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

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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

Figure 1: Ren2 develop systolic dysfunction over time, but this is prevented by Gal3i

Figure 2: Gal3i inhibits the development of fibrosis

Figure 3: Increases in diastolic parameters LVEDP and relaxation constant Tau are attenuated in Ren2 when treated with Gal3i (or ACEi)

Figure 4: 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.

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