# 105 年度生醫系專題研究競賽報名表

年級:生醫三 學號:0317010 姓名:吳佩蓁 指導教授:潘惠錦老師

題目(中文):DM1 模式肌肉表現型之回復

(英文):Recovering muscle phenotypes in the DM1 models

摘要:

Myotonic dystrophy type 1(DM1) characterized by myotonia, muscle weakness and muscle atrophy, is resulted from a (CTG)n expansion in the 3'-untranslated region of DystrophiaMyotonica Protein Kinase (DMPK) gene. The transcribed mRNA with expanded CUG repeats sequesters RNA splicing factor muscleblind-like (MBNL), and these mRNA–protein aggregates form distinct, primarily nuclear foci. Mislocalization of MBNL results in missplicing of pre-mRNAs that are linked to the symptoms found in DM patients. Our lab generated C2C12 myoblast cells and zebrafish models of CUG expansions. The former shows that myoblasts are unable to differentiate into myotubes; and the latter exhibits abnormal swimming patterns associated with impaired muscle structures.We have tested the effects of a number of compounds for alleviating the CUG expansion-induced phenotypes using these models. A β2 -adrenergic receptor agonist known to induce skeletal muscle hypertrophy and attenuate muscle atrophy was selected for further analysis.Pretreat the cells with the compound for one day, and added 2% horse serum to the medium. We found that in the C2C12 model, treatment of this compound stimulated myotube formation in CUG200 cells. Zebrafish models were treated with the β2-agonist as well, two hours after fertilization. Results showed that administration of this compound to CUG-repeat zebrafish improved their motility behaviors such as total distance moved and swimming pattern by usingEthoVision® XTtracking software. Then, thetissue specimens were fixed, sectioned and stained.Histology slidesindicated that loose muscle tissue was more compact after β2-agonistadministration. To elucidate the underlying molecular mechanism, we measured the expression level of proteins related to AKT/mTOR pathway. It is reported that effects of this compound are mediated by activating Akt-mTOR signaling, which can stimulate protein synthesis, promote muscle growth and simultaneously block protein degradation. Both phospho-Akt and phospho-mTOR levels were decreased in CUG200 cells compared with control groups in the C2C12 model. These data indicate that treatment with the β2 agonist alleviated phenotypes in DM1 models and the effects might be mediated through the AKT/mTOR pathway.Zebrafish has plenty of advantages for investigating vertebrate development and for modeling human disease. By virtue of this model, we could have a better and deeper understanding on DM1 disease.