INTERNATIONAL UNION OF TOXICOLOGY

# International Union of Toxicology

**PROPOSAL TO THE NOMINATING COMMITTEE:**
**MEMBERS SUITABLE FOR NOMINATION TO THE IUTOX EXECUTIVE COMMITTEE FOR THE PERIOD 2019-2022**

Proposal due to Barbara Hales at the IUTOX Secretariat by: **November 19, 2018**
Please include a short CV for the nominee

***PROPOSAL SUBMITTED BY***

Member Society: Japanese Society of Toxicology

Name and signature of IUTOX Member Society representative submitting nomination: Akihiko Hirose

Position: Secretary General (JSOT)

Signature: Akihiko Hirose

Date: October 17, 2018

***BIOGRAPHICAL DETAILS OF PROPOSED CANDIDATE***

Name and signature of proposed candidate: Yoshito Kumagai, Ph.D.

Nomination for officer or director may be indicated: Nomination for director

Date of Birth: August 12, 1959

Current Position: President of the JSOT;
Professor, Environmental Biology Laboratory Faculty of Medicine, University of Tsukuba

Address: 1-1-1 Tennodai, Tsukuba, Ibaraki 305-8577 Japan

Nationality: Japan

Scientific Field: Molecular Toxicology

Education:

| | |
|---|---|
| 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 positions held (with dates):

| | |
|---|---|
| 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 |

IUTOX positions held (with dates):

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|---|---|
| 2016-2019 | Executive Committee, International Union of Toxicology (IUTOX) |

Member Society positions held (with dates):

| | |
|---|---|
| 2009-2016 | Director, Japanese Society of Toxicology |
| 2012 | Secretary General, 6th International Congress of Asian Society of Toxicology (ASIATOX) |
| 2012-2015 | Treasurer, ASIATOX |
| 2015-2018 | Councilor & Auditor, ASIATOX |
| 2018- | 15th President, Japanese Society of Toxicology |

Professional memberships and/or 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 |
| 2013 | The Pharmaceutical Society of Japan Award for Divisional Field of Public Health and Environmental Toxicology |
| 2013 | The Japanese Society of Toxicology Pfizer Award |
| 2016 | The Japanese Society of Toxicology Tanabe Award |
| 2018 | The Japanese Society of Toxicology Merit Award |


## Yoshito Kumagai, Ph.D.

Date of Birth: August 12, 1959

Affiliation: Environmental Biology Laboratory, Faculty of Medicine, University of Tsukuba

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http://www.md.tsukuba.ac.jp/environmental_medicine/kibanS/index_en.html


### Academic career

| | | |
|---|---|---|
| 1982 | Department of Pharmaceutical Sciences, | BS in Pharmaceutical Sciences<br>Fukuoka University, Japan |
| 1984 | Department of Pharmaceutical Sciences, | MS in Drug metabolism and Toxicology<br>Fukuoka University, Japan |
| 1988 | Department of Pharmaceutical Sciences, | PhD in Drug metabolism and Toxicology<br>Fukuoka University, Japan |

### Professional experience

| | | |
|---|---|---|
| 1989-1992 | Postdoctoral Fellow | Department of Molecular Pharmacology,<br>UCLA School of Medicine, USA |
| 1992-1994 | Senior Scientist | National Institute for Environmental<br>Studies, Japan |
| 1994-1999 | Lecture | Institute of Community Medicine<br>University of Tsukuba |
| 1999-2003 | Associate Professor | Institute of Comunity Medicine<br>University of Tsukuba |
| 2003-2004 | Professor | Institute of Community Medicine<br>University of Tsukuba |
| 2004-2011 | Professor | Graduate School of Comprehensive<br>Human Sciences, University of Tsukuba |
| 2011-present | Professor | Environmental Biology Laboratory<br>Faculty of Medicine, University of Tsukuba |
| 2014-present | Visiting Professor | China Medical University, China |

| | | |
|---|---|---|
| 2017-present | Director | International Joint Degree Master's Program in Agro-Biomedical Science in Food and Health |

