the D263E desmin, as well as the other ID proteins, retained at high level their proper localization in the myocardium of D263E MHCsTNF mice.

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**Keywords:** Desmin; TNF-α; Aggregates


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**Abstract No. 116**

**Regulation of Calreticulin, a SR chaperone, in human heart failure**

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**Background:** Calreticulin (CRT) is a calcium binding chaperone in the endoplasmic reticulum. Previously, high expression of CRT in transgenic animals resulted in a cardiomyopathic phenotype including decreased systolic function, chamber dilation, and sudden death. The role of CRT in human heart failure has not been characterized yet.

**Methods and results:** Left ventricular myocardial tissue from explanted non-failing hearts (NF; n=17), from terminally failing hearts due to diluted cardiomyopathy (FAIL; n=18; EF: 27.4±2.2%), and myocardial biopsies from compensated hypertrophic hearts due to aortic stenosis (AS; n=18; EF: 51.6±3.3%) were subjected to quantitative Western-blot analysis (data expressed as percent change of NF-levels). Calreticulin expression was significantly increased in both, failing hearts (FAIL: 155.6±8.9%*) and aortic stenosis hearts (AS: 141.4±7.8%*), compared to non-failing myocardium (NF: 100±11.1%; *p<0.05). Calcineurin, a putative downstream effector of calreticulin, was found to be upregulated in a parallel fashion (NF: 100±10.2%; AS: 142.9±6.6%*, FAIL: 180.3±6.6%). Interestingly, like in CRT-overexpressing mice, the gap junctional protein connexin 43 was already significantly down-regulated in myocardium from patients suffering from aortic stenosis (NF: 100±7.1%; AS: 56.7±15.8%*, FAIL: 57.5±8.6%*), which may contribute to the AV-conduction delay found in Calreticulin-overexpression mice as well as in patients suffering from aortic stenosis or heart failure. Since CRT may serve as a SR luminal Ca^{2+} sensor and might be induced by low SR Ca^{2+} load, we co-incubated adult rabbit cardiomyocytes with the SR Ca^{2+} ATPase inhibitor Thapsigargin (10^{-8} M), which resulted in depletion of SR Ca^{2+} and a marked increase of CRT protein expression after 24 h.

**Conclusion:** This is the first study showing upregulated Calreticulin protein levels in human heart failure. Our observations support the role of Calreticulin as a SR calcium sensor.

**Keywords:** Heart failure; SR calcium regulation


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**Abstract No. 117**

**Myocardial protection: Efficacy of RS-C (Aqix®), a novel magnesium-cardioplegia, compared to St Thomas’ hospital solution**

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**Objective:** The current gold standard for myocardial protection is hyperkalemia; however, depolarization can cause myocardial Ca-overload and dysfunction. Alternative cardioplegic solutions, such as the novel Mg-cardioplegia (RS-C) based on RS-I solution (Aqix®); a new perfusion solution formulated to exclude free inorganic phosphate ions and prevent potential deleterious effects, may be beneficial. We compared the efficacy of RS-C to St Thomas’ solution No 2: STH2 (16 mM Mg).

**Methods:** Isolated Langendorff-perfused rat hearts were used, and function measured. In Study 1, the optimal Mg concentration (16, 25, 35 or 50 mM) in RS-C was established after 50 min global 37 °C ischemia compared to STH2. Study 2 compares single-dose RS-C (25 mM Mg) to STH2 at different ischemic durations (20, 30, 40 or 50 min). Study 3 investigated multiple infusions (every 20 min) of RS-C compared to STH2 during 60 min global ischemia. All hearts were reperfused for 60 min and recovery (%) of function determined.

**Results:** In Study 1, LVDP recovery in RS-C (16, 25, 35 or 50 mM Mg) was 48±3, 50±2, 50±3 and 30±3% compared to 51±2% for STH2. Contracture related parameters (time to onset and peak) in 25 mM Mg was 32±1 min (longest) and 35±1 mm Hg (lowest) (p<0.05) vs. STH2 (26±1 min and 43±2 mm Hg). Optimal Mg for RS-C was 25 mM. In Study 2, recovery in RS-C (25) was significantly (p<0.05) higher after 20 min ischemia than with STH2 (81±1% vs. 74±1%); however, there were no differences at 30, 40 or 50 min of global ischemia. In Study 3, RS-C (25) significantly improved recovery compared to STH2 (LVDP: 73±2 vs. 44±1%; LVEDP: 9±2 vs. 45±2 mm Hg; p<0.001).

**Conclusion:** Mg-based cardioplegia, at an optimal Mg concentration of 25 mM, improved protection compared to the hyperkalemic STH2 at a short (20 min) ischemic duration or after 60 min ischemia with multiple infusions. Mg-based cardioplegia may be a beneficial alternative to hyperkalemia under certain specific ischemic conditions.

**Keywords:** Myocardial protection; Cardioplegia; Magnesium