

# Importance of Tenascin-C in Vascular Remodeling Following Myocardial Infarction in Mice

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## Background

Post myocardial infarction (MI) remodeling is known to be mainly driven by neurohormonal stimuli such as the activation of local and systemic renin-angiotensin-aldosterone system (RAAS). The extracellular matrix protein Tenascin-C (TNC) might be an important player in the activation of angiotensin-converting enzyme (ACE). Moreover, we could recently show increased expression of TNC in infarcted heart tissue areas, indicating also its importance in adverse cardiac remodeling.<sup>1</sup>

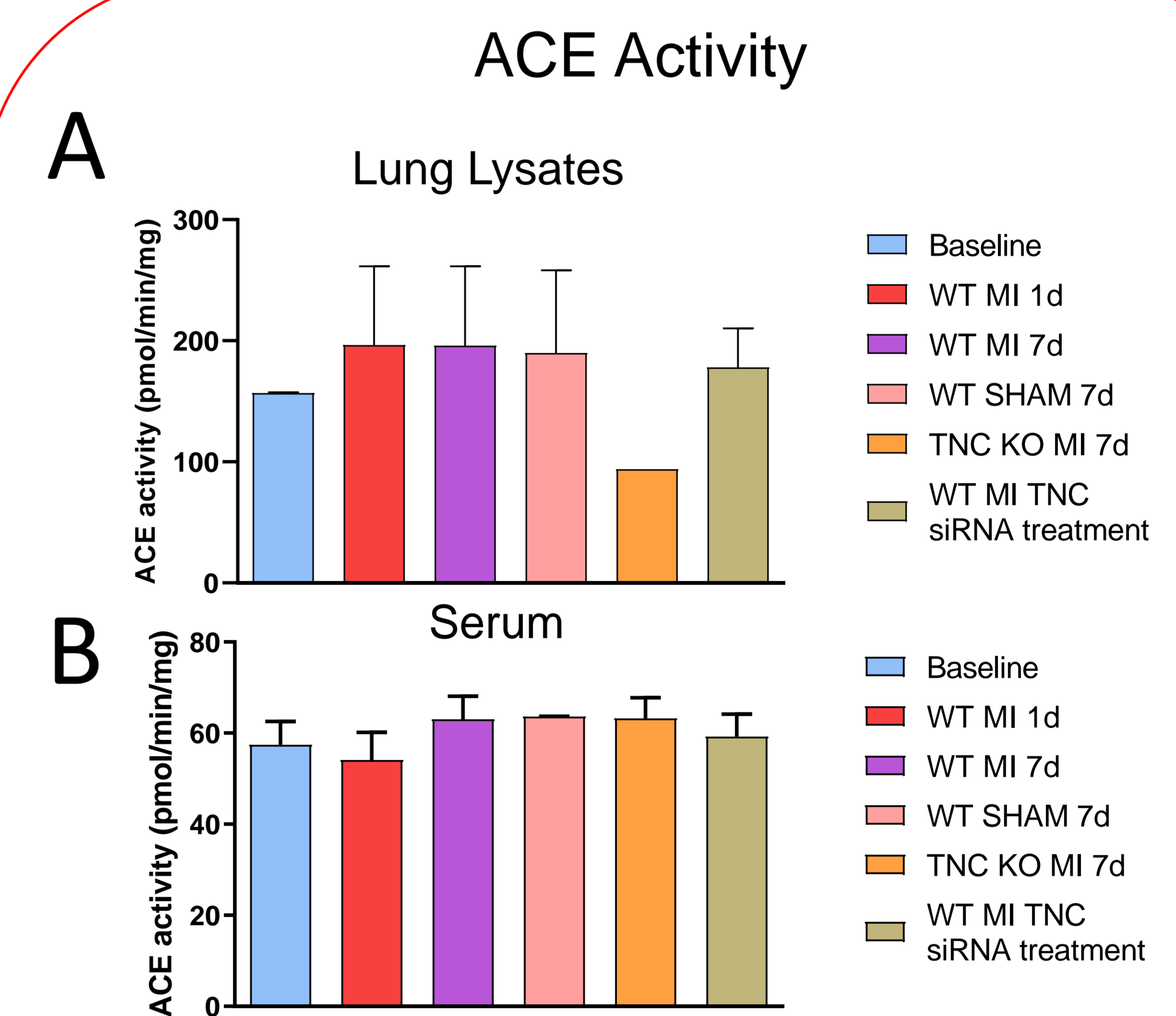
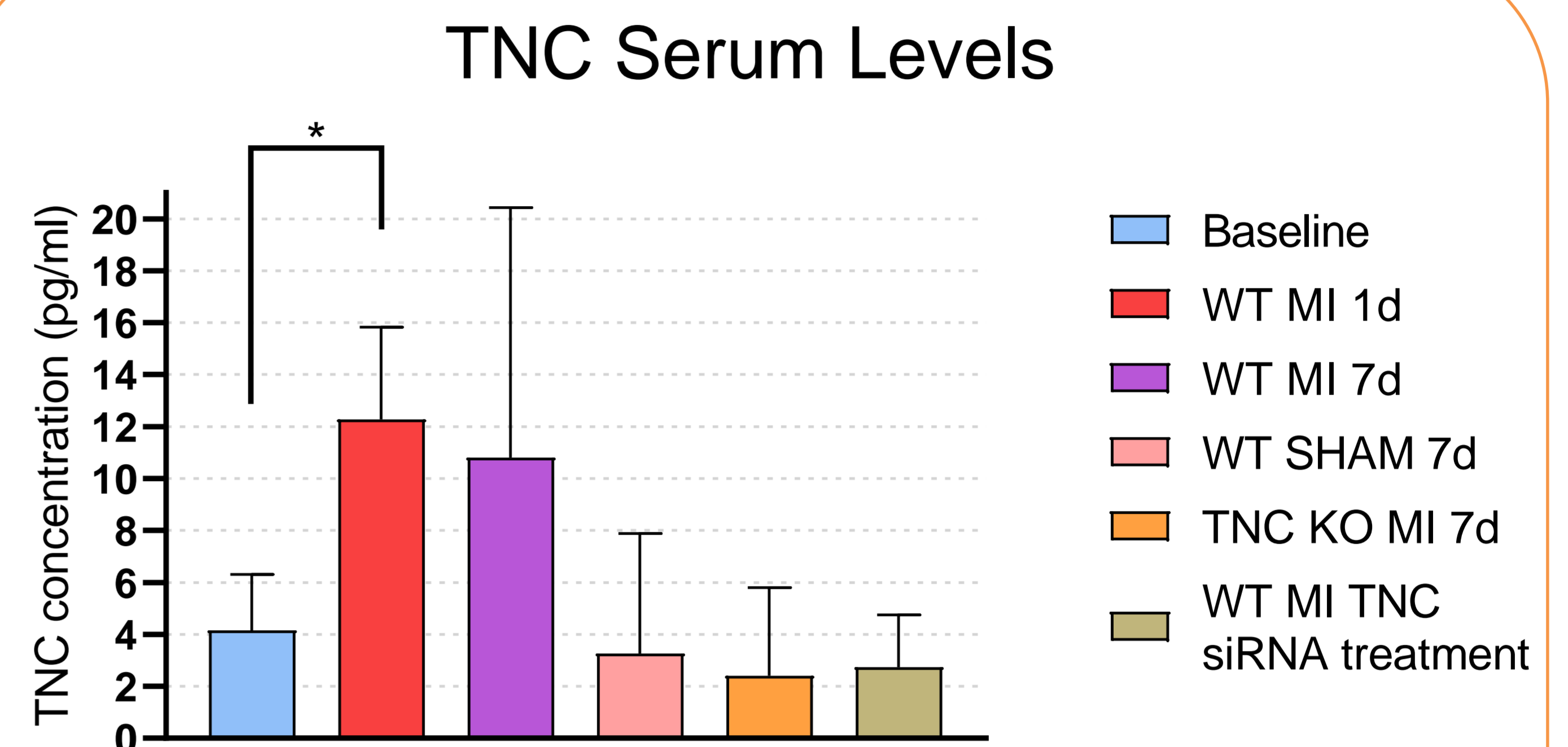
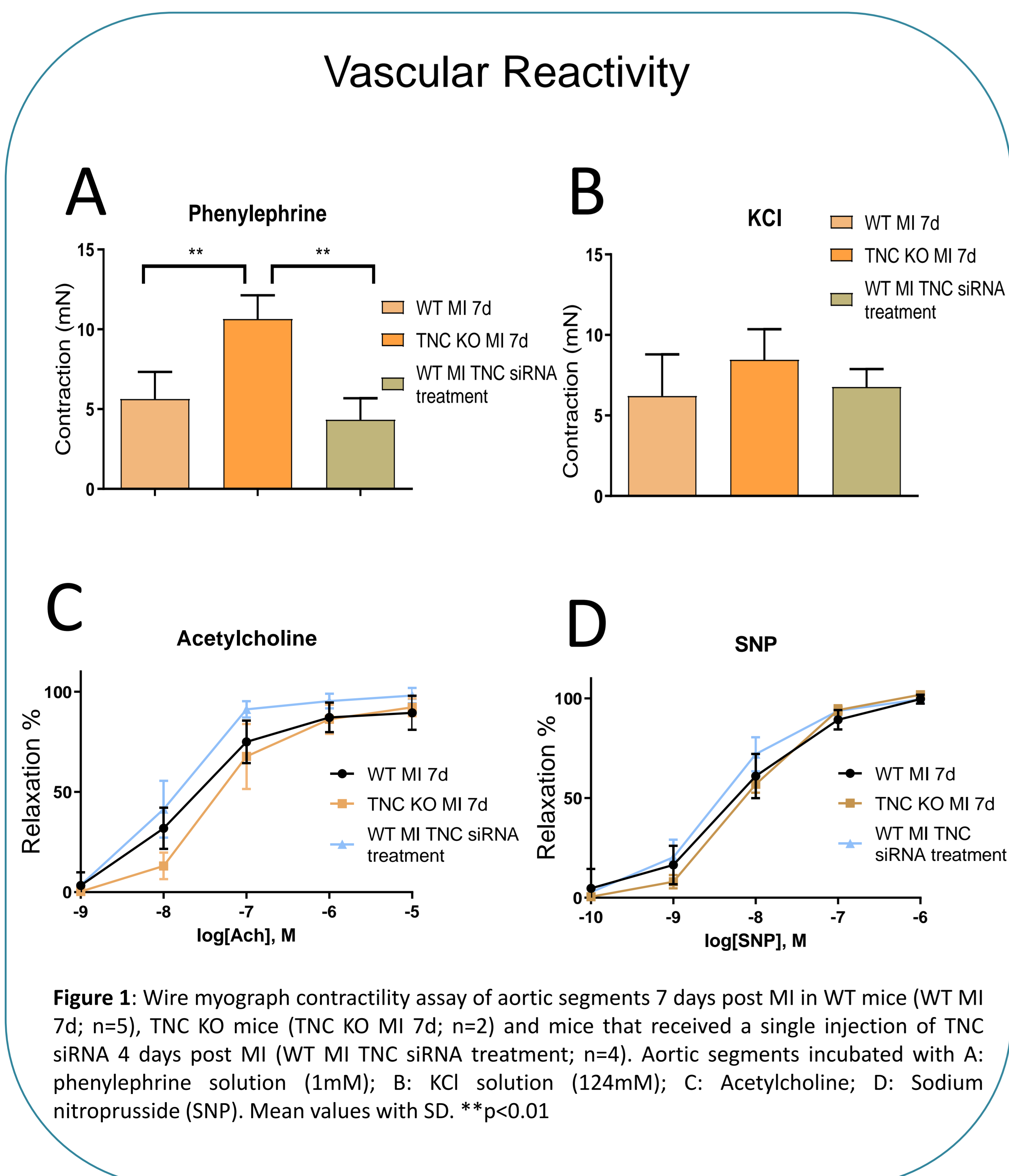
## Aims

