TACSM Abstract

Evaluation of a Vivo-Morpholino Delivery Method to the Brain and the Affect on Physical Activity

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ABSTRACT

Physical inactivity has been shown to be correlated to various disease and conditions. Therefore, there is interest in the genetic mechanisms that control daily physical activity. Vivo-morpholinos are a new molecular biology tool that allows for the transient silencing of specific genes in an animal model, thereby allowing for a systematic method to turn off potential candidate genes involved in the regulation of physical activity. Vivo-morpholinos have not been shown to be effective at silencing genes in the brain due to the fact that the vivo-morpholino cannot cross the blood brain barrier. To counteract this, a tail vein injection (55 ul total volume; 11mg/kg vivo-morpholino; 6.5ug/kg RMP7) was given on three consecutive days containing the bradykinin analog RMP7 and a vivo-morpholino targeting *Vmat2* to male C57/LJ mice (n=6). RMP7 has been shown to increase blood brain barrier permeability while *Vmat2* is a dopamine transporter and is thought to be involved in the regulation of voluntary physical activity. Control animals received either RMP7 plus saline (n=6) or RMP7 plus a vivo-morpholino "scramble" control (n=6). Physical activity was measured by wheel running. Results showed there was not a significant (p=0.24) knockdown in *Vmat2* in the brain with RMP7 administration as compared to control animals. Interestingly there was a significant (p=0.001) knockdown in daily physical activity in the *Vmat2* treated animals compared to the control group. RMP7 may still be a viable option for vivo-morpholino delivery in the brain; however an increased dosage may be required.