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Multi-organ Toxicity and Carcinogenicity Study of Benzene Using Connexin 32 Knockout Mice : Possible Roles of Cx32 Intercellular Gap Junction in the Target Organs

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The possible roles of connexin 32 (Cx32) were evaluated using Cx32 knockout (KO) mice in the benzene-target organs including hemopoietic and respiratory system. Wild type (WT) and Cx32 KO mice were exposed to 300 ppm benzene by inhalation for 6 h per day, 5 days per week for a total of 26 weeks, and then sacrificed to evaluate the organ toxicity or allowed to live out their life span to evaluate the reversibility of the lesions and tumor incidence. Twenty six-week benzene exposure induced significant changes in the number of leukocyte and red blood cell and other blood parameters, and, in the organ weights of heart, lung, spleen, thymus and testes as well as body weight. Notable differences between WT and Cx32 KO mice were found in total body weight and the organ weight of lung and spleen, which was further supported by histopathological examination. The benzene-induced pneumotoxicity, corresponding to the dramatic decrease of body weight following benzene exposure in both types of mouse, was clearly exacerbated in the Cx32 KO mice. Associated with the result, the hyperplastic alveolar epithelial cells positive for CYP2E1 (a critical enzyme for benzene metabolism) were noteworthy, as frequently noted in the lung of benzene-exposed Cx32 KO mice, strongly suggesting an important role of Cx32 in regulating the cell proliferation. However, our results did not indicate any enhancement of tumorigenesis in all the target organs examined including hemopoietic tissues.

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