

Differential modulation of epicardial activation

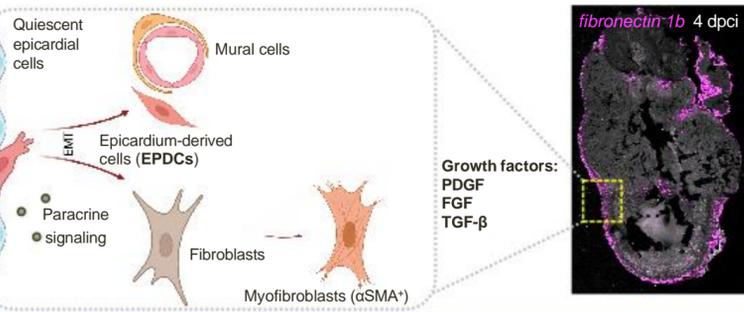
via the Fibulin-2–Nupr1b axis dictates cardiac regeneration after injury

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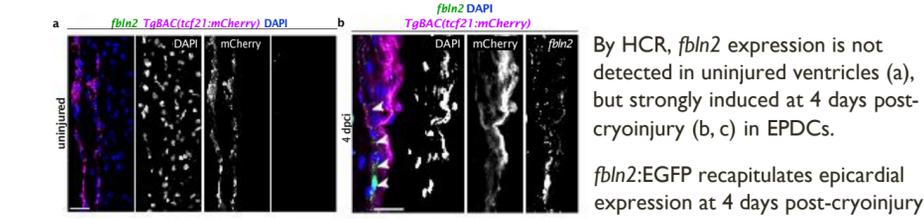
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Background: Epicardial activation promotes both fibrosis and regeneration

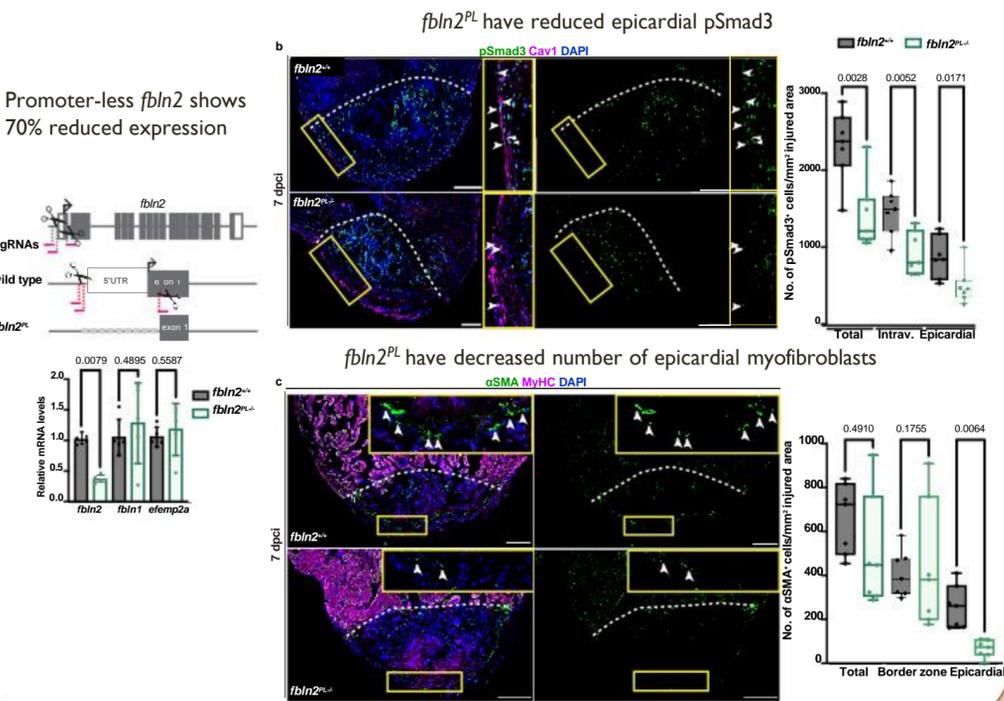
- Myocardial infarction activates fibroblasts, depositing ECM proteins and forming a fibrotic scar.
- Zebrafish hearts regenerate by forming a transient, pro-regenerative fibrotic response.
- A central driver of this response is TGF-β-mediated epicardial activation, but how it balances necessary repair with avoidance of excessive fibrosis remains unclear.



