

GS2-4 **Role of Nrf2/Keap1 system in toxic effects of 1,2-naphthoquinone as environmental electrophile**

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We are exposed to numerous chemical substances that surround us in the environment. It is important to clarify mechanism of toxic effects and biological responses against these chemical substances for health maintenance and improvement of public health. We have identified 1,2-naphthoquinone as an environmental electrophile in air pollutant. When electrophile is covalently bound to protein through thiolate ions ($-S^-$), their structure and function are affected, resulting in disruption of homeostatic functions and expression of toxicity. Therefore, we focus on Nrf2/Keap1 system which negatively regulates electrophiles toxicity. Under normal conditions, Nrf2 is negatively regulated by Keap1. Once Keap1 is modified by an electrophile, leading to Nrf2 activation. The activated Nrf2 translocate to nuclear and then upregulate phase II enzymes and phase III transporters. We examined relation between 1,2-naphthoquinone and Nrf2/Keap1 system by using primary hepatocytes from Nrf2-deficient or liver-specific Keap1-deficient mice. We found that Nrf2 has a crucial role in protection against 1,2-naphthoquinone-induced cytotoxicity through the enhancement of detoxification pathway.