**Society activity**

| | | |
|---|---|---|
| | | Full member, Society of Toxicology |
| | | Member, American Society of Toxicology |
| 2010-2013 | Editor in Chief | Journal of Health Science |
| 2009-2016 | Director | Japanese Society of Toxicology |
| 2010-present | Associate Editor | Journal of Toxicological Sciences |
| 2016-present | Associate Editor | Toxicological Sciences |
| 2012 | Secretary General | 6th International Congress of Asian Society of Toxicology (ASIATOX) |
| 2012-2015 | Treasurer | ASIATOX |
| 2013 | President | 12th Annual Meeting of Society for the Study of Molecular, Preventive and Environmental Medicine |
| 2013-2016 | Vice Dean | Divisional Field of Public Health, Pharmaceutical Society of Japan |
| 2014 | President | 39th Annual Meeting of Divisional Field of Public Health, Pharmaceutical Society of Japan |
| 2015-2018 | Councilor & Auditor | ASIATOX |
| 2016-present | Director | Japanese Society of Nitric Oxide |
| 2016-2019 | Executive Committee | International Union of Toxicology (IUTOX) |
| 2017-present | Director | Japanese Society of Oxidative Stress |
| 2017-present | Associate Editor | Toxicological Sciences, Society of Toxicology |
| 2017 | President | 44th Annual Meeting of Japanese Society of Toxicology in Yokohama |
| 2018 | 15th President | Japanese Society of Toxicology |

## 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

2013 The Pharmaceutical Society of Japan Award for Divisional Field of Public Health and Environmental Toxicology

2013 The Japanese Society of Toxicology Pfizer Award

2016 The Japanese Society of Toxicology Tanabe Award

2018 The Japanese Society of Toxicology Merit Award

## Research interests

We are exposed to a variety of environmental electrophiles through food life, life style and life environment on a daily basis. While it has been reported that such reactive species covalently bind to protein nucleophiles, we found that environmental electrophiles activate redox signaling pathways at lower doses and disrupt these pathways and substantial cytotoxicity at higher doses. It was also found that reactive sulfur species (e.g., persulfides, polysulfides, hydrogen sulfide) negatively regulate modulation of redox signaling and toxicity caused by exposure to environmental electrophiles, presumably through formation of their sulfur adducts.

Exposome has been defined as the cumulative environmental exposures, including diet, lifestyle, pollutants, and others across the life span; however, the full characterization of the exposome throughout the whole lifespan remains an outstanding challenge. In the current study, we attempt modeling an exposome specialized for environmental electrophiles with cultured cells and mice in the absence and presence of reactive sulfur species. We also explore how sulfur adduct derived from methylmercury, a model of environmental electrophiles, undergoes biotransformation by reactive sulfur species, and then is excreted into out of the body.

**ORIGINAL ARTICLE, 190; REVIEW ARTICLE, 22.**

**SELECTED PUBLICATIONS （*, 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**, Nakajima H, Midorikawa K, Homma-Takeda S, Shimojo N. Inhibition of nitric oxide formation by neuronal nitric oxide synthase by quinones: Nitric oxide synthase as a quinone reductase. ***Chemical Research in Toxicology*** 11: 608-613, 1998.

3. Pi JB, ***Kumagai Y**, Sun GF, Yamauchi H, Yoshida T, Iso H, Endo A, Yu LA, Yuki K, Miyauchi T, Shimojo N. Decreased serum concentrations of nitric oxide metabolites among Chinese in an endemic area of chronic arsenic poisoning in Inner Mongolia. ***Free Radical Biology & Medicine*** 28: 1137-1142, 2000.

4. ***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.

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, 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.

8. 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: 1117-1122, 2011.

9. 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.

10. 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.

