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A PROTEIN WITH ANTI-FIBROTIC POTENTIAL FOUND IN THE PROTEOME OF PATIENTS WITH HYPERTENSIVE HEART DISEASE

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Purpose Heart failure with preserved ejection fraction (HFPEF) contributes to 20–50% of the heart failure population. Excessive fibrosis in the cardiac interstitium results in stiffness and reduced compliance of the left ventricle which leads to diastolic dysfunction (DD) and eventual HFPEF. In an effort to discover potential therapies to treat this condition, we performed 2D-DIGE proteomic analysis of at risk hypertensive patients and identified an interesting protein.

Methods The anti-fibrotic potential of this protein (cryptonym: HU1001) was tested in an animal model of hypertensive heart disease. Three groups of 10 animals were treated for 12 weeks; group 1: normotensive Wistar-Kyoto rats treated with vehicle (V-WKY), group 2: spontaneously hypertensive rats treated with vehicle (V-SHR) and group 3: SHRs treated with HU1001 (HU1001-SHR).

Results Echocardiographic analysis of left ventricular mass/tibial length ratio (LVMi) revealed a significant reduction in hypertrophy in treated SHRs compared to untreated SHRs ($p<0.01$). There was no effect of treatment on blood pressure. Perivascular collagen to lumen ratio (PVCi) on picrosirius red stained sections and myocyte cross-sectional area were significantly decreased in the HU1001-SHR group compared to the V-SHR group ($p=0.0016$ and $p<0.01$ respectively). Significant reductions in serum levels of the

neutrophil and monocyte chemotactic proteins CXCL-1 ($p<0.05$) and MCP-1 ($p<0.001$) were found in the HU1001 treated animals.

Conclusions Treatment with HU1001 inhibits deposition of PVC, and reduces myocyte hypertrophy and LVM in SHRs. Lower chemotactic protein concentrations found in HU1001 treated animals may reflect the ability of this peptide to prevent recruitment of pro-fibrotic macrophages.