KEY RESEARCH QUESTION AND/OR CREATIVE PROJECT GOAL

Skeletal muscle is a compound tissue made of individual muscle fibers. To accommodate everyday activities, such as walking, running, jumping, etc., our muscles are composed of several types of fibers, each expressing a unique set of muscle genes. Interestingly, early in development all muscles in the body are made of the same fiber type, but later they acquire different properties. The mechanism of muscle fiber diversity is not clear, although it may be critical in treating muscle-related diseases or enhancing physical performance. The goal of my project is to identify critical genes and possible mechanisms that control the fate of muscle fibers.

METHODS

In our experiments, we used the fruit fly *Drosophila melanogaster* as it is the best available model for gene manipulation. In flies, like in humans, muscle fiber diversity increases during development, which results in highly specialized muscles appearing in adults. For example, the flight muscles are specifically adapted for fast and continuous contractions to generate power for flight. The flight muscles, unlike other muscles in the fly body, do not express the structural muscle gene Act57B. Our lab has created a genetic reporter on the basis of Act57B. We used this molecular tool to screen for genes that influence Act57B activity and, ultimately, flight muscle fate. We were subsequently inactivating ("turning off") candidate genes in the flight muscles, while reading Act57B reporter activity. We were looking to identify genes, whose inactivation resulted in a boost of Act57B expression.

RESULTS (OR ANTICIPATED RESULTS)

We have screened over 200 different genes and identified 10 possible hits, including the transcription factor Mef2 and a variety of factors controlling condensation of nuclear DNA. These hit-producing genes can be sorted into two major categories: regulators and structural components. While structural components condense DNA into a non-active form, the regulators determine what part of the genome needs to be inactivated and recruit structural components.

CONCLUSION/DISCUSSION

Based on the obtained results, we propose the following: chromatin remodelers (e.g. Gug) bind activators of muscle genes (e.g. Mef2) and condense chromatin around some of the muscle genes to cause shut down of unwanted muscle genes. Chromatin structural proteins (Chro) maintain that repression. Given a strong sequence conservation for these proteins, this mechanism can be present in other organisms, including humans. Our future efforts will be applied to validate our findings by alternative methods.