11. ***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.
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. 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.
14. 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.
15. 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.
16. 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.
17. 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*** 156: 412-421, 2017.
18. Abiko Y, Shinkai Y, Unoki T, Hirose R, Uehara T, ***Kumagai Y**. Polysulfide $Na_2S_4$ regulates the activation of PTEN/Akt/CREB signaling and cytotoxicity mediated by 1,4-naphthoquinone through formation of sulfur adducts. ***Scientific Reports*** 7: 4814, 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. Akaike T, Ida T**, Fan-Yan Wei FY**, Nishida M**, **Kumagai Y****, Alam MM, Ihara H, Sawa T, Tetsuro Matsunaga T, Kasamatsu S, Nishimura A, Morita M, Tomizawa K, Nishimura A, Watanabe S, Inaba K, Shima H, Tanuma N, Jung M, Fujii S, Watanabe Y, Ohmuraya M, Nagy P, Feelisch M, Fukuto JM, Motohashi H. Cysteinyl-tRNA synthetase governs cysteine polysulfidation and mitochondrial bioenergetics. ***Nature Communications*** 8: 1177, 2017.
******, These authors contributed equally to this study.

**ORIGINAL ARTICLE (*, corresponding author)**

1. **Kumagai Y**, Ishida T, Toki S. Method for determination of morphinone in urine and bile of guinea pig by high-performance liquid chromatography. *Journal of Chromatography* **421**: 155-160, 1987.
2. Ishida T, **Kumagai Y**, Ikeda Y, Ito K, Yano M, Toki S, Mihashi K, Fujioka T, Iwase Y, Hachiyama S. (8S)-(Glutathion-S-yl)-dihydromorphinone, a novel metabolite of morphine from guinea pig bile. *Drug Metabolism and Disposition* **17**: 77-81, 1989.
3. Ishida T, **Kumagai Y**, Ikeda Y, Ito K, Yano M, Hachiyama S, Toki S. Typical molecular ion peak analysis of morphinone- and codeinone-glutathione adducts with sodium iodide using fast atom bombardment spectrometry. *Organic Mass Spectrometry* **24**: 286-288, 1989.
4. **Kumagai Y**, Todaka T, Yamano S, Toki S. Stimulation mechanism of guinea pig liver-mediated reduction of naloxone by morphine. *Drug Metabolism and Disposition* **18**: 462-466, 1990.
5. Hiramatsu M, **Kumagai Y**, Unger SE, Cho AK. Metabolism of methylenedioxymethamphetamine (MDMA): Formation of dihydroxymethamphetamine and a quinone identified as its glutathione adduct. *Journal of Pharmacology and Experimental Therapeutics* **254**: 521-527, 1990.
6. ***Kumagai Y**, Todaka T, Toki S. A new metabolic pathway of morphine: *In vivo* and *in vitro* formation of morphinone and morphinone-glutathione adduct in guinea pig. *Journal of Pharmacology and Experimental Therapeutics* **255**: 504-510, 1990.
7. **Kumagai Y**, Lin LY, Schmitz DA, Cho AK. Hydroxyl radical mediated demethylenation of (methylenedioxy)phenyl compounds. *Chemical Research in Toxicology* **4**: 330-334, 1991.
8. **Kumagai Y**, Wickham KA, Schmitz DA, Cho AK. Metabolism of methylenedioxyphenyl

compounds by rabbit liver preparations: Participation of different cytochrome P450 isozymes in the demethylenationreaction. *Biochemical Pharmacology* **42**: 1061-1067, 1991.

