



Diesel Exhaust Induces Glucocorticoid Resistance (DIGR)

Ryan Huff (University of British Columbia)

Supervisor: Christopher Carlsten

Asthma Canada - AllerGen Bastable-Potts Graduate Student Research Award

Ryan Huff, a PhD student at the University of British Columbia, plans to investigate the relationship between air pollution and inhaled corticosteroids (ICS) in a rigorous controlled human clinical study. He plans to pursue a career in academic research focused on lung interventions and explore how these treatments impact the immunology and pathophysiology of asthma. His interest in the respiratory system stems from dealing with allergic asthma and moderate-severe seasonal allergies throughout his life.

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Asthma is a chronic disease that affects over 2.5 million Canadians, placing a significant burden on families and the Canadian health care system. Asthma attacks or exacerbations are periods of progressively worsening symptoms due to swelling and closure of the airways, leading to frightening feelings of suffocation, hospitalization, and even death. Inhaling allergens and/or air pollution from various sources such as forest fires or automobile exhaust often provoke these attacks. People with asthma cope with their symptoms using medications broadly called inhaled corticosteroids (ICS). These medications act on cells lining the lungs by turning on and off sets of genes that result in the suppression of airway inflammation and asthma symptoms. However, Asthma Canada estimates that 60% of asthmatics have poorly controlled disease and approximately 250 people die from asthma every year, of which 80% are preventable. Recent studies have suggested that increased air pollution may lead to increased ICS use, and lab research has shown that air pollution interrupts ICS's actions on human lung cells grown on petri dishes.

To further examine this complex interaction between air pollution and ICS function, Huff plans to investigate the relationship between air pollution and ICS in a rigorous controlled human clinical study. In the study, research volunteers will be

exposed for two hours to filtered air or air pollution at a level experienced in major cities such as Beijing or at many Canadian worksites. Following the exposure, volunteers will take a placebo or ICS. Every volunteer will experience each combination of exposure and treatment in a random order over a series of four visits. Cells collected directly from the volunteers' airways will be examined using state of the art gene sequencing techniques to determine which genes have turned on and off. This will enable Huff to investigate how increased air pollution influences ICS effectiveness in people with asthma.

The findings of Huff's study will be significant because they can immediately be used to improve treatment guidelines and inform educational policies aimed at preventing asthma attacks. In addition, discovering which ICS-controlled gene sets are influenced by air pollution could potentially lead to therapeutic targets to the benefit of those unable to avoid polluted environments. Considering that 92% of the world's population live in areas exceeding WHO air pollution guidelines, findings from Huff's research have the potential to impact millions of lives in Canada and abroad.

About Ryan Huff

Ryan Huff is currently completing a PhD in the Experimental Medicine program at the University of British Columbia. His goal is to pursue a career in academic research focused on lung interventions and explore how these treatments impact the immunology and pathophysiology of asthma. His interest in the respiratory system stems from dealing with allergic asthma and moderate-severe seasonal allergies throughout his life. Despite his asthma, he still competed as a varsity athlete in track and field and cross-country during secondary school and his undergraduate degree, mainly with the help of a nasal corticosteroid and a short acting beta-2-agonist. He was always curious about his own asthma, including the biochemical mechanisms by which smog or allergens had restricted breathing in races over the years.

Ryan was excited to join the Chan-Yeung Center for Occupational and Environmental Respiratory Disease (COERD) to study the interaction between environmental exposures and respiratory disease. He hopes that his research project examining how air pollution interrupts the function of inhaled corticosteroids in asthmatic airways can help inform and enhance the treatment of severe asthma.

Ryan previously received his Bachelor of Medical Sciences in Biochemistry from the University of Western Ontario, and completed his MSc in Medical Genetics at the University of British Columbia in 2015 under the supervision of Dr. Marco Marra at Canada's Michael Smith Genome Sciences Centre. His MSc thesis focused on using genome-engineering tools to investigate the gene KMT2D, which encodes an epigenetic modifier frequently mutated in non-Hodgkin's lymphoma.

Outside of the lab he is an avid long distance runner, and enjoys hiking and backcountry skiing.