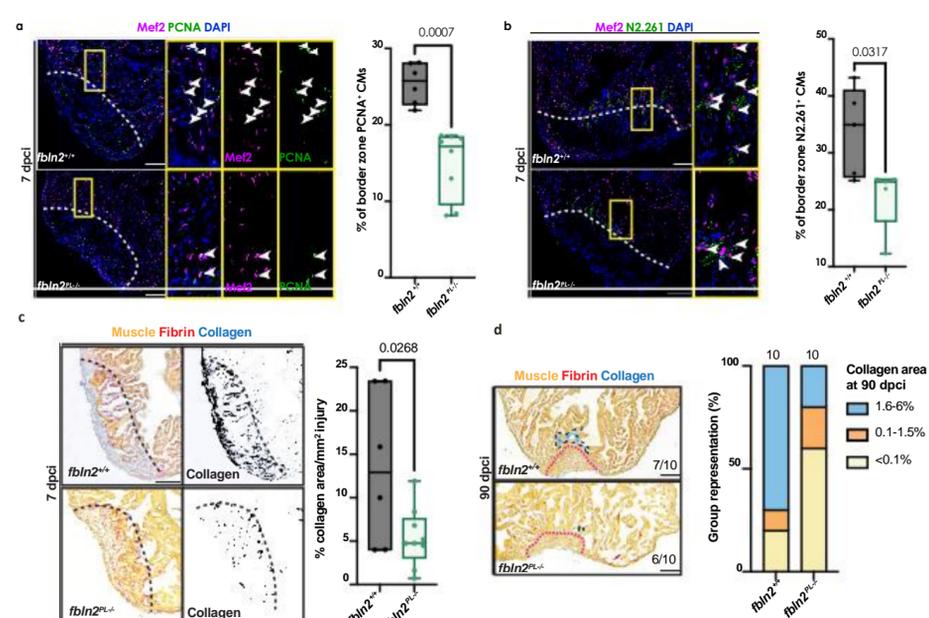
Fibulin-2: an injury-induced secreted matricellular protein



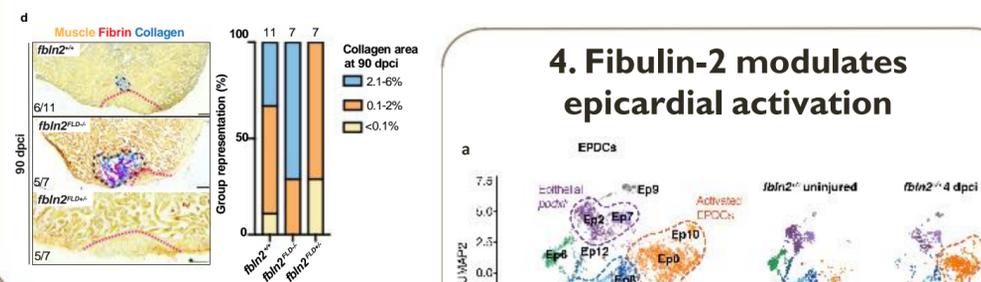
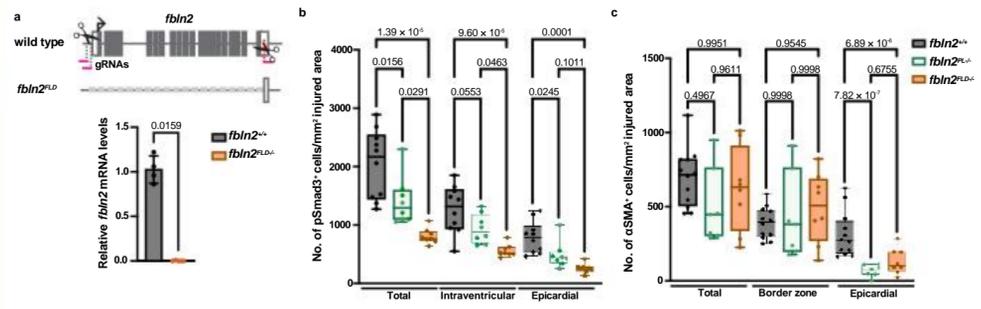
1. Fbn2 regulates epicardial TGF-β signaling and myofibroblast numbers



