THE HARTWELL FOUNDATION

2014 Individual Biomedical Research Award

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Harnessing Lymphocyte Cooperativity for the Treatment and Prevention of Asthma

Over the past four decades, Western societies have borne witness to a dramatic and troubling trend of increased autoimmunity, allergy, and asthma. The increase in asthma has been so severe that it has become the most common chronic condition in children, and is the leading cause of school absences. Asthma accounts for nearly 25% of all emergency room visits, consuming more than $18 billion in healthcare costs in the US each year. For mild asthma, limiting exposures to triggers and the use of fast-acting inhaled medications called bronchodilators is adequate. For moderate asthma, blocking inflammation to control symptoms with regular and long-term use of inhaled corticosteroids is necessary. Severe asthmatics, lack responsiveness to corticosteroid treatment and have a low quality of life stemming from the lack of available treatment options. With the rising tide of asthma among our nation's children, the development of alternative effective therapies is imperative. One popular explanation for the increase in asthma suggests our increasingly sanitized environment alters the types of everyday exposure to bacteria and other microbes, which may lead to a dysfunctional immune system that is unprepared to respond properly to the usual triggers for asthma. Recently, Brian has been examining this effect in a mouse model system and his efforts have led to a serendipitous and exciting discovery. He found that a specific subset of immune cells can produce a regulatory molecule that instructs other immune cells within a target tissue to resist inflammation, revealing a novel suppressive pathway that is fundamental to the immune system. His early data suggests that the molecule is not a steroid, but rather a naturally occurring protein. Most significant, the administration of cells producing this protein seems to render mice completely resistant to asthma. He now seeks to identify and characterize this protein, and to test its potential as a new asthma drug in pre-clinical trials using multiple animal models of mouse asthma. If Brian is successful, his therapeutic intervention would represent a novel non-steroidal treatment for the long-term suppression of asthmatic inflammation in both moderate (steroid responsive) and severe (steroid nonresponsive) asthma patients, directly benefitting the 9% of affected children in the US currently suffering from this condition. It is also conceivable that induction of the suppressive pathway by such a drug could have important applications in lupus, rheumatoid arthritis, type I diabetes, multiple sclerosis, atherosclerosis, Crohn's disease, as well as other autoimmune or inflammatory disorders characterized by an over-exuberant immune system.