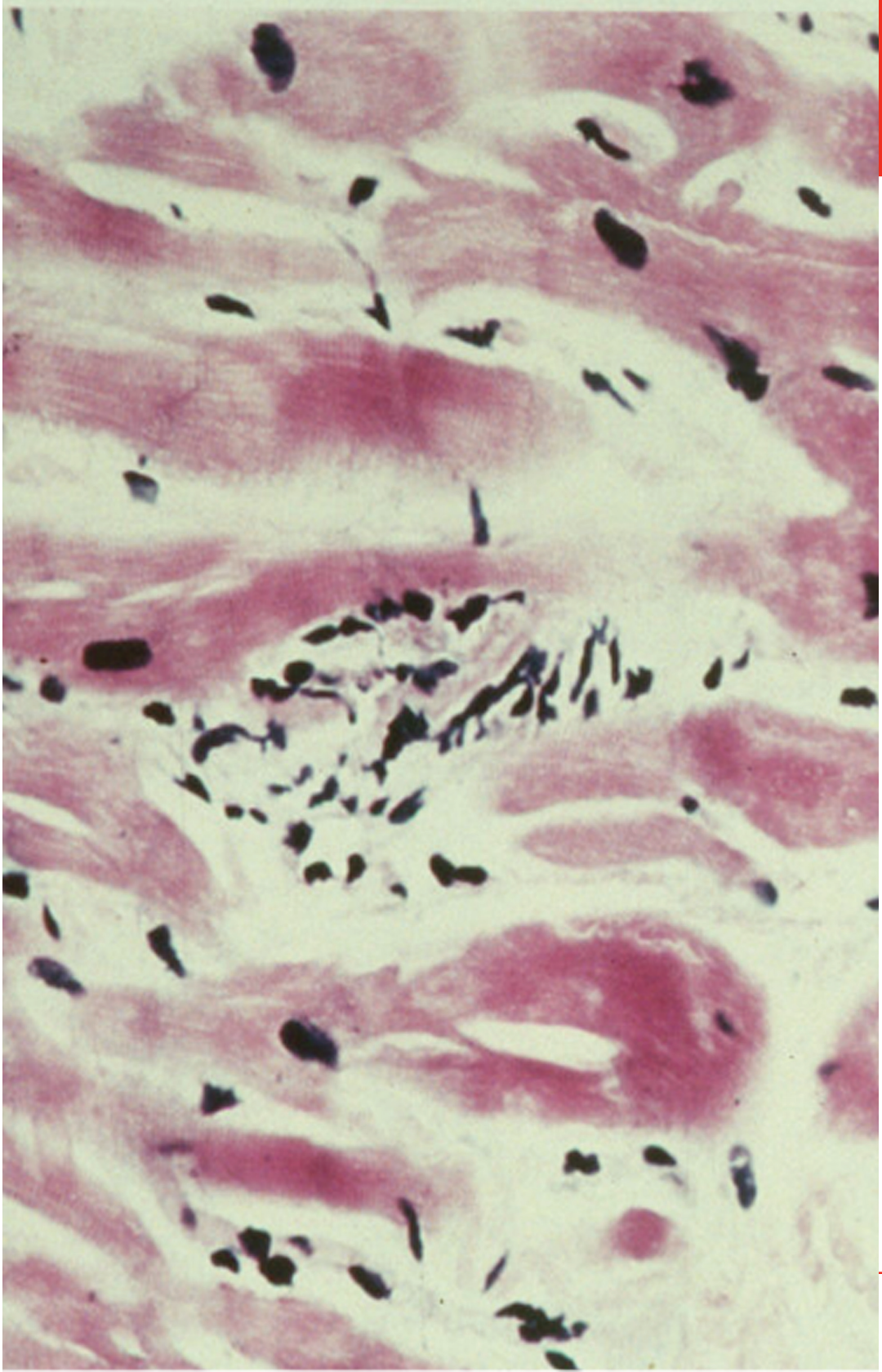
# INTRODUCING
HeartGen5YP and
HeartGenMYO

**Personalized Medicine for Heart Failure**
New molecular diagnostics for dilated cardiomyopathy and myocarditis



# Heart Failure Facts and Solutions

## Heart Failure Facts

- 600,000 new cases are diagnosed in the United States each year.
- Heart failure is the number one cause of hospital admission in the U.S. and has the highest degree of morbidity and mortality of any disorder in the western world.[i]
- According to a Congressional Budget Office report, the costs associated with heart failure constitute approximately 43% of the entire Medicare budget.

## Management of Heart Failure Lacks a Personalized Approach

- Accurate biomarkers are lacking for assessing patient prognosis and applying personalized medicine.
- The current standard-of-care in cardiology is unable to distinguish accurately between cardiomyopathy patients with an excellent long-term prognosis from those who will develop, within 5 years, a sudden circulatory collapse and require cardiac transplantation, or those who are at risk for sudden (arrhythmic) cardiac death.[ii]
- Specific and treatable causes such as myocarditis (inflammation of the heart muscle) are difficult to diagnose even with endomyocardial biopsy.
- Inadequate diagnostic and prognostic biomarkers contribute to death, disability, and healthcare costs.

