

GATA3: A Regulator of Renin Cell Development and Blood Pressure

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Category: Basic Research

Background: Renin cells are precursors for other cell types in the kidney and show high plasticity in postnatal life in response to challenges to homeostasis. Our previous study revealed that the dual-zinc finger transcription factor *Gata3*, is important for cell lineage commitment, differentiation, and identity of the cells of the renin lineage. We found *Gata3* is expressed in juxtaglomerular, mesangial, and smooth muscle cells under normal conditions and homeostatic threat. In addition, we identified a decrease in renin expression, leading us to believe *Gata3* is crucial for the expression of renin and the regulation of blood pressure.

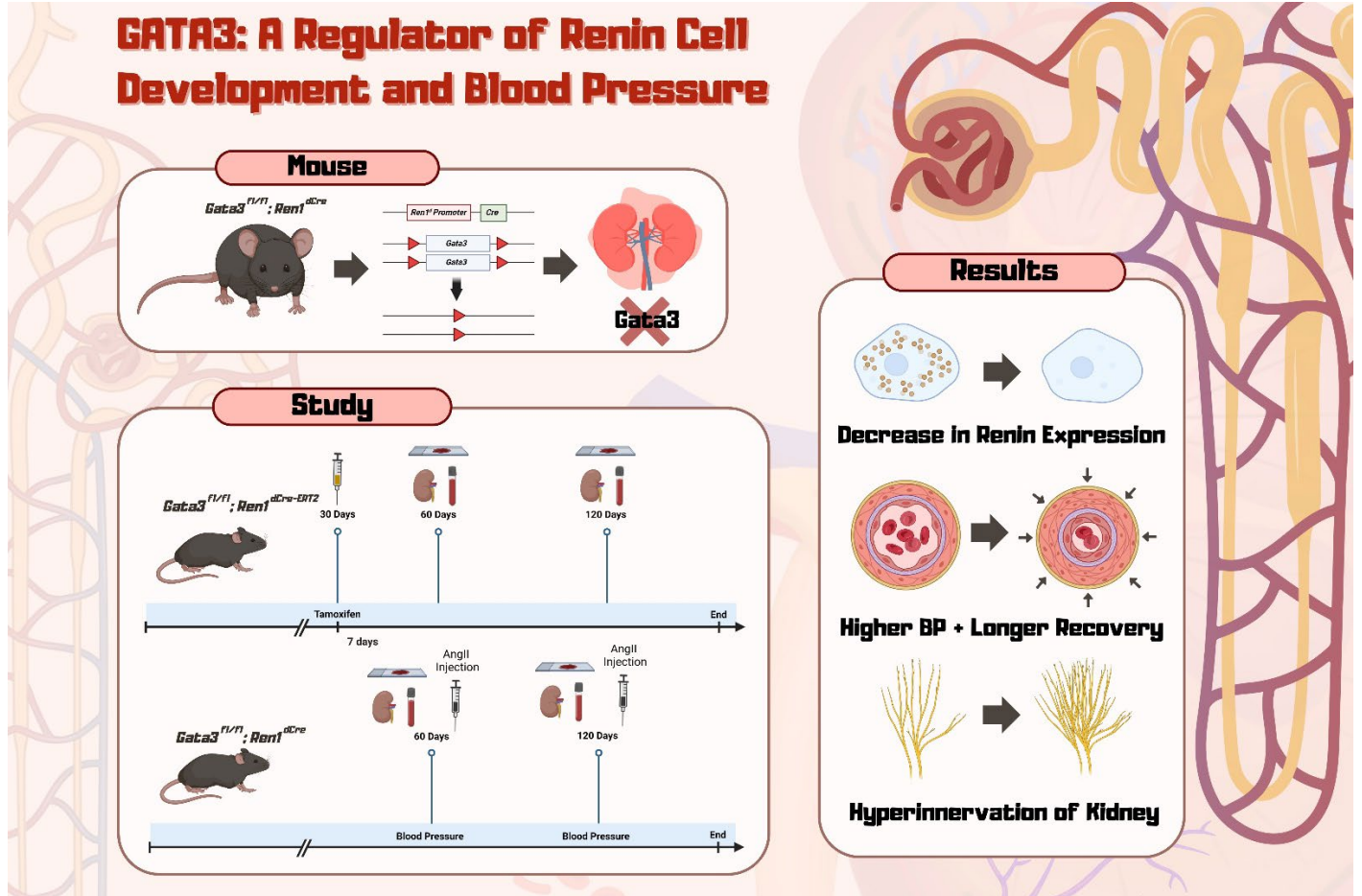
Objective: To determine whether GATA3 has a role in the regulation of blood pressure.

Design/Methods: We studied 60 and 120-day-old mice with a non-inducible (constitutive) and inducible deletion (tamoxifen injections at 1 month) of *Gata3* in renin cells: *Gata3^{fl/fl};Ren1^{dCre/+}* (*Gata3-cKO*) and control *Gata3^{fl/fl};Ren1^{d+/+}* counterparts, and *Gata3^{fl/fl};Ren1^{dCre-ERT2}* (*Gata3-cKO*) and control *Gata3^{fl/fl};Ren1^{d+/+ERT2}* respectively. For lineage tracing, *Gata3^{fl/fl};Ren1^{dCre/+};R26^{mTmG}* mice were generated. Plasma renin levels were measured by Elisa from blood samples collected by cardiac puncture. Systolic, diastolic, and mean arterial pressure were measured. Blood pressure was also measured upon acute injection of angiotensin II. *Ren1*, *Acta2*, *Gata3*, and *Tubb3* were visualized in kidney sections by immunostaining & immunofluorescence using specific antibodies and DAB color reaction. Histological analysis was performed on adult kidney sections with hematoxylin and eosin (H&E) staining.

Results: *Gata3-cKO* constitutive deletion mice have: 1) a marked reduction of *Ren1* mRNA levels in renin cells compared to controls; 3) a significant decrease in circulating plasma renin compared to controls under basal conditions and physiological threat; 4) no significant difference in blood pressure at 2 and 4 months of age; 5) a significant mean blood pressure increase, faster blood pressure elevation, and increased recovery period to baseline blood pressure when subjected to acute angiotensin II injections; 6) No significant difference of *AT1aR* mRNA levels in renin cells compared to controls; 7) Increase of *Tubb3* staining, indicative of hyperinnervation at 2 and 4 months of age under basal conditions. *Gata3-cKO* inducible deletion mice demonstrate: 1) glomeruli with decreased positive renin staining in the Bowman's capsule compared to constitutive mice 2) no histology abnormalities in renal tissue compared to *Gata3-cKO* constitutive deletion mice 3) a marked reduction of *Ren1* mRNA levels in renin cells compared to controls; 4) a significant decrease in circulating plasma renin compared to controls under basal conditions and physiological threat.

Conclusion: Our results suggest that *Gata3* influences the regulation of blood in postnatal life and is crucial in the proper development of renal vasculature. In addition, our data suggests that *Gata3* serves a role in regulating renin cell innervation.

Concept Figure



Summary

- **Objective:** To determine whether GATA3 has a role in the regulation of blood pressure.
- **Conclusions:** Our results suggest that *Gata3* influences the regulation of blood in postnatal life and is crucial in the proper development of renal vasculature. In addition, our data suggests that *Gata3* serves a role in regulating renin cell innervation.
- **Implications for Children:** Understanding the role of the GATA3 signaling pathway in renin cells and kidney development may lead to insights for developing new therapies for children with kidney disease or hypertension.

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