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PR013 REDUCES HYPEREMIA IN MURINE MODELS OF ALLERGIC CONJUNCTIVITIS AND BOTH HISTAMINERGIC/ NONHISTAMINERGIC ITCH IN VITRO

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Introduction: PR013 is a proprietary formulation of hypochlorous acid (HOCl) being developed for treatment of allergic conjunctivitis (AC). AC is induced by exposure to allergens resulting in hyperemia, inflammation, and pruritis. The goal of this study was to elucidate whether PR013 reduces hyperemia in an AC murine model and inhibits neuronal signaling *in vitro*.

Methods: Murine CAC™ Model: Symptoms of AC were induced by injection and ocular application of short ragweed allergen (SRW) in BALB/c mice. On challenge days, PR013 was instilled into the eyes followed 60 minutes later by SRW. Hyperemia was evaluated at baseline and 18 minutes after ocular challenge. Dorsal Root Ganglia (DRG): DRG were isolated from untreated BALB/c mice. Changes in intracellular Ca^{2+} were measured by microscopy after exposure to PR013 followed by various pruritogens.

Results: Dosing prior to allergen challenge did not result in hyperemia, indicating that PR013 was well tolerated. Treatment after SRW challenge resulted in significant, dose-dependent, reduction in hyperemia compared to vehicle. Results demonstrated better control of hyperemia than olopatidine (0.1%) and similar efficacy to prednisolone (1%). Concentrations of PR013 lower than 0.05% did not demonstrate significant reduction in hyperemia. Treatment with PR013 resulted in a significant reduction in the response of DRG neurons to pruritogens known to stimulate both histamine-dependent and histamine-independent signaling pathways.

Conclusion: Treatment with HOCl significantly reduces hyperemia associated with AC in a murine model, similar to prednisolone (1%) and reduces neuronal signaling *in vitro,* suggesting its ability to manage both histaminergic and nonhistaminergic itch.

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INCONGRUITY IN DETECTING DOG SENSITIZED INDIVIDUALS BETWEEN SKIN PRICK AND SPECIFIC DOG IGE TESTING

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Introduction: Allergies to furry animals is a critically important clinical problem. There are over 70 million dogs in US households alone with the frequency of animal allergies increasing worldwide. The accuracy in the diagnosis of dog allergies is critical. Immediate hypersensitivity skin testing (IHST) with dog extracts and dog specific IgE (sIgE) has been used to identify sensitized individuals. We wished to determine how well IHST results correlate with dog sIgE using a cut off of 0.35kU/L as positive.

Methods: This retrospective chart review studied patients who had skin and blood testing for sensitization to dogs. Tests were considered positive if the wheal was >3x3mm or dog sIgE was >0.35kU/L.

Results: Since 2008, 430 subjects have both data from IHST and sIgE. Of those, 18.5% (n=67) of patients tested had skin testing that did not match dog sIgE results.

Conclusions: IHST and blood dog specific IgE do not correlate well with over 18% incongruity. Current methodology in testing for dog sensitization is not accurate. It remains unclear how many individuals are symptomatic to dog exposure, but test negative. A dog sIgE >0.35kU/L may not be sensitive enough to identify sensitized patients. Current crude extracts may not contain all dog allergens at high enough concentrations to detect sensitized individuals.

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METHODS FOR HOMOGENIZING FELD1 LEVELS IN A CAT ALLERGEN EXPOSURE CHAMBER

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Introduction: Exposure chambers assess allergic responses within a controlled environment. Limited facilities exist to expose subjects to controlled levels of Fel d1. Our purpose is to ensure stable and consistent levels of Feld1 in our cat chamber.

Methods: The chamber, volume 520 ft^3 (14.7 m^3) contains two neutered male cats. Air samples were obtained at 3 locations 4 feet above the floor using sampling pumps (Gillian 5000) with glass fiber filters (Millipore), flow rate 4 L/min. Filter Feld1 was quantified using ELISA (Indoor Biotechnologies). To evaluate air circulation as a means to homogenize allergen levels, two fans were placed 7.0 or 1.5 feet above the floor and thirty-minute samples taken 1, 2 and 4 hours after starting the fans.

Results: When the fans were near the ceiling (7.0ft), allergen levels were not consistent across the room. The room average for Feld1 levels was 18.3, 19.6, and 0.0 ng/m^3, respectively after 1, 2 and 4 hours of running the fans. Whereas, greater consistency was seen when the fans were lowered closer to the floor at 1.5 feet, such that Feld1 levels were 6.7, 7.6, and 13.2 ng/m^3 after 1, 2 and 4 hours. There was no clear indication that the length of time the fans operated, prior to making measurements, improved allergen distribution or increased Feld1 levels. Feld1 values are consistent with lower levels of home exposure.

Conclusion: The live-cat-room challenge better represents subject's home exposure; however, refinement of fan positioning is needed to provide more consistent levels of airborne Feld1.

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ANATOMIC DISTRIBUTION OF FELD1 AND FELD4 IN DOMESTIC HOUSE CATS

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Introduction: Cat dander is one of the most potent allergens. Subjects may be sensitized to several allergens in dander, but 80% of individuals have IgE antibodies to Feld1 and/or Feld4. Our purpose was to measure Feld1 and Feld4 in cat saliva, fur and urine and determine if differences depend on breed, gender, or age.

Methods: Cats from a local animal hospital were volunteered by owners who signed an informed consent. Twenty-six cats were recruited in four cohorts: neutered males, neutered females, females and males. Breed, age, weight and health status was recorded. Allergen was extracted from the samples and assayed in triplicate by ELISA.

Results: Thirteen male and 13 female cats, aged 5.6 ± 4.3 years (mean ± SD) were studied. Nine were a long hair breed, 3 medium hair and 14 short hair. Data was analysed by Wilcoxon rank sum test; values given as median, 25-75 percentile. Urine was obtained from 18 cats. Feld1 (0.02, 0.065-0.071 ug/ml,) and Feld4 (<0.4 ug/ml, the limit of detection) levels were low. In fur, n=26, Feld4 (0.09, 0.03-0.19 ug/g) was much lower than Feld1 (12.24, 5.0-25.0 ug/g), ($p<0.001$). Conversely, Feld4 was higher than Feld1 in saliva, n=21, (7.62, 1.32-18.5 vs. 2.45, 0.75-5.73 ug/ml, respectively, $p=0.039$). Allergen levels were not dependent on age, gender or breed. Neutering did not affect allergen levels but there were few non-neutered males.

Conclusion: Distribution of Feld4 differs from that of Feld1 in domestic cats. How this affects the allergic response is unknown.