

July 16, 2007

Dear Mr. Gant;

I am delighted to write a letter commenting upon the exciting research involving MARCKS-directed peptides and their strong potential as effective therapeutic agents for treatment of pulmonary inflammatory diseases being conducted by Dr. Kenneth B. Adler from North Carolina State University and BioMarck Corporation in North Carolina.

As you know, chronic obstructive pulmonary disease (COPD) is one of the major causes of human suffering not only in the United States but also worldwide. Dr. Adler, one of the foremost established and well-respected researchers in the world in the field of airway disease, has generated an impressive body of work that has focused upon mechanisms of bronchial epithelial cell inflammation and mucus production, and has painstakingly detailed the significant cellular signaling pathways by which these processes proceed. Dr. Adler was recently recognized by the American Thoracic Society when he was presented with the "Recognition Award for Scientific Accomplishments" by this organization at their annual meeting in San Diego in spring of 2006.

The clinical implication of this work is the real hope of generating new therapeutic targets to limit or regulate abnormal mucus hypersecretion. At this time, there are no effective therapies that effectively block mucus secretion in this and other pulmonary diseases, and current pharmacological treatments can induce only slight improvements in COPD patients. The peptides that Dr. Adler discovered and described in the articles his laboratory published in the prestigious journals *Nature Medicine* 10:193-196, 2004 and *The Journal of Biological Chemistry* 276:40982-40990, 2001, and recently shown to enhance lung function in a mouse model of mucus hypersecretion (*Journal of Applied Physiology* 102:399-405, 2007) raise the strong possibility that new and effective therapies based on his discovery of new cellular targets associated with these diseases can be developed.

I am also aware of the recent work done by Dr. Adler's laboratory in which it was shown that the MARCKS-related peptides can also reduce inflammation, the 2nd main component of COPD. Current drugs offer only slight improvement in COPD patients, while the BioMarck drug based on Dr. Adler's peptides can be a significant therapeutic advance. I cannot emphasize how important these findings are. They represent a true paradigm shift in our understanding of the pathogenetic mechanisms associated with airway inflammatory diseases, and can serve as the basis for a new generation of specific therapies designed to more effectively treat the millions of patients worldwide who suffer from these disorders. The truly exciting aspect of these studies is that these drugs are directed toward specific

cellular targets that have been identified by Dr. Adler as regulating mucus secretion, a perfect example of the bridging of state-of-the-art bench research and research directed toward a family of diseases. This is a wonderfully exciting and a potentially major advance in pulmonary medicine.

I am available if you wish to discuss Dr. Adler's discovery and more recent work, or if you need additional information.

Sincerely,

A handwritten signature in black ink that reads "Joe G.N. Garcia M.D." The signature is written in a cursive style with a large initial "J" and "G".

Joe G.N. Garcia, M.D.
Lowell T. Coggeshall Professor of Medicine
Chairman, Department of Medicine