PD-38

Effect of Low-dose 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin on Host Resistance to Influenza Virus in Mice

Keiko Nohara [1,2], Hiroyuki Izumi [2,3], Shin-ichi Tamura [4] , Ryoichi Nagata [3], Chiharu Tohyama [1,2]

[1]Environmental Health Sciences Division, National Institute for Environmental Studies, [2]CREST, JST, [3]Shin Nippon Biomedical Laboratories, Ltd, [4]Department of Pathology, National Institute of Infectious Diseases

Introduction: Dioxins, including 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD), the most toxic congener, exert diverse biological effects in humans and animals. Host resistance, especially to virus infections, is considered one of the most sensitive targets of TCDD-toxicity, while a recent study showed that the vulnerability to TCDD of host resistance to viruses varied from experiment to experiment. Burleson et al. (Fundam. Appl. Toxicol. 29, 40, 1996) reported that a single oral dose as low as 10 ng TCDD/kg increased the mortality of mice infected with influenza A virus. If this value had been adopted as the basis for the tolerable daily intake (TDI) of dioxins, the TDI of 1-4 pg toxic equivalent (TEQ)/kg/day recommended by WHO would have to be lower. In the present study, we used the same experimental protocol described by Burleson et al. to determine whether low-dose TCDD consistently compromises the host resistance of mice infected with influenza A virus.

Materials and Methods: Four strains of mice, B6C3F1 (C57B1/6 x C3H), BALB/c, C57B1/6N and DBA/2, were purchased from Japan Charles River Inc. (Shiga, Japan). They were dosed with either corn oil or TCDD (Cambridge Isotope Laboratories, Inc., Andover, MA) by gavage at 8-weeks old. Seven days later, mice were lightly anesthetized with diethyl ether and infected intranasally with the mouse-adapted strain of influenza virus A/PR/34/8 (H1N1). After virus inoculation, mice were observed for health conditions and mortality twice a day.

Results and Discussion: In a previous study, Burleson et al. (1996) administered TCDD to female B6C3F1 mice (8 weeks old) 7 days prior to the virus infection, infected them with influenza A virus (A/Hong Kong/8/68) at doses causing 30% or fewer deaths, and found that a dose as low as 10 ng TCDD/kg increased mortality. We repeated their experiments by using the same protocol for TCDD-exposure and infection in the same strain, sex, and age of mice infected with influenza A virus (A/PR/34/8). However, a TCDD dose as high as 500 ng/kg did not increase the mortality.

We also investigated the sex- and strain-dependency of host resistance in male B6C3F1 mice and in female C57B1/6, Balb/c, and DBA/2 mice by administering the same dose range of TCDD. The results showed that TCDD doses up to 500 ng/kg did not increase the mortality of virus-infected mice in any of the strains.

Further studies on the mechanism underlying the toxicity of TCDD are needed to assess the risk of exposure to this compound in influenza A virus infection.