9. Patel N, **Kumagai Y**, Unger SE, Fukuto JM, Cho AK. Transformation of dopamine and a-methyldopamine by NG108-15 cells: Formation of thiol adduct. *Chemical Research in Toxicology* **4**: 421-426, 1991.
10. Fukuto JM, **Kumagai Y**, Cho AK. Determination of the mechanism of demethylenation of (methylenedioxy)phenyl compounds by cytochrome P450 using deuterium isotope effects. *Journal of Medicinal Chemistry* **34**: 2871-2876, 1991.
11. **Kumagai Y**, Schmitz DA, Cho AK. Aromatic hydroxylation of methylenedioxybenzene (MDB) and methylenedioxymethamphetamine (MDMA) by rabbit cytochrome P450. *Xenobiotica* **22**: 395-403, 1992.
12. **Kumagai Y**, Ikeda Y, Toki S. Hydroxyl radical-mediated conversion of morphine to morphinone. *Xenobiotica* **22**: 507-513, 1992.
13. **Kumagai Y**, Lin LY, Philpot RM, Yamada H, Oguri K, Yoshimura H, Cho AK. Regiochemical differences in cytochrome P450 isozymes responsible for the oxidation of methylenedioxyphenyl groups by rabbit liver. *Molecular Pharmacology* **42**: 695-702, 1992.
14. Lin LY, **Kumagai Y**, Cho AK. Enzymatic and chemical demethylenation of (methylenedioxy) amphetamine and (methylenedioxy)-methamphetamine by rat brain microsomes. *Chemical Research in Toxicology* **5**: 401-406, 1992.
15. Inamura T, Pardridge WM, **Kumagai Y**, Black KL. Differential tissue expression of immunoreactive dehydropeptidase I, a peptidyl leukotriene metabolizing enzyme. *Prostaglandins Leukotrienes and Essential Fatty Acids* **50**: 85-92, 1994.
16. **Kumagai Y**, Lin LY, Hiratsuka A, Narimatsu S, Suzuki T, Yamada H, Oguri K, Yoshimura H, Cho AK. Participation of cytochrome P450-2B and -2D isozymes in the demethylenation of methylenedioxy-methamphetamine enantiomers by rats. *Molecular Pharmacology* **45**: 359-365, 1994.
17. ***Kumagai Y**, Shinyashiki M, Sun GF, Shimojo N, Sagai M. An efficient method for purification of cuprozinc superoxide dismutase from bovine erythrocytes. *Experientia* **50**: 673-676, 1994.
18. ***Kumagai Y**, Taira J, Sagai M. Apparent inhibition of superoxide dismutase activity *in vitro* by diesel exhaust particles. *Free Radical Biology & Medicine* **18**: 365-371, 1995.
19. Lin L. Y, **Kumagai Y**, Hiratsuka A, Narimatsu S, Suzuki T, Funae Y, DiStefano EW, Cho AK. Cytochrome P450 2D isozymes catalyze the 4-hydroxylation of methamphetamine

enantiomers. *Drug Metabolism and Disposition* **23**: 610-614, 1995.

20. Narimatsu S, Watanabe T, Mochida M, Masubuchi Y, Horie T, **Kumagai Y**, Cho AK, Imaoka S, Funae Y. Characterization of chemically reactive propranolol metabolite that binds to microsomal proteins of rat live. *Chemical Research in Toxicology* **8**: 721-728, 1995.
21. Chu T, **Kumagai Y**, DiStefano EW, Cho AK. The disposition of MDMA and three metabolites in the brains of different rat strains and their possible roles in acute 5HT depletion. *Biochemical Pharmacology* **51**: 789-796, 1996.
22. Homma-Takeda S, Shinyashiki M, Nakai I, Tohyama C, **Kumagai Y**, Shimojo N. Direct detection of mercury-bound metalloproteins (metallothionein and Cu,Zn-superoxide dismutase) using a combination of gel electrophoresis and one dementional synchrotron radiation X-ray fluorescence analysis. *Analytical Letters* **29**: 601-611, 1996.
23. Homma-Takeda S, Shinyashiki M, **Kumagai Y**, Shimojo N. A new method for detection of mercury-bound protein using a combination of gel electrophoresis and one dimentional synchrotron radiation X-ray fluorescence analysis. *Journal of Occupational Health* **38**: 118-119, 1996.
24. Inayama T, **Kumagai Y**, Sakane M, Saito M, Matsuda M. Plasma protein-bound sulfhydryl groups oxidation following full-marathone race. *Life Sciences* **59**: 573-578, 1996.
25. Mori Y, Murakami S, Sagae T, Hayashi H, Sakata M, Sagai M, **Kumagai Y.** Inhibition of catalase activity in vitro by diesel exhaust particles. *Journal of Toxicology, Environmental Health* **47**: 125-134, 1996.
26. Arimoto T, Yoshikawa T, Komori Y, **Kumagai Y.** Inhibition of rat constitutive nitric oxide synthase by benexate. *Life Sciences* **59**: 953-959, 1996.
27. Shimojo N, **Kumagai Y**, Homma-Takeda S, Shinyashiki M, Takasawa N, Kushida K. Isozyme selective induction of mouse pulmonary superoxide dismutase by the exposure to mercury vapor. *Environmental Toxicology and Pharmacology* **2**: 35-37, 1996.
28. Shinyashiki M, ***Kumagai Y**, Homma-Takeda S, Nagafune J, Suzuki J, Matsuzaki I, Satoh S, Sagai M, Shimojo N. Selective inhibition of the mouse brain Mn-SOD by methylmercury. *Environmental Toxicology and Pharmacology* **2**: 359-366, 1996.
29. Inamura T, **Kumagai Y**, Sagai M, Matsuda M. Effect of low- and high-molecular components contained in human plasma and superoxide dismutase activity. *Sangyo Eiseigaku Zasshi* **38**: 260-261, 1996.
30. ***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.

