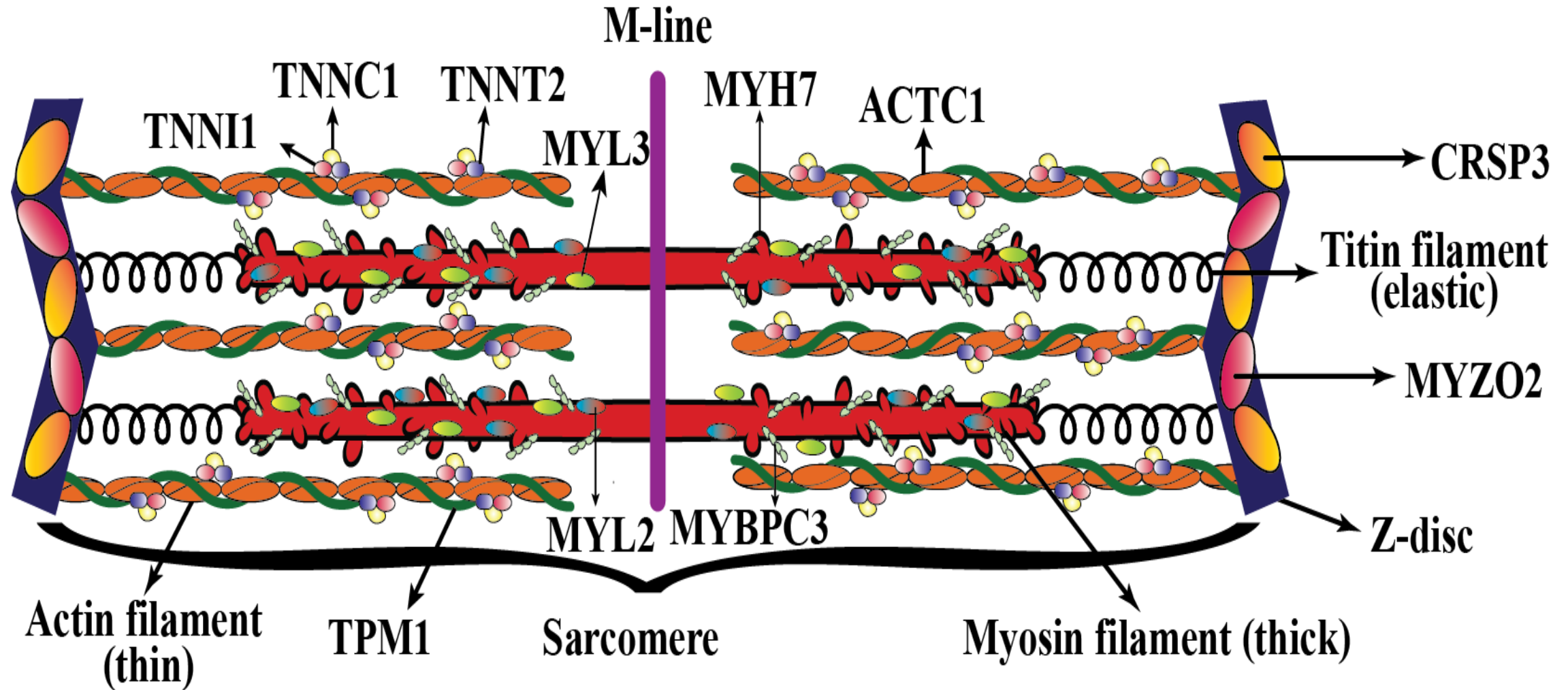


The sarcomere gene mutation locations in HCM and location of gene, protein and function



I. Thin myofibril proteins ($\approx 5\%$): ACT1, TPM1, TNNI3, TNNC1, TNNT2

II. Thick myofibril proteins ($\approx 45\%$): MYBPC3 (20%), MYH7(20%), MYL2(<1%), MYL3(<1%).

III. Z disk protein ($\approx 1\%$) CRSP3, MYZO2.

Genes Implicated in HCM Established causal gene HCM (large families)

Gene	Protein	Function
<i>MYH7</i>	β -Myosin heavy chain	ATPase activity, force generation
<i>MYBPC3</i>	Myosin-binding protein C	Cardiac contraction
<i>TNNT2</i>	Cardiac troponin T	Regulator of actomyosin interaction
<i>TNNI3</i>	Cardiac troponin I	Inhibitor of actomyosin interaction
<i>TPM1</i>	α -Tropomyosin	Places the troponin complex on cardiac actin
<i>ACTC1</i>	Cardiac α -actin	Actomyosin interaction
<i>MYL2</i>	Regulatory myosin light chain	Myosin heavy chain 7-binding protein
<i>MYL3</i>	Essential myosin light chain	Myosin heavy chain 7-binding protein
<i>CSRP3</i>	Cysteine- and glycine-rich protein 3	Muscle LIM protein (MLP), a Z disk protein

Likely causal genes for HCM (small families)

Gene	Protein	Function
<i>JPH2</i>	Junctophilin-2	Intracellular calcium signaling
<i>LDB3</i>	Lim domain binding 3	Z disk protein
<i>MYH6</i>	Myosin heavy chain α	Sarcomere protein expressed at low levels in the adult human heart
<i>MYLK2</i>	Myosin light chain kinase 2	Phosphorylate myosin light chain 2
<i>NEXN</i>	Nexilin	Z disc protein
<i>TNNC1</i>	Cardiac troponin C	Calcium-sensitive regulator of myofilament function

Gene	Protein	Function
<i>FHL1</i>	Four-and-a-half LIM domains 1	Muscle development and hypertrophy
<i>MYOZ2</i>	Myozenin 2 (calsarcin 1)	Z disk protein
<i>PLN</i>	Phospholamban	Regulator of sarcoplasmic reticulum calcium
<i>TCAP</i>	Tcap (telethonin)	Titin capping protein
<i>TRIM63</i>	Muscle ring finger protein 1	E3 ligase of proteasome ubiquitin system
<i>ACTN2</i>	Actinin, $\alpha 2$	Z disk protein
<i>ANKRD1</i>	Ankyrin repeat domain 1	A negative regulator of cardiac genes
<i>CASQ2</i>	Calsequestrin 2	Calcium-binding protein
<i>CAV3</i>	Caveolin 3	A caveolae protein
<i>VCL</i>	Vinculin	Z disk protein