In the present study we aimed to clarify the impact of TNC on RAAS activation and vascular (dys)function in a mouse model of MI.

## Materials and Methods

MI was induced by permanent ligation of the left anterior descending coronary artery in TNC-knockout (TNC KO) and wild-type (WT) AJ mice. One or seven days after MI, animals were sacrificed and heart, lung, aorta and serum were taken for further analyses. Additionally one WT group was treated with a single i.p. injection of TNC siRNA on day 4 after MI to knock down TNC expression. Vascular function (contraction and relaxation) was assessed in isolated aortic segments using a DMT wire myograph (Figure 1). Circulating levels of TNC were evaluated using an ELISA kit (Figure 2). Finally, ACE activity measurements were performed in lung lysates and serum using a fluorescence assay (Figure 3).

## Results



## Conclusions

Lack of TNC was associated with an increase of aortic segments contraction 7 days post-MI (Figure 1). This may indicate the importance of TNC in vascular remodeling. Treatment of infarcted mice with TNC siRNA 4 days post OP resulted in lower circulating levels of TNC (Figure 2). However ACE activity in lung and serum as well as vascular reactivity were not affected by this treatment (Figure 3). These findings may imply that vascular remodeling may already evolve within the first days post MI. Further studies are warranted to clarify the underlying mechanisms and biological significance.

## References

[1] Gonçalves, Inês F.; Acar, Eylem; Costantino, Sarah; Szabo, Petra L.; Hamza, Ouafa; Tretter, Eva V. et al. (2019): Epigenetic modulation of tenascin C in the heart: implications on myocardial ischemia, hypertrophy and metabolism. In: Journal of hypertension 37 (9), S. 1861-1870. DOI: 10.1097/HJH.0000000000002097.