

Environmental Biology

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Major Scientific Interests of the Group

This laboratory addresses the mechanisms by which environmental electrophiles such as naphthoquinones, (E)-2-alkenals, 1,4-benzoquinone, crotonaldehyde, methylmercury and cadmium affect living systems by interacting with redox sensor proteins with reactive thiols (thiolate ions) through covalent modification. The observations obtained by this group regarding environmental electrophiles have lent new insight into mechanisms of redox-dependent signal transduction pathways that are regulated by reactive sulfur species (persulfides and polysulfides) in the body.

Projects for Regular Students in Doctoral or Master's Programs

- 1) Activation of redox signal transduction pathways (e.g., PTP1B/EGFR, Keap1/Nrf2, HSP90/HSF1 and PTEN/Akt) during exposure to environmental electrophiles.
- 2) Isolation and identification of phytochemicals with reactive sulfur species that can capture environmental electrophiles, resulting in inactivation of these chemicals.

Selected Publications

- 1) **Kumagai Y**, Abiko Y. Environmental electrophiles: protein adducts, modulation of redox signaling and interaction with persulfides/polysulfides. *Chem Res Toxicol* 30: 203-219, 2017.
- 2) Akaike T, Ida T, Fan-Yan Wei FY, Nishida M, **Kumagai Y**, Alam MM, Ihara H, Sawa T, 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 Commun* 8: 1177, 2017.
- 3) 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. *Sci Rep* 6: 28944, 2016.
- 4) 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. *Proc Natl Acad Sci USA* 111: 7606-7611, 2014.
- 5) **Kumagai Y**, Shinkai Y, Miura T, Cho AK. The chemical biology of naphthoquinones and its environmental implications. *Annu Rev Pharmacol Toxicol* 52: 221-247, 2012.
- 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. *J Biol Chem* 282: 33396-33404, 2007.