Title of Research:

12_S01-03-3

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

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Summary of Research:

The purpose of this project was to establish an animal model for predicting respiratory sensitizers and for evaluating their relative respiratory sensitizing potency. To this end, we developed a respiratory sensitization test using an intratracheal administration method in mice. The degree of Th2 type-allergic response in the lungs was determined using allergic inflammation scores based on histopathological grading. With this method, mice were sensitized with three concentrations of a test substance 5 days per week for 3 weeks. Three days following the last administration, mice were challenged with one concentration for three days, and were sacrificed 2 days later.

Next, we investigated the differences resulting from the different sensitization and elicitation treatment regimens in order to determine conditions that cause obvious allergic reactions. Interestingly, we found that allergic reactions tended to be reduced in mice sensitized with the highest concentration of a test substance. Therefore, we examined the influence of lower substance concentrations on eliciting responses based on the hypothesis that overdosing of the test substances in the sensitization and elicitation treatments suppressed allergic reactions. We also investigated the influence of the frequency of sensitization and elicitation treatments on those reactions. We found that toluene diisocyanate (TDI) and trimellitic anhydride (TMA) elicited allergic responses at lower concentrations than those of conventional elicitation. Additionally, both test substances resulted in allergic inflammation scores that were greater than or equal to conventional scores when eliciting concentrations were lower than those of conventional elicitation.

These results indicate that lower elicitation concentrations contributed to enhanced allergic reactions in our model system, which could be used to obtain obvious inflammatory responses by excluding primary irritation. Upon examining the influence of lowered sensitization and elicitation treatment frequency on inflammatory responses, we found that multiple elicitation treatments were required similar to the conventional elicitation study design. we will proceed with detailed studies to elucidate the influence of conditions such as frequency and duration on sensitization.

Timeline:

March 1, 2015 – February 29, 2016

Topics:

Publications: