Targeted drug therapy to provide effective and localised anticoagulation without impairing haemostasis

Xiaowei Wang¹,², Donny Hanjaya-Putra³, Carolyn Haller³, Amy Kate Searle¹, Karlheinz Peter¹,², Elliot L. Chaikof³

¹Atherothrombosis and Vascular Biology, Baker Heart & Diabetes Institute, Melbourne, Victoria, Australia; ²Department of Medicine, Monash University, Victoria, Australia; ³Beth Israel Deaconess Medical Center (BIDMC), Harvard Medical School, Boston, Massachusetts

INTRODUCTION
- Current dual combination therapy using anti-platelet; anti-thrombotic; and/or anti-coagulation agents offers the promise of treatment and improved thrombotic protection
- Substantial risk of major bleeding hampers widespread use

METHODS
- Single chain antibody
  - Targeting blocks activated GPIIb/IIIa complex on activated platelets (scFvTarg)
  - Non-binding mutated control (scFvNon-targ)
  - Tick anticoagulant peptide (TAP)
  - Potent direct inhibitor of FXa
  - scFvTarg + TAP = Targ-TAP
  - scFvNon-targ + TAP = Non-targ-TAP

RESULTS

Targ-TAP binds to activated platelets and retains anti-FXa activity after fusion

Targ-TAP prevents thrombosis in vitro

Targ-TAP colocalises with CD42b

Targ-TAP increases time to occlusion without bleeding in vivo

CONCLUSION
- Activated platelet targeted TAP
  - Prevents thrombosis in vitro and in vivo
  - Overcomes bleeding complications
  - Enables prophylactic strategy to be employed

xiaowei.wang@baker.edu.au