

## Cardiomyopathy

Chronic heart failure is a debilitating condition of the cardio-vascular system in which the heart no longer fulfills its pumping function adequately. Despite enormous efforts in health care, the mortality associated with this disease remains extraordinarily high, indicating that current therapies are far from effective.

A major constraint in the development of effective drug treatment for chronic heart failure has been the lack of suitable cell-based assays with physiological relevance. Over the last decade, ventricular cardiomyocytes prepared from neonatal rats have been used to characterize the myopathic phenotype *in vitro*

. However, the extensive use of rat cardiomyocytes in drug development has been difficult because of their cumbersome handling properties and their limited availability for intense screening campaigns.

At the cellular level, hypertrophic cardiomyocytes are characterized by increased cell size, enhanced protein synthesis, and enhanced organization of the contractile apparatus

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. These phenotypic changes are due to a switch in the cardiomyocytes'

gene expression pattern: genes are activated that, in normal conditions, would only be expressed during early embryonic development

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## MyCor - Induced cardiac hypertrophy

Cor.At® cardiomyocytes faithfully recapitulate these characteristics of diseased cardiomyocytes *in vitro* when

stimulated with specific agonists

. Upon stimulation with agonists like

endothelin-1 and

phenylephrine,

Cor.At®

cardiomyocytes increase in cell size (

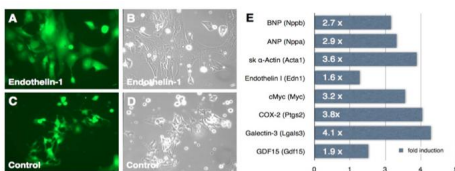
Fig. 1), up-regulate the expression of the hypertrophic marker genes

ANP and

BNP (

Fig. 2

) as well as other specific marker genes for hypertrophy (Fig. 2).



**Figure 2: Gene expression analysis of ET-1 induced Cor.At hypertrophy**  
 ET-1 (100 nM; A, B) was used to induce hypertrophic phenotype of Cor.At cells, after 24h starvation and cultivation on gelatine-coated dishes. 24h after ET-1 induction, microscopic pictures were taken (GFP fluorescence (A, C), phase contrast (B, D)) and total RNA was prepared (Qiagen RNeasy).  
 RNA expression analysis was performed using the Affymetrix GeneChip Mouse Gene 1.0 ST Array. ET-1 induced expression of hypertrophic marker genes is given in comparison to untreated control (fold induction).  
 BNP (Nppb) = b-type natriuretic peptide; ANP (Nppa) = a-type natriuretic peptide; sk α-actin (Acta1) = skeletal muscle α-actin; endothelin-1 (Edn1); cMyc (Myc); COX-2 (Ptgs2) = cyclooxygenase-2 or prostaglandin synthase-2; galectin-3 (lgals3); GDF15 (Gdf15) = growth differentiation factor 15

Together with Axiogenesis' safety pharmacology and toxicology portfolio the My.Cor system is a sound profiling platform that integrates the discovery of new active pharmaceutical ingredients (APIs) for cardiac hypertrophy therapy, and will be used for internal drug discovery efforts and as a drug discovery service for the pharmaceutical industry.

My.Cor is a patented customizable *in vitro* assay that provides a model for cardiomyopathy in embryonic stem cell (ESC)-derived cardiomyocytes

My.Cor

makes the drug discovery process more convenient and efficient, thereby helping to facilitate the development of better drugs for chronic heart failure.

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