



Enhancing Cardiac Function Using Short Protein Inhibiting DNAs and RNAs (20120271, Dr. Michael Bowser)

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Cardiomyopathy Treatment

A new class of oligonucleotides can be used to treat cardiomyopathy. The short, protein-interacting DNAs and RNAs (SPIDRs) are designed to selectively bind to phospholamban (PLN), a compound that inhibits SERCA, which is a necessary function for cardiac health.

Results show that ssDNA and RNA interact strongly with PLN, thereby inhibiting its effect on SERCA. Furthermore, the length of SPIDR sequences varies and allows tunable heart function control: a longer SPIDR sequence more fully restores SERCA function while shorter sequences restore SERCA function to a lesser extent. These new oligonucleotides may serve as a platform for developing effective drugs.

Restores SERCA Functionality during Diastole

The SERCA/PLN complex is a prime target for treating heart disorders. SERCA clears Ca^{2+} from the cytosol to initiate the diastolic (relaxation) phase of the heart contraction cycle. While many treatments target the contraction phase of the cardiac cycle, none currently exist that target diastole. Phospholamban (PLN) inhibits SERCA activity by down regulating the rate of Ca^{2+} clearance. By selectively binding to PLN, this technology blocks the inhibitory effect PLN has on SERCA, essentially restoring SERCA activity, speeding diastole and enhancing overall heart function.

BENEFITS AND FEATURES:

- Treats cardiac disease/cardiomyopathy
- Selectively binds to PLN; inhibits PLN activity on SERCA
- SPIDR sequence length affects SERCA functionality
- Tunes SERCA inhibition and Ca^{2+} transport

APPLICATIONS:

- Cardiac disease treatment
- Improving myocyte relaxation and/or improvement of myocyte relaxation
- Reducing time required to return to baseline after contraction

Phase of Development - Pre-clinical validation

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