sciences Fukuoka University, Japan
1984	Department of Pharmaceutical Sciences,	MS in Drug metabolism and Toxicology Fukuoka University, Japan
1988	Department of Pharmaceutical Sciences,	PhD in Drug metabolism and Toxicology Fukuoka University, Japan

Professional experience

1989-1992	Postdoctoral Fellow	Department of Molecular Pharmacology, UCLA School of Medicine, USA
1992-1994	Senior Scientist	National Institute for Environmental Studies, Japan
1994-1999	Lecture	Institute of Community Medicine University of Tsukuba
1999-2003	Associate Professor	Institute of Community Medicine University of Tsukuba
2003-2004	Professor	Institute of Community Medicine University of Tsukuba
2004-2011	Professor	Graduate School of Comprehensive Human Sciences, University of Tsukuba
2011-present	Professor	Environmental Biology Laboratory Faculty of Medicine, University of Tsukuba

2014-present	Coordinator	Global Innovation Joint Degree Program (GIP-TRIAD)

Awards

1990	Special Investigator's Award, Merck Sharp & Dohme Research Laboratories, USA
2002	Young Investigator's Award, Japanese Society for Hygiene
2009	The Pharmaceutical Society of Japan Award for Divisional Scientific Promotions
2011	The Japanese Society of Toxicology Tanabe Award
2013	The Pharmaceutical Society of Japan Award for Divisional Field of Public Health
2013	The Japanese Society of Toxicology Pfizer Award

Research interests

Our laboratory addresses the mechanisms by which chemicals causing oxidative stress and environmental electrophiles such as polycyclic aromatic hydrocarbon quinones and methylmercury affect living systems by interacting with sensor proteins with reactive thiols (thiolate ions) through chemical modification. The observations obtained by this group regarding environmental electrophiles have lent new insight into mechanisms of redox-dependent cellular signalings such as cell survival, cell proliferation and cell damage. We are also interested in role of reactive sulfur species (e.g., hydrogen sulfide, persulfides and polysulfides) in regulation of the redox signal transduction pathways mediated by environmental electrophiles.

Selected publications (Original article, 180; Review, 19; Book, 19)

***, corresponding author**

1. ***Kumagai Y**, Arimoto T, Shinyashiki M, Shimojo N, Nakai Y, Yoshikawa T, Sagai M. Generation of reactive oxygen species during interaction of diesel exhaust particles components with NADPH-cytochrome P450 reductase and involvement of the bioactivation in the DNA damage. *Free Radical Biology & Medicine* **22**: 479-487, 1997.
2. ***Kumagai Y**, Hayashi T, Miyauchi T, Endo A, Iguchi A, Kiriya-Sakai M, Sakai S, Yuki K, Kikushima M, Shimojo N. Phenanthraquinone inhibits eNOS activity and suppresses vasorelaxation. *American Journal of Physiology* **281**: R25-R30, 2001.
3. ***Kumagai Y**, Koide S, Taguchi K, Endo A, Nakai Y, Yoshikawa T, Shimojo N. Oxidation of proximal protein sulfhydryls by phenanthraquinone, a component of diesel exhaust particles, *Chemical Research in Toxicology* **15**: 483-489, 2002.

