BIGGER ISN’T BETTER: RISKS & REASONS FOR AN ENLARGED HEART

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Myosin Molecular Motor
Genetic Defects in Myosin Motor

Leading cause of sudden death in young adults.

1 in 500 people have genetic defect (1,250 Vermonters)
Hypertrophic Cardiomyopathy (HCM)  
Normal  
Dilated Cardiomyopathy (DCM)  

Seidman and Seidman Cell (2001)
Myosin Genetic Mutations

R403Q  →  S532P

2000 amino acids

● Hypertrophic

● Dilated
Power = Force x Velocity

Myosin Molecular Motor
Motility Assay

Actin Filament Velocity ~ Muscle Velocity

http://motility.york.ac.uk/
Star Trek Tractor Beam

Laser Trap

**INTERRUPT**

**STAR TREK DEEP SPACE NINE**

**ACTIVATE TRACTOR BEAM**

“Tractor beam” is the common term for the focused linear graviton force beam installed on most starships.

Plays on your ship with Tractor Beam; it may tow any ship present which is yours or is empty. **OR** Plays on your outpost or ship; adds Tractor Beam (but may not carry ships aboard).
Single Molecule Laser Trap Assay
Laser Trap Assay

Detector

Trap

Actin

Myosin

Coverslip Surface
Heart is the Ultimate Power Generator!

450 Million Revolutions

3 Billion Beats

Engine Power and Torque Curves

Power

Torque

Torque (NM)

Power (kW)

Speed (RPM)
Power vs. Force Relation

- **P\(_{\text{max}}\)**
- **Normal**
- **HCM R403Q**
- **DCM S532P**

**Axes:**
- **Force/myosin (pN)**
- **Power**
Depressed Motor Function

Enhanced Motor Function

DCM

HCM

Function

+-

Enhanced Motor Function

Depressed Motor Function
CARDIOMYOPATHIES: DEFECTS IN THE MOLECULAR MOTORS THAT POWER THE HEART

Future Perspectives

1. Genetic Testing or Simple EKGs

2. Precision and Individual Therapeutics:

   Enhance Myosin Power in Dilated Cardiomyopathy

   Reduce Myosin Power in Hypertrophic Cardiomyopathy
Throttling back the heart’s molecular motor

A small molecule inhibits mutated forms of myosin that cause cardiac hypertrophy

By David M. Warshaw