

# Activated Platelets as Promising Imaging Tool

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Cardiovascular disease remains the main cause of death worldwide. Novel diagnostics are urgently needed to identify patients at risks. Progress in diagnostic imaging is driven by the application of antibodies for molecular and functional imaging using various modalities. Nanomedicine plays an increasing role in the development of antibody diagnostics because of the potential for increased payload of contrast agents and imaging tracers.

Platelets are cell fragments derived from megakaryocytes and play a major role in haemostasis, thrombosis and inflammation. Targeting the platelet integrin receptor  $\alpha\text{IIb}\beta\text{3}$  is well established in clinical practice however all approved agents bind to the receptor regardless of the activation state thereby visualising all platelets in circulation.

We have previously generated confirmation-specific single-chain antibodies (scFvs) against  $\alpha\text{IIb}\beta\text{3}$  that exclusively bind to activated platelets. These scFvs are not only targeting an epitope that is specific for platelets but also to the activated form of the  $\alpha\text{IIb}\beta\text{3}$  receptor thereby providing unprecedented specificity. This allows the development of diagnostic approaches for the detection of thrombosis or emboli as well as many inflammatory processes in which platelets are involved such as atherosclerotic plaque instability and ischemia reperfusion injury.

To enable clinical translation, we have pioneered universal bioconjugation approaches to couple various tracers and nanoparticles to these scFvs. These include genetic, biological (e.g. sortase coupling) and chemical (e.g. click chemistry) approaches. The coupled products include effector molecules and imaging reagents for molecular imaging using PET/CT system.

In conclusion, radiolabelled scFv holds great promise to provide major advances in various fields of diagnostic imaging and might open a new area in combination with therapeutics in personalised *theranostic* approaches.

## Acknowledgements

This work has been supported by the Australian National Health and Medical Research Council, Australian Research Council and National Heart Foundation