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Theme

- Adaptive response and protection against electrophilic stress

Keyword Electrophilic stress, protein adduct, Redox signaling, Reactive sulfur species

Highlight

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.

Other Faculty Members

Associate Professor Yasuhiro Shinkai
Associate Professor Norihiko Obayashi
Assistant Professor Yumi Abiko

Applications and Prospects

- Since we are daily exposed to a variety of environmental electrophiles via living environment, life style and dietary habits, understanding such reactive chemicals-mediated activation and disruption of redox signaling pathways through covalent modification of cellular proteins is a critical issue for human health.

Literature, intellectual property, work

- Akiyama M, Unoki T, Shinkai Y, Ishii I, Ida T, Akaike T, Yamamoto M, Kumagai Y. Environmental electrophile-mediated toxicity in mice lacking Nrf2, CSE, or both. *Environ Health Perspect* 127: 67002, 2019.
- Shinkai Y, Kumagai Y. Sulfane Sulfur in Toxicology: A Novel Defense System Against Electrophilic Stress. *Toxicol Sci* 170: 3-9, 2019.
- Kumagai Y, Abiko Y. Environmental electrophiles: protein adducts, modulation of redox signaling and interaction with persulfides/polysulfides. *Chem Res Toxicol* 30: 203-219, 2017.
- 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.