31. Shimojo N, Matsuzaki I, Tabata T, Shinyashiki M. Sun GF, Homma-Takeda S, Iida A, **Kumagai Y.** A novel hair analysis for trace elemnts on hair cross section by synchrotron radiation X-ray fluorescence imaging with X-Ray microprobe. *Journal of Occupational Health* **39**: 64-65, 1997.
32. Homma-Takeda S, Ishido M, **Kumagai Y**, Takenaka Y, Shimojo N. Exposure of rat to inorganic mercury induces DNA fragmentation responsible for apoptosis. *Journal of Occupational Health* **39**: 70-71, 1997.
33. Narimatsu S, Arai T, Watanabe T, Masubuchi Y, Horie T, Suzuki T, Ishikawa T, **Kumagai Y**, Cho AK. Covalent binding of a metabolite derived from propranolol and its active metabolite 4-hydroxypropranolol to hepatic microsomal proteins of the rat. *Chemical Research in Toxicology* **10**: 289-295, 1997.
34. Sun GF, Shimojo N, Pi JB, Lee S, **Kumagai Y.** Gene deficiency of glutathione S-transferase m isoform associated with susceptibility to lung cancer in a Chinese population. *Cancer Lette*rs **113**: 169-172, 1997.
35. Yamada H, Shiiyama S, Soejima-Ohkuma T, Honda S, **Kumagai Y**, Cho AK, Oguri K, Yoshimura H. Deamination of amphetamines by cytochrome P450: Studies on substrate specificity and regioselectivity with microsomes and purified CYP2C subfamily isozymes. *Journal of Toxicological Sciences* **22**: 67-74, 1997.
36. Shimojo N, Homma-Takeda S, Ohuchi K, Shinyashiki M, **Kumagai** Y**.** Mercury dynamics in hair of the rats exposed to methylmercury by synchrotron radiation X-ray fluorescence imaging. *Life Sciences* **60**: 2129-2137, 1997.
37. Shiiyama S, Soejima-Ohkuma T, Honda S. **Kumagai Y**, Cho AK, Yamada H, Oguri K, Yoshimura H. Major role of the CYP2C isozymes in deamination of amphetamine and benzphetamine - Evidence for the quinidine-specific inhibition of the reactions catalyzed by rabbit enzyme. *Xenobiotica* **27**: 379-387, 1997.
38. ***Kumagai Y**, Tsurutani Y, Shinyashiki M, Homma-Takeda S, Yoshikawa T, Nakai Y, Shimojo N. Bioactivation of lapachol responsible for DNA scission by NADPH-cytochrome P450 reductase. *Environmental Toxicology and Pharmacology* **3**: 245-250, 1997.
39. ***Kumagai Y**, Mizukado S, Nagafune J, Shinyashiki M, Homma-Takeda S, Shimojo N. Post-transcriptional elevation of mouse brain Mn-SOD by mercuric chloride. *Brain Research* **769**: 178-182, 1997.

40. Takenaka Y, Homma-Takeda S, **Kumagai Y**, Shimojo N. A dose-response study on inorganic mercury-induced DNA fragmentation in rat kidney. *Sangyo Eiseigaku Zasshi* **39**: 184-185, 1997.

41. Homma-Takeda S, **Kumagai Y**, Shinyashiki M, Shimojo N. Application of synchrotorn radiation X-ray fluorescence imaging combined with periodic acid schiff staining to renal section of mercury-treated rats. *Journal of Synchrotron Radiation* **5**: 57-59, 1998.

