Title:

A Novel Regenerative Therapeutic Strategy to Reverse Advanced Heart Failure in Chronic Chagas Disease and Other Cardiomyopathies

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Abstract:

Development of regenerative therapeutic strategies to reverse the progression of advanced heart failure is a most urgent clinical need in this century. Trypanosoma cruzi is a protozoan parasite that causes chronic cardiomyopathy in millions of people worldwide, estimated to cost about $7.19 billion per year. The only cure for the cardiomyopathy, characterized by intense inflammation and fibrosis, is hearts transplant, but this therapy is impractical due to the extreme difficulty in securing heart for transplant. However, cardiomyopathy occurs in only 30% infected individuals as the other 70% remain asymptomatic and show no cardiac pathology, implying the existence of strong regenerative mechanisms in Chagas disease progression. We have identified in T cruzi itself a surface molecule that potently promotes renewal of cardiac progenitor/stem cells (CPCs) ex vivo, concomitantly inducing secretion of anti-inflammatories, particularly TSG-6. Intravenous administration of a recombinant form of this unique CPC renewal and anti-inflammatory stimulating factor in mice bearing chronic Chagas cardiomyopathy dramatically reverses cardiac inflammation, inflammatory cytokines and fibrosis. These results suggest 1) that the T cruzi-modeled CPC renewal factor is a mechanism underlying pathology-free progression in Chagas disease progression, and 2) a novel regenerative therapeutic opportunity to reverse heart failure not only in Chagas but also in other cardiac diseases such as postmyocardial infarction.