

Title of Research:

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Establishment of animal testing for the prediction of respiratory sensitizing potential of chemicals

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Summary of Research:

Currently, there is no test for evaluating the respiratory sensitizing potential of chemicals. The purpose of this project is the establishment of animal testing methods for predicting respiratory sensitizers and for evaluating their relative respiratory sensitizing potency. We have developed a respiratory sensitization testing method using intratracheal administration.

In the second stage, we verified the effectiveness of the testing method using several new but known respiratory sensitizers. Test substances used were phthalic anhydride (PA), methyl tetra hydrophthalic anhydride (MTHPA), maleic anhydride (MA), and hexamethylene diisocyanate (HDI), which are well-known respiratory sensitizers. We used oxazolone (OX) and chlorobenzene (CB), which are a skin sensitizer and non-sensitizer, respectively. Mice were sensitized by intratracheal instillation of individual chemicals, each at three concentrations, on 5 days per week for 3 weeks. Three days following the last installation, mice were challenged with the corresponding agents for three days, and were sacrificed 2 days later. The degree of Th2 type-allergic inflammation in lungs was determined using an allergic inflammation score based on the histopathological grading.

PA and MTHPA elicited weak Th2-type allergic inflammatory responses in a dose-related manner. It was difficult to identify a respiratory sensitizing potency for MA under the test conditions, although Th2-type allergic inflammatory responses were elicited in the lungs of mice sensitized with MA. With HDI, Th2-type allergic inflammatory responses were elicited in elicitation-control and low-concentration groups; the reason for this is unknown. OX showed the same levels of allergic inflammation scores as the vehicle-control group. No allergic inflammatory reaction to CB was found at non-sensitizing potency. The relative sensitizing potency, based on the relationship between sensitizing concentrations and allergic inflammation scores, could be used to compare the potency of PA, MTHPA, OX, and CB. Thus, the present test method could separate PA and MTHPA from OX and CB, and confirmed the usefulness of evaluating relative sensitizing potency. Further studies should be conducted on enhancing the elicitation reaction for weak respiratory sensitizers.

Timeline:

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Topics:

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Publications:

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