4. Pi JB, Yamauchi H,***Kumagai Y**, Sun GF, Yoshida T, Aikawa H, Hopenhayn-Rich C, Shimojo N. Evidence for induction of oxidative stress caused by chronic exposure of Chinese residents to arsenic contained in drinking water. *Environmental Health Perspectives* **110**: 331-336, 2002.
5. Kikuno S, Taguchi K, Iwamoto N, Yamano S, Cho AK, Froines JR, ***Kumagai Y.** 1,2-Naphthoquinone activates vanilloid receptor 1 through increased protein tyrosine phosphorylation, leading to contraction of guinea pig trachea. *Toxicology and Applied Pharmacology* **210**: 47-54, 2006.
6. Iwamoto N, Sumi D, Ishii T, Uchida K, Cho AK, Froines JR, ***Kumagai Y**. Chemical knockdown of protein tyrosine phosphatase 1B by 1,2-naphthoquinone through covalent modification causes persistent transactivation of epidermal growth factor receptor. *Journal of Biological Chemistry* **282**: 33396-33404, 2007.
7. Taguchi K, Fujii S, Yamano S, Cho AK, Kamisuki S, Nakai Y, Sugawara F, Froines JR, ***Kumagai Y.** An approach to evaluate two-electron reduction of 9,10-phenanthraquinone and redox activity of the hydroquinone associated with oxidative stress. *Free Radical Biology & Medicine* **43**: 789-799, 2007.
8. Taguchi K, Shimada M, Fujii S, Sumi D, Pan XQ,Yamano S, Nishiyama T, Hiratsuka A, Yamamoto M, Cho AK, Froines JR, ***Kumagai Y**. Redox cycling of 9,10-phenanthraquinone to cause oxidative stress is terminated through its monoglucuronide conjugation in human pulmonary epithelial A549 cells. *Free Radical Biology & Medicine* **44**: 1645-1655, 2008.
9. Toyama T, Shinkai Y, Yasutake A, Uchida K, Yamamoto M, ***Kumagai Y**. Isothiocyanates reduce mercury accumulation via an Nrf2-dependent mechanism during exposure of mice to methylmercury. *Environmental Health Perspectives* **119**: 1117-1121, 2011.
10. Yoshida E, Toyama T, Shinkai Y, Sawa T, Akaike T, ***Kumagai Y**. Detoxification of methylmercury by hydrogen sulfide producing enzyme in mammalian Cells. *Chemical Research in Toxicology* **24**: 1633-1635, 2011.
11. Miura T, Kakehashi H, Shinkai Y, Egara Y, Hirose R, Cho AK, ***Kumagai Y.** GSH-mediated S-transarylation of a quinone glyceraldehyde-3-phosphate dehydrogenase conjugate. *Chemical Research in Toxicology* **24**: 1836-1844, 2011.
12. Nishida M, Sawa T, Kitajima N, Ono K, Inoue H, Ihara H, Motohashi H, Yamamoto M, Suematsu M, Kurose H, Van der Vliet A, Freeman BA, Shibata T, Uchida K, **Kumagai Y**,

Akaike T. Hydrogen sulfide anion regulates redox signaling via electrophile sulfhydration. *Nature Chemical Biology* **8**: 714-724, 2012.

13. ***Kumagai Y**, Shinkai Y, Miura T, Cho AK. The chemical biology of naphthoquinones and its environmental implications. *Annual Review of Pharmacology and Toxicology* **52**: 221-247, 2012.
14. Ida T, Sawa T, Ihara H, Tsuchiya Y, Watanabe Y, **Kumagai Y**, Suematsu M, Motohashi H, Fujii S, Matsunaga T, Yamamoto M, Ono K, Devarie-Baez NO, Xian M, Fukuto JM, Akaike T. Reactive cysteine persulfides and S-polythiolation regulate oxidative stress and redox signaling. *Proceedings of the National Academy of Sciences, USA* **111**: 7606-7611, 2014.
15. Abiko Y, Mizokawa M, ***Kumagai Y**. Activation of the Keap1/Nrf2 pathway through covalent modification of the 2-alkenal group of aliphatic electrophiles in Coriandrum sativum L. *Journal of Agricultural and Food Chemistry* **62**: 10936-10944,2014.
16. Abiko Y, Yoshida E, Ishii I, Fukuto JM, Akaike T, ***Kumagai Y**. Involvement of reactive persulfides in biological bismethylmercury sulfide formation. *Chemical Research in Toxicology* **28**: 1301-1306, 2015.
17. Unoki T, Abiko Y, Toyama T, Uehara T, Tsuboi K, Nishida M, Kaji T, ***Kumagai Y.** Methylmercury, an environmental electrophile capable of activation and disruption of the Akt/CREB/Bcl-2 signal transduction pathway in SH-SY5Y cells. *Scientific Reports* **6**: 28944, 2016.
18. Abiko Y, Sha L, Shinkai Y, Unoki T, Luong NC Tsuchiya Y, Watanabe Y, Hirose R, Akaike T, ***Kumagai Y**. 1,4-Naphthoquinone activates the HSP90/HSF1 pathway through the S-arylation of HSP90 in A431 cells: Negative regulation of the redox signal transduction pathway by persulfides/polysulfides. *Free Radical Biology & Medicine* **104**: 118-128, 2017.
19. ***Kumagai Y**, Abiko Y. Environmental electrophiles: protein adducts, modulation of redox signaling and interaction with persulfides/polysulfides. *Chemical Research in Toxicology* **30**: 203-219, 2017.
20. Shinkai Y, Masuda A, Akiyama M, Xian M, ***Kumagai Y**. Cadmium-mediated activation of the HSP90/HSF1 pathway regulated by reactive persulfides/polysulfides. *Toxicological Sciences* 2doi: 10.1093/toxsci/kfw268, 2017.