



Genetic disruption of Galectin-3 prevents adverse cardiac remodeling

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Introduction and Aim

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

Hypothesis – Genetic disruption of the Galectin-3 pathway inhibits the development of adverse cardiac remodeling and progression to heart failure.

Methods

➤ We employed 8 weeks old mice that are deficient for the gene encoding Galectin-3 (Gal3KO, N=48), and transgene negative controls (WT).

➤ We induced cardiac remodeling by two interventions: 1) administration of angiotensin II (AngII, 2.5µg/gr/day) via osmotic minipump for 14 days, and 2) transverse aortic constriction (TAC) for 28 days. Control mice received saline (via minipump, 14 days).

➤ We measured cardiac function with echo (fractional shortening, FS%). Prior to sacrifice, invasive hemodynamics were recorded. Ventricular collagen deposition was quantified as fibrosis score (%) by histological analysis, and we measured markers of collagen metabolism in plasma by ELISA (procollagen type I/III N-terminal propeptides, PINP and PIIINP, respectively).

Results

Figure1: AngII and TAC increase heart weight (A), but causes cardiac dysfunction in WT mice only (B)

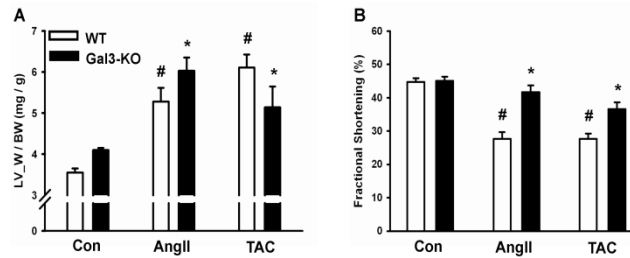


Figure2: LV relaxation parameters LVEDP and Tau were increased by AngII and TAC in WT mice, but to a lesser extent in Gal3KO mice

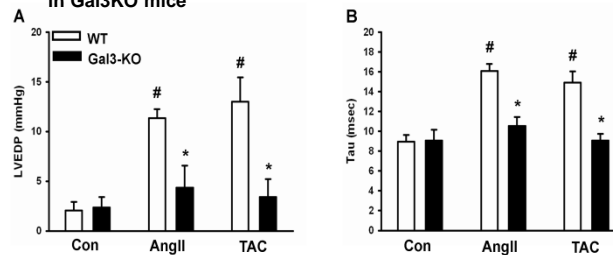
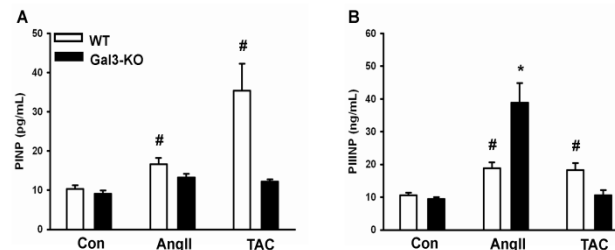
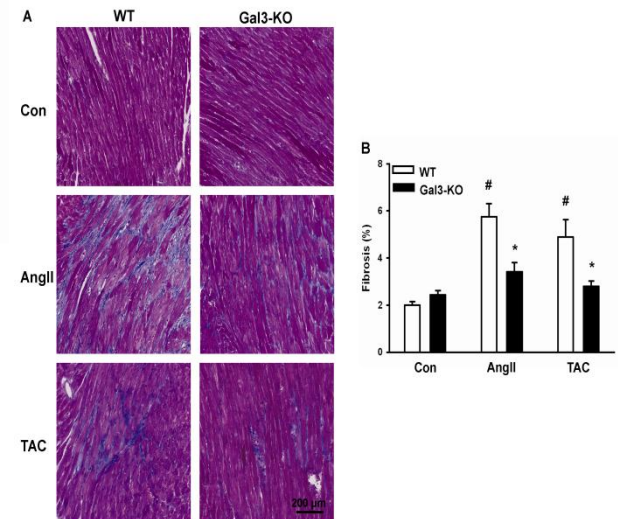


Figure3: Plasma PINP and PIIINP were increased by AngII and TAC in WT mice, but to a lesser extent in Gal3KO mice



Results (continued)

Figure 4: AngII and TAC increased fibrosis from ~2% to ~6% in WT mice; Gal3KO mice have much less fibrosis



* P<0.05 vs. WT (any condition)
P<0.05 WT-con vs. WT-AngII or WT-TAC.

Conclusion

Genetic disruption of Galectin-3 attenuates the development of adverse cardiac remodeling, associated with a decrease in fibrosis. These findings suggest that Galectin-3 is involved in the pathophysiology of adverse cardiac remodeling and heart failure.