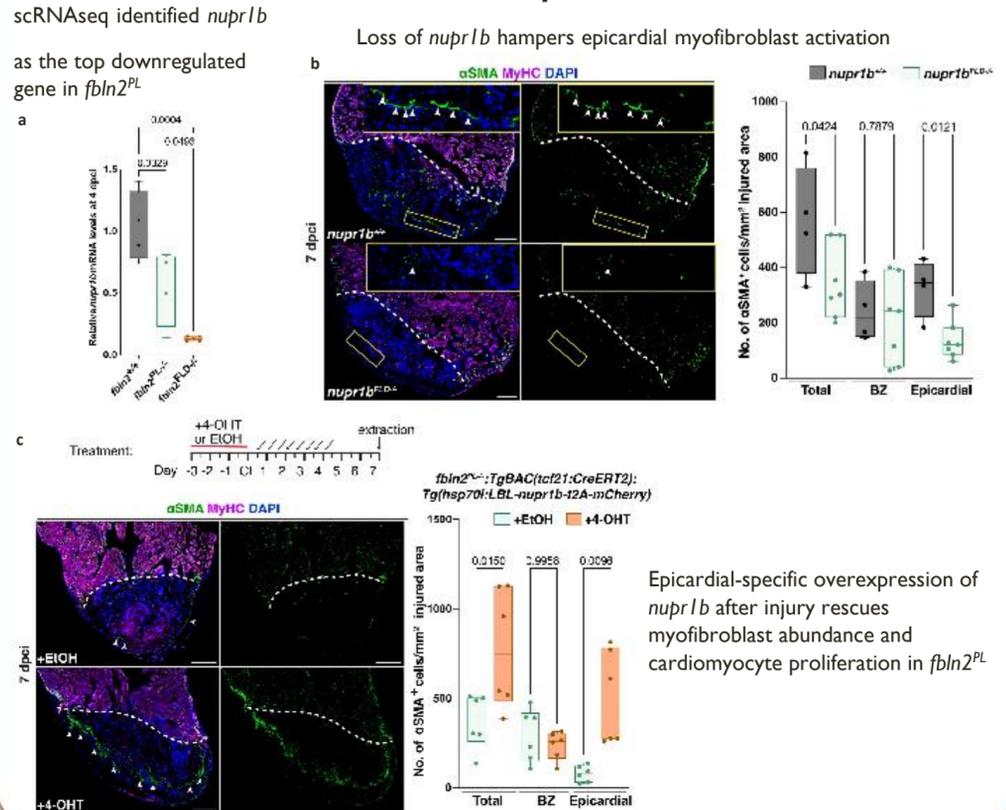
2. fbn2^{PL} present reduced cardiomyocyte regeneration but retain smaller collagen deposits



3. Complete ablation of fbn2 further decreases TGF-β but results in scarring



5. Nupr1b drives epicardial myofibroblast abundance and rescues mutant fbn2 defects



Conclusion

Regenerative and fibrotic functions of epicardial activation are tightly regulated



Attenuation of epicardial activation can be beneficial

Fibulin-2

Disruption of the balance is detrimental



- Improved fibrosis resolution

- Insufficient transient fibrosis
- Compromised regeneration
- Scarring

Can we use Fbn2 as a potential therapeutically actionable element to limit maladaptive fibrosis while sparing, or enhancing regeneration?

References

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Funding

Fonds de Recherche du Québec Postdoctoral Fellowship to G. Kayman #310928
Canadian Institutes of Health Research Grant to R. Marin-Juez #PJT-178037