



A Humanized Mouse Model of Severe Asthma

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SUMMARY

UCLA researchers have developed two transgenic mouse models that mimic the allergic response to be used for studying asthma and other allergic and inflammatory diseases.

BACKGROUND

Asthma, a chronic inflammatory disease of the lung, affects an increasingly larger population every year and presents a major public health problem in terms of morbidity and cost. The cause and mechanisms of asthma and allergic diseases are not yet understood. As the spontaneous development of asthma in a non-human animal is next to impossible, the ability to engineer mouse models of the disease remains critical to the understanding and treatment of the disease.

INNOVATION

UCLA researchers have developed 2 novel transgenic mouse models of the allergic response by using knock-in mutagenesis to create Q576R and Y709F mutants of the endogenous murine IL-4R . The Q576R mice, a human genetic polymorphism that is associated with severe and fatal and near-fatal asthma, developed severe allergic airway disease modeling human asthma. The Y709F mice, a key regulatory residue in the IL-4R alpha chain immunoreceptor tyrosine based inhibitory motif (ITIM), exhibited heightened allergic responses and allergic airway disease. Both mutations were found to promote IL-4 production by Th2 cells and IgE responses.

APPLICATIONS

- To study mechanisms of asthma and other allergic diseases
- To develop and test treatments of allergic diseases, including asthma, food allergy, and inflammatory bowel disease

ADVANTAGES

- Mouse models containing single mutations help examine the role of specific pathways involved with the disease.

STATE OF DEVELOPMENT

The mouse models are fully developed. The researchers plan to employ the model in studies of asthma and food allergies including drug screening

RELATED MATERIALS

- Reference for the Q576R mouse Tachdjian R, Mathias C, Al Khatib S, Bryce PJ, Kim HS, Blaeser F, O'Connor BD, Rzymkiewicz D, Chen A, Caplan B, Holtzman MJ, Hershey GK, Garn H, Harb H, Renz H, Oettgen HC, Chatila TA. Pathogenicity of a Disease-Associated Human IL-4 Receptor Allele in Experimental Asthma, Journal of Experimental Medicine. vol. 206 (10): 2191 (2009).
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- Reference for IL-4 receptor signaling pathways in asthma: Chatila TA. "Interleukin 4 Receptor Signaling Pathways in Asthma Pathogenesis," Trends in Molecular Medicine, Vol. 10. p. 493-9 (2004).

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OTHER INFORMATION

KEYWORDS

Animal, Biomedical, Asthma, Mouse model

CATEGORIZED AS

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 - Disease: Autoimmune and Inflammation
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