

Title: Translational control of repeat-associated non-AUG translation by eIF5-mimic protein (5MP)

The translational regulatory protein 5MP is a general inhibitor of translation, but also serves as a translational rheostat suppressing non-AUG initiation through counteracting the effect of eIF5 which increases non-AUG translation. We test the hypothesis that 5MP suppresses a special mode of non-AUG translation termed repeat-associated non-AUG (RAN) translation. The expansion of CGG repeats by replication errors or genetic recombination, such as those found in the leader region of fragile X mental retardation 1 (FMR1), causes neurodegenerative diseases. Others' studies recently characterized RAN translation in the leader region of FMR1. Initiation of the +1 (CGG) reading frame occurs at ACG codon or GUG codon 5' to the repeat. Initiation of the +2 (CGG) reading frame appears to occur within the repeat at GCG to make a polyAlanine protein. 0 CGG reading frame is not translated because polyArginine protein stalls the ribosome and is quickly degraded. Here we examine the effect of 5MP1 and eIF5 overexpression on CGG NanoLuciferase RAN reporter plasmids in HEK293T. Based on NanoLuciferase assay subsequent to transient transfection of the reporter plasmids, we obtained preliminary data suggesting that 5MP1 suppresses and eIF5 increases RAN translation from either +1 (CGG) and +2 (CGG) reading frames. More repeats are necessary to substantiate these effects with statistical significance and thereby to draw conclusions, but we are excited to obtain promising data.

Personal Note: Throughout the course of this experiment, I learned a great deal about biological research and research techniques as well as how to conduct myself professionally in the lab.