

**Asthma and Adiposity**

*P.I.: Patricia L. Hopkins-Price, Ph.D.*

*Funding Agency: American Lung Association of Illinois-Iowa*

Asthma and adiposity (fatness or obesity) are major public health problems in the United States today. Asthma affects more than 17 million Americans. More than 97 million people have excessive body fat, and both these diseases have risen in prevalence in the United States over the last 20 years. In addition, patients with asthma commonly have obesity and vice versa. Yet it is still unclear if adiposity, by itself, relates to asthma occurrence. Several studies have shown improved lung symptoms, lung functions, and need for medications following weight loss in obese subjects with asthma. However, it is still uncertain whether this improvement is due to a change in airway sensitivity, or improvement in chest restriction from loss of excessive fat, or just an improvement in the feeling of shortness of breath.

This study will evaluate the effect of weight loss in obese subjects with asthma during obesity management programs in central Illinois. In addition, this study will also identify whether weight loss in obese subjects with asthma is associated with a change in the inflammatory state of the airways and of the body, as a whole. The focus of this study will be the change in airway sensitivity following weight loss. Other study measures will include changes in levels of feeling of shortness of breath, markers of inflammation in the body and in the airways, and of chest restriction caused by excessive fat. This study will enroll obese subjects with asthma who are participating in obesity management programs for weight reduction. They will be in the study for 12 months. Each subject's measurements will be compared before and after weight loss. If excessive body fat is identified as a possibly modifiable risk factor in asthma management, preventive steps focused on weight

control may help reduce the considerable and increasing suffering from asthma in the United States.



**Does Growth Hormone Treatment Abolish Caloric Restriction Benefits in Long-Lived Ames Dwarf and Normal Mice?**

*P.I.: Michal Masternak, Ph.D.*

*Funding Agency: SIU Central Research Committee*

The long-term objectives of this research are to determine whether growth hormone (GH) will abolish the benefits of caloric restriction (CR) and longevity gene mutation in Ames dwarf and normal mice. Ames dwarf mice are long-lived, hypoinsulinemic, hypoglycemic and exhibit enhanced insulin sensitivity. Ames dwarf mice are deficient in GH, prolactin and thyroid stimulating hormone. Dwarf mice live approximately 50 percent longer than normal siblings. Reducing caloric intake by 30 percent significantly extended the lifespan in normal animals and extended the lifespan of Ames dwarf mice.

Studies in mutant mice and in animals subjected to CR add to the evidence that GH and insulin/IGF1 signaling are important in the control of aging in different species. Caloric restriction, GH deficiency or disruption of GH signaling reduce circulating IGF1, increase insulin sensitivity and increase longevity.

Dr. Masternak hypothesizes that suppression of GH release is an important mediator of CR effects on longevity. His work also has shown that the improvement of insulin sensitivity by CR in Ames dwarf mice was eliminated by treatment with high dose of GH. He is studying the effects of GH treatment and 30 percent CR combined with GH treatment in these long-lived mutants. He is investigating the insulin-signaling pathway, known to be affected by CR and also identified as a longevity marker in many

studies. The results of these studies will provide novel information on the role of somatotropic axis in mediating the effects of CR on insulin signaling and likely also on longevity.



**Nerve Growth Factors in Laryngeal Denervation**

*P.I.: Gayle Woodson, M.D.*

*Funding Agency: SIU Central Research Committee*

Laryngeal paralysis is a disabling condition, and efforts aimed at restoring normal function have yielded disappointing results. The long-term goal of this research is to improve the functional outcome of reinnervation (the restoration of nerve control of a paralyzed muscle). Prior research indicates that a major obstacle to clinical success is that regenerating nerve fibers "successfully" reinnervate muscles that close the larynx, yet fail to adequately reinnervate the muscles that open it. Thus, the larynx is fixed in a closed position, and breathing is compromised as a result. This study will assess the potential role of neurotrophins (NT) in improving the specificity of laryngeal reinnervation. Dr. Woodson's team will document changes in NT receptor expression in the recurrent laryngeal nerve and NT levels in their target muscles over a period of time subsequent to transection. Dr. Woodson hypothesizes that the NT response to denervation differs significantly between the opening and closing laryngeal muscles and these differences could account for disparities in the reinnervation of these two muscles. Strategies to enhance the efficiency and specificity of reinnervation could improve results of reinnervation.



For more information about these projects, contact the Office of Research and Faculty Affairs at 217-545-7936.