

BDR SEMINAR (Kobe/online hybrid)

Mathias Francois

The Centenary Institute, Sydney, Australia

Tuesday, December 6, 2022

11:00-12:00

1F Auditorium, DB Building C, Kobe / Broadcast online via Zoom

Zoom meeting URL will be announced on the event day by e-mail.

✧This seminar is open only to BDR members.

Endothelial cell transcription: from developmental genetics to drug repurposing

Summary

Modulation of transcription factor (TF) activity holds great promise for the development of targeted therapeutics, because these proteins act at the point of convergence for cell signalling and directly orchestrate gene expression. Many transcription factors depend on interactions with partner proteins for their activity, and so attempts to develop therapeutics have focused on disrupting interactions critical for nuclear shuttling, post-translational modification or dimerization. However, isolating and targeting one specific interaction is often insufficient to generate a biological effect, due to redundancies in regulatory pathways in which transcription factors are involved. During the presentation, I will show a novel function for SOXF transcription factor during cardiac endothelial cell differentiation which instructs cardiac morphogenesis. Then I will report a novel molecular strategy that is efficient to interfere with the SOX18 TF activity to perturb its function and therefore impairs vascular outgrowth in pre-clinical model systems. Further, using this new strategy we have identified an FDA-approved drug that has been successfully repurposed to manage two rare vascular diseases in human. Our work provides a proof of therapeutic utility for a novel strategy to inhibit transcription factor activity, re-establishing this class of protein as a viable class of molecular targets for small molecules in therapeutic settings.



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