A Cut and Paste Method for Modification of Cmybp-C in Muscle Sarcomeres

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Title: A Cut and Paste Method for Modification of cMyBP-C in Muscle Sarcomeres

Invention: This technology utilizes a new mice strain created using CRISPR/Cas9 that allows a desired modification of cardiac myosin binding protein-c (cMyBP-C) to be introduced at the exact location of the native cMyBP-C. This method relies on unique “spy” proteins that allow researchers to effectively “cut and paste” desired cMyBP-C sequences that could include a variety of modifications such as point mutations and FRET probes.

Background: cMyBP-C is an essential regulator of heart muscle contraction. Mutations in the gene that encodes cMyBP-C are a leading cause of abnormal thickening of the heart muscle known as hypertrophic cardiomyopathy (HCM). cMyBP-C has an abundance of dynamic interactions that occur with binding partners in the sarcomere, making the study of this protein extremely complex. Furthermore, manipulation of large, thick filaments such as myosin, titin, and cMyBP-C within muscle cells is very difficult. It is widely recognized that this obstacle is the single most important barrier to progress in cMyBP-C research. This technology uses a new approach to potentially overcome this barrier and improve cMyBP-C research.

Applications:

• Research tools
• cMyBP-C and hypertrophic cardiomyopathy research
• Skeletal muscle MyBP-C research
• Research for a variety of sarcomeric proteins

Advantages:

• Makes genetic modifications in the native position of cMyBP-C in the sarcomere
• Potential to lay the framework for manipulation of other hard to modify sarcomeric proteins
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