



Pharmacological inhibition of Galectin-3 attenuates adverse cardiac remodeling and heart failure



L. Yu¹, W.P. Ruirok¹, H.H.W. Sillje¹, E. Bos², H. Van Goor², D.J. Van Veldhuisen¹, W.H. Van Gilst¹, R.A. De Boer¹

(1) University Medical Center Groningen, Department of Cardiology, Groningen, Netherlands (2) University Medical Center, Department of Pathology

Department of Cardiology, University Medical Center Groningen, University of Groningen, Groningen, the Netherlands. Contact: L.yu@umcg.nl

Introduction and Aim

Galectin-3 is a carbohydrate binding protein which has been implicated as a mediator of liver and kidney fibrosis. Elevated levels of Galectin-3 are associated with poor prognosis in human heart failure. Additionally it has been shown that exposing the myocardium to galectin-3 induces cardiac fibrogenesis and compromises function.

Hypothesis – Treatment with a carbohydrate with high affinity to may effective to inhibit myocardial fibrogenesis, adverse cardiac remodeling, and heart failure.

Methods

➤ We employed homozygous TGR(mREN)27 rats (REN2, N=33), which spontaneously develop HF, and compared them to control (Sprague Dawley, SD) rats.

➤ We treated with N-acetyllactosamine, which has strong affinity to galectin-3 's carbohydrate recognition domain (CRD), as a Galectin-3 inhibitor (Gal3i). To include a golden standard, we treated some rats with the ACE-inhibitor lisinopril (ACEi).

➤ We measured cardiac function with echo (fractional shortening, FS %), and prior to sacrifice invasive hemodynamics were recorded.

➤ Ventricular collagen deposition was quantified as fibrosis score (%) by histological analysis. Gene expression of collagen-I and III (Col-I, Col-III) were measured by quantitative real-time PCR (RT-PCR).

Results

Figure1: Ren2 develop systolic dysfunction over time, but this is prevented by Gal3i

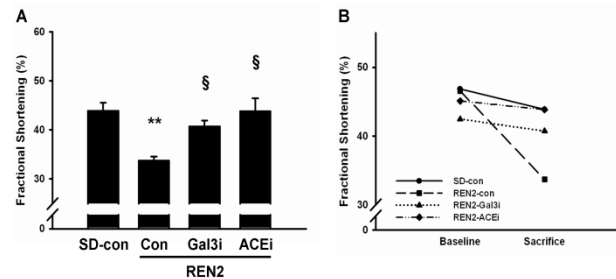
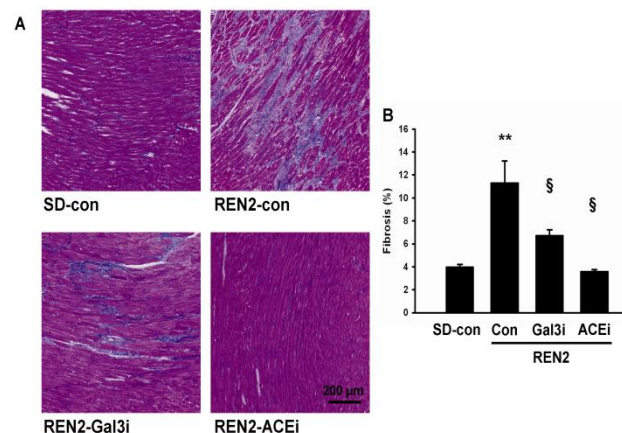


Figure2: Gal3i inhibits the development of fibrosis



➤ ** P<0.05 vs. SD-con, § P<0.05 vs. REN2-con.

Results (continued)

Figure3: Increases in diastolic parameters LVEDP and relaxation constant Tau are attenuated in Ren2 when treated with Gal3i (or ACEi)

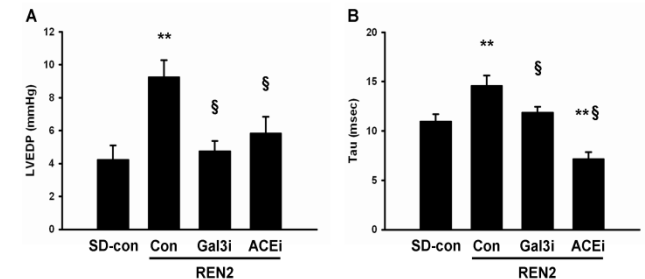
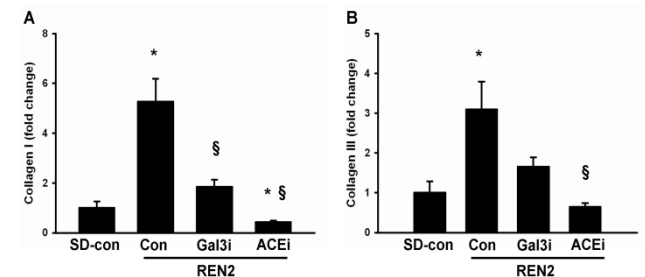


Figure4: Expression of Collagens I and III were reduced in the Gal3i-treated Ren2 compared with untreated Ren2



Conclusion

Pharmacological inhibition of Galectin-3 attenuates adverse cardiac remodeling and heart failure. Drugs which bind to the galectin-3 CRD may reduce cardiac fibrogenesis and are candidates for prevention or treatment of heart failure.

