UCSD Researchers Show Immunostimulatory DNA Reverses Airway Scarring and Inflammation in a Mouse Model of Asthma

September 26, 2005 |

The structural changes including airway scarring and inflammation that contribute to severe breathing problems associated with asthma were significantly reversed in mice treated with immunostimulatory sequences of DNA (ISS), a novel therapy developed by researchers at the University of California, San Diego (UCSD) School of Medicine.

Published in the December 15, 2004 issue of the Journal of Immunology (Volume 173, No. 12), the study demonstrated that systemic administration of ISS to mice with scarred and inflamed airways significantly reduced the degree of blockage and scarring. The researchers also determined the specific mechanisms used by ISS to reverse structural changes caused by asthma in the lung.

Asthma is a chronic lung disorder affecting upwards of 20 million Americans, characterized by narrowed, scarred, or mucus-obstructed airways in the lungs, leading to severe difficulty in breathing. According to the American Academy of Allergy, Asthma & Immunology, even mild asthma can be life-threatening.

Jae Youn Cho, M.D., Ph.D., Assistant Project Scientist, UCSD Department of Medicine, and the study's first author, noted that "repeated episodes of asthma can induce structural changes in the airway, so that the airways constrict more easily and cause asthmatics to have breathing problems. We found that ISS therapy actually reversed these structural changes."

Developed by Eyal Raz, M.D., a UCSD professor of medicine and one of the co-authors of the paper in the Journal of Immunology, ISS are short synthetic DNA molecules that mimic the properties of bacterial DNAs in stimulating a specific type of immune response to allergens or toxic substances. In previous studies, ISS was shown to prevent the inflammation and airway obstruction in mouse models of asthma. The new study is the first to investigate the therapy's role in reducing already established scarring and inflammation in a model of allergen induced asthma.

Over a three month period, the scientists administered an allergen by inhalation, which resulted in mucus and collagen build-up, with the characteristic hyperreactive and inflamed airways of asthma. One group of mice which had already developed scarring and inflammation of their airways was given ISS every other week for one or three months, while a second group of mice received a placebo. Several laboratory methods were used to study the lungs of both groups of mice. Mice that received ISS had less scarring of their bronchial tubes, reduced thickness of the smooth muscle layer surrounding the bronchial tubes which contributes to constriction of the airways, and less mucus production.

In further studies, the researchers found that the mechanism used by ISS to reverse airway blockage was threefold. It reduced the expression of TGF-beta 1, a growth factor that is associated with excess fibrous tissue growth in the tissue surrounding the bronchial tubes. ISS also reduced levels of an immune-response regulatory protein called thymus- and activation-regulated chemokine (TARC), which is involved in recruiting immune cells to the airway. In addition, ISS reduced the number of white cells called eosinophils and peribronchial CD4+ lymphocytes, which contribute to the immune and inflammatory response.

The study's senior author, David H. Broide, M.D., UCSD professor of medicine, noted that the "National Institutes of Health's Immune Tolerance Network, which supports translational research, has just awarded UCSD a grant to study a derivative of this therapy (ISS conjugated to ragweed) in human subjects with ragweed-induced asthma. As ragweed is not endemic to San Diego the clinical component of the study will be conducted at research sites in the Northeast, while mechanistic studies on sputum specimens will be performed at UCSD."

In addition to Broide, Cho and Raz, authors of the paper were Marina Miller, M.D.; Kwang Je Baek, M.D.; Ji Won Han, M.D.; Jyothi Nayar, B.S.; Sook Young Lee, M.D.; Kirsti McElwain, B.S.; and Shauna McElwain, B.S.. The study was supported by the National Institutes of Health.

News Media Contact Sue Pondrom 619-543-6163

UCSD Health Sciences Communications HealthBeat: /news/

Share This Article

Related News

First Clinical Trial to Assess Alzheimer's Gene Therapy Receives $5 Million

5/25/2021

Cross Border Effort to Vaccinate 10,000 Maquiladora Workers
5/25/2021

Superficial Relationship: Enzymes Protect the Skin by Ignoring Microbes and Viruses
5/21/2021

UC San Diego Health Joins Call to Don't Delay HPV Vaccinations, Save Lives
5/20/2021

View All News >

Follow Us

Follow @ucsdhealth