

L6 RAT SKELETAL MUSCLE CELLS (RDLP#429)

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Technology description

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BACKGROUND

Approximately 40% of people with diabetes develop disease complications due to hyperglycemia, including blindness, kidney failure, lower-extremity amputations and cardiovascular disease. It is important to identify drugs that can help reduce blood glucose levels, preferably by increasing glucose uptake into muscle. It is estimated that the total number of cases of diabetes will reach 239 million worldwide by 2010.

DESCRIPTION OF THE INVENTION

The inventors have subcloned an L6 myoblast cell line that was selected for high fusion capacity as these cells differentiate into myotubes. Glucose uptake in L6 myotubes is stimulated by insulin with a 1.5 to 2-fold increase of their maximal response above basal (unstimulated) rates. Glucose uptake in L6 cells also responds rapidly to stimulation by IGF-I in much the same manner as insulin (a 2-fold maximal stimulation above basal). In addition, prolonged exposure of L6 cultures to insulin or IGF-I induces hypertrophy of L6 myotubes, glucose transporter biosynthesis, and 3 to 4-fold increases in glucose uptake. Insulin-stimulated glucose uptake measurements in isolated rat and mouse EDL and soleus muscle are typically 3 to 4-fold and 2 to 3-fold above basal rates, respectively. Thus, L6 myotubes in culture have a significant glucose uptake response to insulin that is within the range established for isolated rodent skeletal muscle preparations.

Advantages

This technology provides a L6 muscle cell line that can differentiate with high reliability into a myotube muscle cell phenotype that naturally expresses the GLUT4 glucose transporter protein, and has a significant insulin-stimulated glucose uptake biological response. The cell line can be used as the basis for a high throughput screen in the search for novel anti-diabetic compounds by measuring their effect on glucose uptake, thus providing an efficacious alternative to isolated skeletal muscle tissues or primary skeletal muscle cell cultures. The L6 myotube cell line is the best-characterized cellular model of skeletal muscle origin to study glucose uptake and GLUT4 translocation. The cell line is amenable for transient transfection by plasmid-based gene transfer and viral infection protocols (retrovirus and

adenovirus). Stable transfectants can be differentiated into myotubes. Adenovirus infection can be performed in myotubes.

Institution

[The Hospital For Sick Children](#)

Inventors

[Amira Klip](#)

联系我们



叶先生

电话 : 021-65679356

手机 : 13414935137

邮箱 : yeyingsheng@zf-ym.com