## The Heart Genomics Solution

- Heart Genomics biomarkers employ "RNA expression profiling" in its Diagnostic Tests.[iii,iv]
- HeartGen5YP and HeartGenMYO measure panels of genes or "gene signatures" which provide a highly accurate assessment of diagnosis and prognosis of patients with heart failure.

**Left**

*Close up of heart tissue affected by Myocarditis*

# HeartGen5YP

Heart Genomics' 5 Year Prognosis Diagnostic Test (HeartGen5YP) is a laboratory based test performed at a CLIA facility that analyzes heart tissue from biopsies and then provides a score (the "5YP Score"), accurately telling the patient and physician whether the patient has a "Bad Prognosis (BP)" or "Good Prognosis (GP)" for the 5 year period. The test provides an accurate diagnosis, enabling the physician to make individualized, optimal therapeutic decisions for patients with heart failure due to cardiomyopathy.[ii]

If the HeartGen5YP indicates a bad 5 year prognosis, both the patient and physician can intervene to improve the patient's outcome probabilities. This information can help decisions about listing the patient for heart transplantation, implanting an artificial device or considering the use of experimental therapies. A good prognosis 5YP Score can provide reassurance that conventional medications and lifestyle modification can lead to years of good quality of life and fewer hospitalizations to treat heart failure exacerbations.

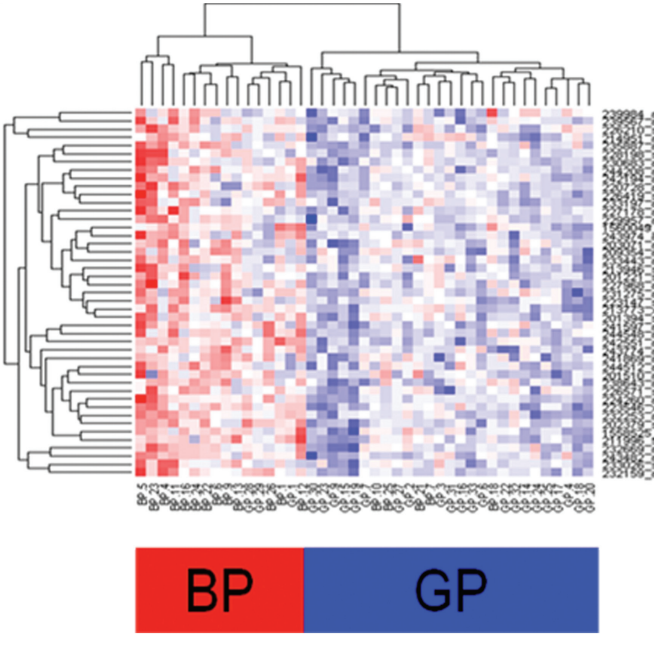



**Figure 1A**

*Microarray transcriptomic analysis reveals a gene signature that predicts with a high degree of accuracy a Good Prognosis ("GP") long term event free survival as compared to a Bad Prognosis ("BP") manifesting as death or need for heart transplantation within 2 years. (From Heidecker B, et. al: Transcriptomic biomarkers for individual risk assessment in new-onset heart failure. Circulation 118:238-246, 2008. Copyright 2008, American Heart Association).*

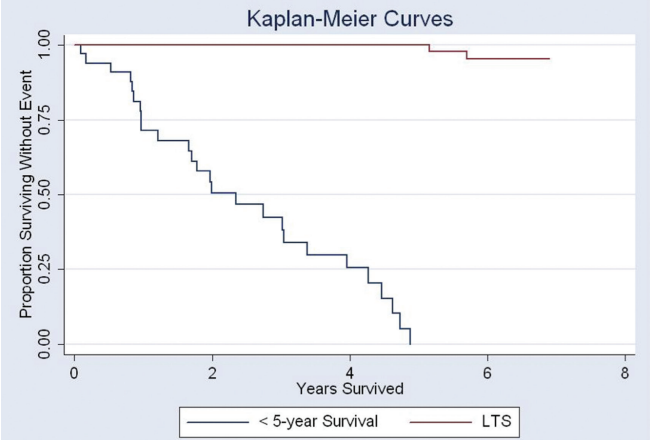



**Figure 1B**

*As diagnosed by HeartGen5YP, good prognosis patients have outstanding 5 year survival (zero mortality,) whereas poor prognosis patients have a 50% chance of dying within 2 years.*[iii]

The HeartGen5YP enables better and more accurate treatment decisions that will not only improve patients lives and prevent unnecessary treatments, but can also cut healthcare costs. For example, many heart failure patients presenting with an ejection fraction of 25% or less frequently receive an empiric defibrillator. As the 5YP Score can predict EF improvement, it can potentially obviate the need for a defibrillator. It is possible, therefore, that the HeartGen5YP test could allow more effective tailoring for a decision to implant a defibrillator.

