Undergraduate Scholarly Showcase Speech

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Introduction

Good morning, my name is Olivia Spencer, and I am a third year studying Medical Laboratory Science: Pre-Medicine. My research took place in the Immunobiology Department at Cincinnati Children's Hospital. I want to give thanks to the Lewkowich Lab for taking me in, and particularly to my mentor Dr. Jackie McAlees for putting up with me each day.

Relevance

I want you to look to your left and right. Chances are, someone in the row of seats next to you has struggled with asthma. This disease affects individuals of all backgrounds. However, its burden is uneven.

Asthma is disproportionately impacting women after puberty, with the diagnosis in adult females nearly doubling the number in adult males.

Additionally, asthma severely impacts children. The disease is in the top 3 reasons for ER visits of minors, and Cincinnati Children's Hospital alone gets roughly 4000 ER visits per year. Asthma is also the #1 cause of missed school days for chronic illness in children, accounting for more than 7.9 million days in 2018.

Finally, asthma is the #1 most racially disparate disease, surpassing heart disease, obesity, COPD, and Type 2 diabetes. People of color are at a much higher risk of developing asthma, suffering from asthma complications, and ultimately have a 2.8x greater risk of death from the disease.

Because of this, the economic burden of asthma in the United States is substantial, costing around $81.9 billion annually. Furthermore, this does not include the unquantifiable losses contributed to asthma, such as increased pain and suffering, limitation of physical activities, and job changes that lead to decreased quality of life.

The primary goal of our lab is to understand the underlying physiological mechanism of allergic asthma to narrow these disparities.

Abundance

There is a proven genetic basis for the development of the disease, however, as you can see the rate of diagnosis is increasing too quickly to be driven by genetics alone. This suggests and environmental impact on asthma incidence.

Industrialization in first-world countries may contribute to these numbers. The hygiene hypothesis suggests that reduced exposure to parasites in modern, sanitized environments may lead to immune system dysregulation. This theory highlights the complex interplay between environmental factors, immune responses, and the prevalence of allergic conditions in developed societies.

Physiology

So, what does asthma look like? A healthy airway is smooth and open wide, with moderate mucus secretion and response to stimuli. However, asthmatic airways are hyperresponsive to stimuli, ultimately causing smooth muscle constriction around the airway, inflammation, and increased mucous production. Because of this, the millions of patients impacted by this chronic disease must deal with symptoms such as shortness of breath, chest tightness, and persistent coughing for the rest of their lives.

Objectives

Today, there is still no cure, specific treatment, or prevention for asthma.

Additionally, there is no universally accepted definition nor is there a single test to definitively diagnose asthma. For diagnosis in the US, we say “Here take this medication, if it works you have asthma, if it doesn’t you don’t”.

Asthma treatment is a stepladder of medications that patients climb until their asthma is under control. During this time, patients experience the disruptive, uncomfortable, and even life-threatening symptoms mentioned earlier. This is nonspecific, inefficient, and detrimental to patient care.

Finally, there is little information on the identification of types of asthma within the population, who is at risk for developing asthma, and any mechanism of prevention for the disease.

Understanding the physiological mechanism of allergic asthma will significantly aid in the diagnosis, treatment, and prevention of the disease by helping to identify specific cellular targets that trigger asthma and predict environmental susceptibilities to the disease. As research develops, one day we could find a cure.

Project Overview

Specific experiments in our lab manipulate allergen exposure, weight, antibiotic exposure, and cellular signals.

Allergens

It is important to understand and characterize responses to allergens in asthmatic vs normal lungs. House dust mite is a microscopic organism and common allergen found in areas with high amounts of dead skin cells such as carpet and bedding. Without your knowledge, virtually everybody is exposed to them each day. However, some people develop an asthmatic response to house dust mite while others do not. We are trying to understand this distinction and identify susceptibilities to allergic asthma.

By exposing the mice in our lab to house dust mite or a saline control, we are able to measure asthmatic response to allergens. We also manipulate the mode of exposure via direct contact with skin or through inhalation and aim to understand how the parent's exposure to an allergen impacts their children. So far we have found that mice exposed to an allergen have a higher chance of developing asthma, and even more so if their parents had a history of prior exposure as well.

Obesity

Virtually in parallel, the rise in obesity is accompanied by the rise in allergic asthma. Theories such as fatty tissue on the chest wall, disordered sleep breathing, and systemic inflammation may contribute to this development. In our lab, Mice with high-fat diets have been analyzed and show a greater risk for asthma, particularly in females. Not only that, but obesity reduces the effectiveness of typical asthma medication, putting patients at higher risk for asthma complications. This highlights the need for novel drug therapies with specific cellular targets for allergic asthma.

Antibiotics

The hygiene hypothesis indicates that early childhood exposure to pathogens helps build a strong immune system and protects against the development of allergies. It is understood that good bacteria in our gut and on our skin help shape our immune system and how we respond to bad bacteria. However, modern sanitation has extremely limited the diversity of these pathogens in our environment.

Through the use of chemicals and antibiotics, we can model modern sanitation by creating an ultra-clean environment in our mouse model. This disrupts their microbiome similar to ours, and its effect on allergic asthma can be compared.

Cellular Signals

Finally, cellular signals that activate the immune system can be turned on and off. This allows us to understand what is happening inside the cell. The current asthma treatment is medications that use steroids to nonspecifically suppress the entire immune system putting patients at a higher risk of infection. By mapping the signaling pathway, we can find potential targets for drug therapies specific to allergic asthma.

Acknowledgments

Countless hours of hard work and dedication by the Lewkowich laboratory and other partners have been put in to gather evidence on the environment's role in asthma development. Moving forward, our objective is to translate these findings into improved diagnostic methods, targeted treatments, and ultimately, a potential cure for asthma.

Nobody is immune to the harmful impact asthma has had on society, and it is only getting worse as the years go by. The millions of people affected by this disease deserve a chance to finally breathe freely. Thank you.