

**TITLE: Melanocortin Receptor Targets in an Experimental Murine model of Inflammatory Myositis**

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**RESEARCH PROJECT DESCRIPTION**

The inflammatory myopathies, dermatomyositis (DM) and polymyositis (PM), are diseases characterized by inflammatory infiltration of muscles. Interestingly, adrenocorticotrophic hormone (ACTH) gel, a long-acting formulation of porcine ACTH hormone that contains within its sequence several pro-opiomelanocortin peptides, was first granted approval for treatment of PM and DM in 1952, prior to the FDA requiring rigorous testing. However, ACTH gel has not been widely used by clinicians, as the data supporting use are limited to a recent case series of five myositis patients who were recalcitrant to traditional treatments and who demonstrated improved muscle strength on ACTH therapy. At the *in vitro* level, one of the melanocortin peptides in ACTH gel,  $\alpha$ -MSH, attenuates inflammation via selective activation of melanocortin receptors (MCR1 and MCR3). This proposal will examine whether the therapeutic benefits of ACTH gel can be reproduced by injection of a single melanocortin peptide,  $\alpha$ -MSH. The proposed experiments will test the hypothesis that selective activation of MCR1 alters disease activity in a mouse model of inflammatory myositis. Our goal is to generate preliminary data with  $\alpha$ -MSH and compare results to those obtained by stimulation of other melanocortin receptors with ACTH and  $\gamma$ -MSH. Outcome measures will include assessment of muscle weakness, inflammation and necrosis in a well-characterized experimental model of myositis in mice.

**ROLE OF MEDICAL STUDENT** – The medical student will perform experiments that evaluate muscle strength in mice and will be responsible for analysis and interpretation of the resulting data.

**FUNDING SOURCE** – Gatorade Pilot Project

**RELEVANT PUBLICATIONS** –

1. Catania, A., Gatti, S., Colombo, G. & Lipton, J.M. Targeting melanocortin receptors as a novel strategy to control inflammation. *Pharmacol Rev* 56, 1-29 (2004).
2. Levine, T. Treating refractory dermatomyositis or polymyositis with adrenocorticotrophic hormone gel: a retrospective case series. *Drug Des Devel Ther* 6, 133-139 (2012).
3. Allenbach, Y., et al. Role of regulatory T cells in a new mouse model of experimental autoimmune myositis. *Am J Pathol* 174, 989-998 (2009).

COMPLETE DESCRIPTION SHOULD BE NO MORE THAN APPROXIMATELY  
500 WORDS

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