HeartGen5YP's MSA-based approach has undergone initial validation in clinical Proof-of-Concept studies, validating its accuracy in determining the 5-year prognosis of heart failure patients.

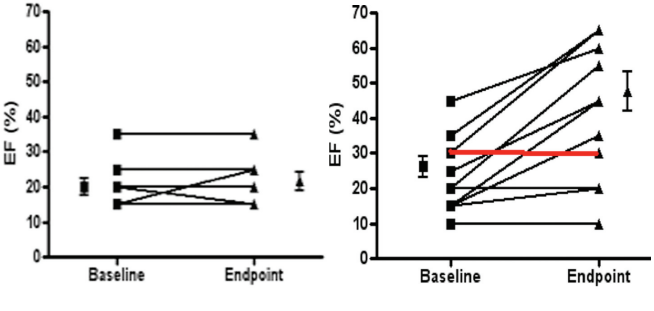



**Figure 2**

*Patients with gene signature predicting favorable outcome undergo reverse remodeling and have dramatic improvements in ejection fraction. (From Heidecker B, et. al: Transcriptomic biomarkers for individual risk assessment in new-onset heart failure. Circulation 118:238-246, 2008. Copyright 2008, American Heart Association).*

# HeartGenMYO

The HeartGenMYO is a laboratory based test performed at a CLIA facility that detects whether a patient has myocarditis.[iv] Myocarditis is a form of inflammation of heart muscle that afflicts 30% of new heart failure cases. Importantly, myocarditis is treatable and potentially reversible. The endomyocardial biopsy is the gold standard method of diagnosis. Pathological inspection requires multiple biopsies and can still be inaccurate. The HeartGenMYO diagnoses myocarditis from a single biopsy with substantially increased accuracy. The increased certainty can help guide tailored therapy for inflammatory heart disease.[v]

HeartGenMYO's MSA-based approach has undergone initial validation in clinical Proof-of-Concept studies, validating its accuracy in diagnosing myocarditis.

The HeartGenMYO study was chosen in March 2012 by the editors of *Circulation Heart Failure* as one of the Most Important Papers in Pathopysiology and Genetics,[vi] stating:

> [this technology] can substantially improve the diagnostic accuracy of heart biopsy for myocarditis…[and] provide treating physicians with important and accurate diagnostic information about individual patients and could provide tools for personalized treatment or monitoring. Given emerging treatment strategies for viral and inflammatory myocarditis, accurate diagnostic tools are of increased importance.

The editors concluded that:

> these findings demonstrate that transcriptomic biomarkers from a single endomyocardial biopsy can improve the clinical detection of patients with inflammatory diseases of the heart. This approach advances the clinical management and treatment of cardiac disorders with highly variable outcome.

**For more information, contact**
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**REFERENCES**

i Lloyd-Jones D, Adams RJ, Brown TM, Carnethon M, Dai S, De SG et al. Executive summary: heart disease and stroke statistics--2010 update: a report from the American Heart Association. Circulation 2010; 121(7):948-954.

ii Parakh K, Kittleson MM, Heidecker B, Wittstein IS, Judge DP, Champion HC, Barouch LA, Baughman K, Russell SD, Kasper EK, Sitammagari KK, Hare JM. The variable natural history of idiopathic dilated cardiomyopathy. Israeli Medical Association Journal 2012, 14:666-672.

iii Similar diagnostic tests using MSA techniques are now in standard use for the management of patients with cancer, most notably breast cancer, as well as for diseases such as heart transplantation and have shown that they augment current clinical practices, allowing for more effective, individualized patient management.

iv See Kittleson MM, Ye SQ, Irizarry RA, Minhas KM, Edness G, Conte JV, Parmigiani G, Miller LW, Chen Y, Hall JL, Garcia JGN, Hare JM. Identification of a gene expression profile that differentiates ischemic and nonischemic cardiomyopathy. Circulation 2004;110:3444-3451. See also Heidecker B, Kasper EK, Wittstein IS, Champion HC, Breton E, Russell SD, Kittleson MM, Baughman KL, Hare JM. Transcriptomic Biomarkers for Individual Risk Assessment in New Onset Heart Failure. Circulation 2008; 118:238-46.

v Heidecker B, Kittleson MM, Kasper EK, Wittstein IS, Champion HC, Russell SD, Hruban RH, Rodriguez ER, Baughman KL, and Hare JM. Transcriptomic Biomarkers for the Accurate Diagnosis of Myocarditis. Circulation. 2011 Mar 22;123(11):1174-84. Epub 2011 Mar 7.

vi Kocoil RD. Circulation: Heart Failure Editors Picks, Most Important papers in pathophysiology and genetics. Circ Heart Failure 2012;5:e32-e49


www.heartgenomics.com