## Cooperative ETS transcription factors enforce adult endothelial cell fate and cardiovascular homeostasis.

Jesus M. Gomez-Salinero, Tomer Itkin, Sean Houghton, Chaitanya Badwe, Yang Lin, Viktoria Kalna, Neil Dufton, Claire R. Peghaire, Masataka Yokoyama, Matthew Wingo, Tyler M. Lu, Ge Li, Jenny Zhaoying Xiang, Yen-Michael Sheng Hsu, David Redmond, Ryan Schreiner, Graeme M. Birdsey, Anna M. Randi & Shahin Rafii Nat Cardiovasc Res (2022).
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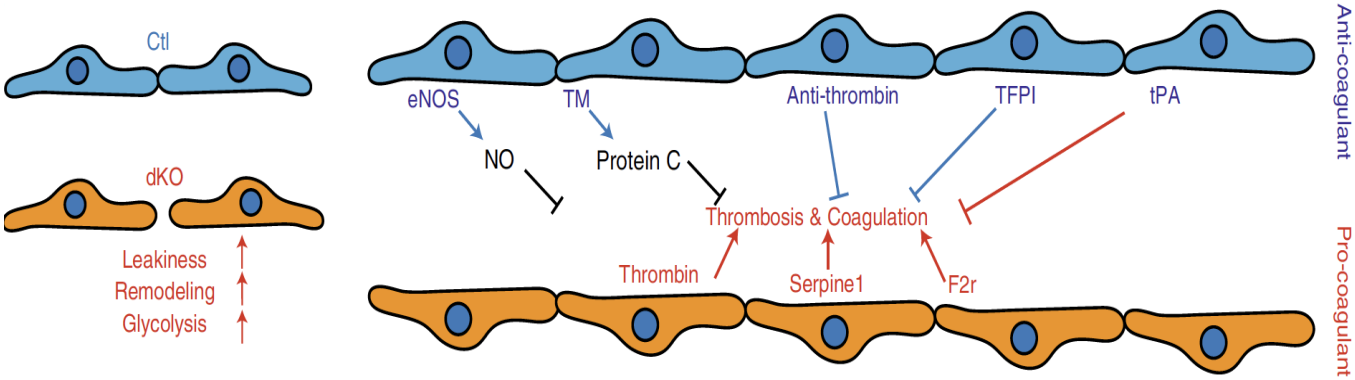


*Figure displaying phenotype differences between Erg/Fli1 double-knockout mice and their respective control animals.*

**Key findings:**

Gomez-Salinero and colleagues challenge with their article the current dogma that claims that endothelial cells (ECs) are limited to a steady homeostatic state during adulthood.

This recent publication indicates that fate decisions in ECs as well as their functionality rely on cross-signaling of the two ETS transcription factors (TFs), ERG and Fli1.

Deletion of either ERG or Fli1 leads to only subtle vascular dysfunction, however, their combined genetic deletion in adult ECs results interestingly in acute vasculopathy and multi-organ failure.

The authors are able to show that this dual TF loss further results in hyperinflammation and spontaneous thrombosis, resulting consequently in death. ERG and Fli1 co-deficiency causes rapid transcriptional silencing of pan and organotypic vascular core genes, with dysregulation of inflammation and coagulation pathways.

Vascular hyperinflammation leads to impaired hematopoiesis with myeloid skewing. Accordingly, enforced ERG and FLI1 expression in adult human mesenchymal stromal cells activates vascular programs and functionality, enabling in vivo engraftment of a perfusable vascular network.

Of translation value, GWAS analysis identified vascular diseases being associated with FLI1/ERG mutations. Constitutive expression of ERG and Fli1 upholds EC fate, physiological function and resilience in adult vasculature, whereas their functional loss can contribute to systemic human diseases.