The Effect of p38 On GLUT1 DHA Transport and ROS Levels in Muscle Cells  
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ABSTRACT

Glucone transporter 1 (GLUT1) handles a large portion of basal glucose transport and is the primary dehydroascorbic acid (DHA) transporter in skeletal muscle. DHA is the oxidized form of the cellular antioxidant, ascorbic acid (vitamin C). The objective of this study is to determine the effects of p38 on GLUT1 mediated DHA transport and on reactive oxygen species in skeletal muscle cells. Increased p38 activity is hypothesized to decrease DHA transport and to increase ROS levels. It is also hypothesized that decreased p38 activity will lead to increased DHA transport into cells and to decreased ROS levels. Decreased ROS levels increase the cellular antioxidant, ascorbic acid (vitamin C). The objective of this study is to determine the effects of p38 on GLUT1 mediated DHA transport and the level of induced ROS in mouse SOL and EDL muscle cells. Increased p38 activity is hypothesized to decrease DHA transport and to increase ROS levels. It is also hypothesized that decreased p38 activity will lead to increased DHA transport into cells and to decreased ROS levels. These findings of the current study provide evidence that p38 effects GLUT1 DHA transport and the level of induced ROS in muscle cells.

INTRODUCTION

GLUT1:
- GLUT1 is a large portion of basal glucose transporter that is present in all tissue types.
- It is a high facilitative membrane glucose transporter.
- GLUT1 is a primary transporter of DHA.

DHA:
- DHA is a 12 transmembrane spanning integral membrane protein.
- GLUT1 is a primary transporter of DHA.
- p38 is a mitogen activated protein kinase (MAPK).
- It is activated by cellular stress such as inflammatory cytokines, or ultraviolet radiation.

p38:
- p38 is a mitogen activated protein kinase (MAPK).
- Anisomycin (ANS) is a p38 inhibitor.
- ANS has been found to increase phosphorylated p38.

SB203580 (SB):
- SB is a specific inhibitor of p38.
- SB inhibits p38 by binding to its ATP binding pocket.
- Pyrogallol is a super oxide donor.
- It induces reactive oxygen species.

HYPOTHESIS:
- Increased p38 activity is hypothesized to decrease DHA transport and to increase ROS levels.
- It is also hypothesized that decreased p38 activity will lead to increased DHA transport and decreased ROS levels.

RESULTS

GLUT1 Transport by SB:
- Cells were incubated in radioactive transport media for 10 minutes.
- L6 DHA TRANSPORT:
- Cells were incubated in radioactive transport media for 10 minutes.
- Cells were incubated in radioactive transport media for 10 minutes.

DHA Transport by ANS:
- DHA transport increased in muscle cells when treated with p38 inhibitor SB.
- DHA transport increased in muscle cells when treated with p38 inhibitor SB.
- DHA transport increased in muscle cells when treated with p38 inhibitor SB.

DISCUSSION

- ANS activated p38 and increased phosphorylated p38.
- DHA transport increased in muscle cells when treated with p38 inhibitor SB.
- DHA transport decreased in L6 myoblasts when treated with p38 activator ANS.
- Inhibited p38 leads to increased DHA transport into cells.
- Cells with inhibited p38 also had increased reactive oxygen species (ROS).
- DHA converts to ascorbic acid which reduces ROS thus potentially reducing the effects of type 2 diabetes.
- p38 inhibition could be a strategy to reduce reactive oxygen species in patients with type 2 diabetes.

FUTURE STUDIES

- ANS DHA transport in mouse SOL and EDL muscle
- Immunoprecipitation assays to see possible association between STOM and GLUT1
- Glucose transport studies to determine substrate specificity switch
- Cell-based assays

LITERATURE CITED