42. ***Kumagai Y**, Nakajima H, Midorikawa K, Homma-Takeda S, Shimojo N. Inhibition of nitric oxide formation by neuronal nitric oxide synthase by quinones: Nitric oxide synthase as a quinone reductase. *Chemical Research in Toxicology* **11**: 608-613, 1998.

43. **Kumagai Y**, Pi JB, Lee S, Sun GF, Yamanushi T, Sagai M, Shimojo N. Serum antioxidant vitamins and risk of lung and stomach cancers in Shenyang, China. *Cancer Letters* **129**: 145-149, 1998.

44. Shinyashiki M, ***Kumagai Y**, Nakajima H, Nagafune J, Homma-Takeda S, Sagai M, Shimojo N. Differential changes in rat brain nitric oxide synthase in vivo and in vitro by methylmercury. *Brain Research* **798**: 147-155, 1998.

45. Lim H-B, Ichinose T, Miyabara Y, Takano H, **Kumagai Y**, Shimojo N, Devalia JL, Sagai M. Involvement of superoxide and nitric oxide on airway inflammation and hyperresponsiveness induced by diesel exhaust particles in mice. *Free Radical Biology and Medicine* **25**: 635-644, 1998.

46. ***Kumagai Y**, Midorikawa K, Nakai Y, Yoshikawa T, Kushida K, Homma-Takeda S, Shimojo N. Inhibition of nitric oxide formation and superoxide generation during reduction of LY83583 by neuronal nitric oxide synthase. *European Journal of Pharmacology* **360**: 213-218, 1998.

47. Homma-Takeda S, Liao ZQ, **Kumagai Y**, Shimojo N. Effects of dichloromethane on metylmercury-induced toxicity of rat C6 glioma cells. *Sangyo Eiseigaku Zasshi* **40**: 37-38, 1998.

48. Kanda H, **Kumagai Y**, Nakajima H, Takenaka Y, Homma-Takeda S, Shimojo N. Various changes in nitric oxide synthase and arginase II in rat kidney caused by inorganic mercury. *Sangyo Eiseigaku Zasshi* **40**: 212-213, 1998.

49. Li S, **Kumagai Y**, Kiriya-Sakai M, Shimojo N. Acetylation of 4-amino-2,6-dinitrotoluene, a major metabolite of 2,4,6-trinitrotoluene by liver cytosol of SD rats. *Sangyo Eiseigaku Zasshi* **40**: 252-253, 1998.

50. Kugenuma Y, Homma-Takeda S, **Kumagai Y**, Shimojo N. methylmercury-induced DNA

fragmentation in rat genital organs. *Sangyo Eiseigaku Zasshi* **40**: 250-251, 1998.

51. Kiriya-Sakai M, **Kumagai Y**, Li S, Shimojo N. Generation of hydrogen peroxide during reduction of 2,4,6-trinitrotoluene and its related compounds. *Sangyo Eiseigaku Zasshi* **41**: 11-12, 1999.
52. Homma-Takeda S, Takenaka Y, **Kumagai Y**, Shimojo N. Selective induction of renal proximal tubular cells caused by inorganic mercury in vivo. *Environmental Toxicology and Pharmacology* **7**: 179-187, 1999.
53. Pi JB, ***Kumagai Y**, Sun GF, Yamauchi H, Yoshida T, Iso H, Endo A, Yu LA, Yuki K, Miyauchi T, Shimojo N. Decreased serum concentrations of nitric oxide metabolites among Chinese in an endemic area of chronic arsenic poisoning in Inner Mongolia. *Free Radical Biology & Medicine* **28**: 1137-1142, 2000.
54. Pi JB, ***Kumagai Y**, Sun GF, Shimojo N. Improved method for extraction and determination of L-arginine and its mono- and di-methylated metabolites in biological samples by high-performance liquid chromatography. *Journal of Chromatography* **742**: 199-203, 2000.
55. ***Kumagai Y**, Wakayama T, Li S, Shinohara A, Iwamatsu A, Sun GF, Shimojo N. z-crystallin catalyzes reductive activation of 2,4,6-trinitrotoluene to generate reactive oxygen species: A proposed mechanism for the induction of cataracts. *FEBS Letters* **478**: 295-298, 2000.
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