Modeling the Transport of Nuclear Proteins Along Single Skeletal Muscle Cells

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Principal's reference number

1

Description

The purpose of this study was to define the factors that control the distribution of nuclear proteins in multinucleated skeletal muscle cells (myotubes). Nuclear-targeted red fluorescent proteins of different molecular weights were used as a model protein. Changes in their distributions were quantified as a result of perturbations causing myotube hypertrophy, atrophy, and diminished nuclear import rates. A computational model was developed to simulate nuclear protein distribution using a combination of empirical values and data from the literature. Finally, the results from the model system were then validated using muscle-related transcription factors ARNT and Six1.

These data were generated to study the distribution of nuclear proteins within multi-nucleated skeletal muscle cells. Myotubes were produced by differentiating primary mouse myoblasts that were sparsely transfected to express a nuclear protein from a single nucleus. From the microscopy images, we measured the protein intensity in all nuclei along with the distance of each nucleus from the brightest one, which was assumed to be the transfected nucleus. We used these distribution profiles to study the relationship between protein size and its transport behavior. We also studied the effect of treatments that induce cell hypertrophy (capsaicin), atrophy (dexamethasone), and diminished nuclear import (importazole) on the transport of the nuclear proteins. We also developed a mathematical model to simulate how changes in cell and protein properties affect protein transport. These data form the basis of the figures in the associated manuscript, and the detailed methods pertaining to their collection can be found there. The data have been organized according to their corresponding figure.

Figure 1 - Nuclear protein transport dynamics
Using time-lapse microscopy, we captured the transport of the DsRed red fluorescent protein (RFP) at 6, 12, 18, and 24 hours after induction of expression (Fig 1 - 1-4). We also included a Hoechst nuclear counterstain at the final timepoint (24 hours, Fig 1 - 5)

Figure 2 - Molecular weight affects nuclear protein transport
These data show the distribution profiles of mCherry, tdTomato, and DsRed RFP variants in myotubes after three days of differentiation and one day of expression. The images are fluorescence microscopy

images with one channel containing the RFP signal and the other a nuclear counterstain. The filenames indicate which RFP is used.

Figure 3 - Perturbing nuclear import affects nuclear protein transport
In these images, cells were treated as previously with the addition of 5 µM importazole added during the final 24 hours to reduce the rate of protein import into nuclei. The filenames indicate which RFP is used.

Figure 4 - Cell morphology affects nuclear protein transport
In these images, cells were treated as previously with the addition of either 10 µM capsaicin or 10 µM dexamethasone during the final 24 hours to induce hypertrophy or atrophy, respectively. The drugs modulated cell width, which in turn affected the distribution profiles of the nuclear proteins. The filenames indicate which drug and RFP are used.

Figure 5 - Mathematical model to simulate nuclear protein transport
Here, a computational MATLAB model was developed to simulate the effects of various cell and protein properties on nuclear protein distribution.

Figure 6 - Transport of muscle transcription factors
To validate the results derived with RFP nuclear proteins, we repeated the experiments using ARNT-CFP and Six1-myc transcription factors expressed in muscle. ARNT-CFP has a similar size to DsRed, while Six1-myc is similar to mCherry. The images contain two channels (either ARNT-CFP signal and DRAQ5 nuclear coutnerstain or Six1-myc and Hoechst nuclear counterstain). The filenames indicate which transcription factor is used.

Language

English

Unit of analysis

Cells

Population

Myotubes derived from primary mouse myoblasts

Study design

Experimental study

Data format / data structure

Still image

Software

Responsible department/unit

Department of Medical Biochemistry and Biophysics

Contributor(s)

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Research area

Medical and health sciences (Standard för svensk indelning av forskningsämnen 2011)

Keywords

Skeletal muscle, Myonuclear domain, Nuclear transport, Mathematical model

Publications

Modeling the transport of nuclear proteins along single skeletal muscle cells. Hermes Taylor-Weiner, Christopher L. Grigsby, Duarte M. S. Ferreira, José M. Dias, Molly M. Stevens, Jorge L. Ruas, Ana I. Teixeira. Proceedings of the National Academy of Sciences, Jan 2020, 201919600; DOI: 10.1073/pnas.1919600117
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