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Area of research

Regulation of platelet signalling and activation.

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Summary

How does platelet stimulation by a variety of agonists lead to activation and platelet aggregation? We are interested in elucidating the signalling pathways that are involved in platelet activation, in particular those that may play a role in platelet hyperactivity in conditions such as obesity and diabetes. Platelets are able to respond to a wide range of agonists and when activated at the site of injury they rapidly aggregate to form a platelet haemostatic plug. Increased or inappropriate platelet activation, however, will lead to thrombosis and vascular complications. Risk factors such as obesity and some genetic factors lead to a resistance to insulin, which is the major underlying cause of type II, adult-onset diabetes, the most common type of diabetes. Type II diabetes is associated with an increased risk of cardiovascular complications, which is the main cause of morbidity and mortality in these patients. There is substantial evidence for platelet hyperactivity in patients with diabetes, which is thought to play a contributory role in diabetic heart disease. Although, the pathogenesis of diabetic cardiovascular disease is not yet fully understood, it is likely to involve the clustering of certain risk factors, often called the insulin resistance syndrome, which is associated with type II diabetes. In our lab, we are interested in investigating the contribution of these risk factors to making platelets hyper responsive.

Activities / Findings

- mTORC2-dependent phosphorylation of S473 is not required to activate Akt1 in human platelets. [Read more >](#)

Memberships

Organisations

[School of Physiology, Pharmacology & Neuroscience](#)

[Bristol Heart Institute](#)

Other sites

- [Bhi](#)

Research Areas

- [Signalling in platelets](#)

Links

-  [Bristol Platelet Group](#)

Selected publications

- Moore, SF, Williams, CM, Brown, E, Blair, TA, Harper, MT, Coward, RJ, Poole, AW & Hers, I, 2015, '[Loss of the insulin receptor in murine megakaryocytes/platelets causes thrombocytosis and alterations in IGF signalling](#)'. *Cardiovascular Research*.
- Moore, SF, Hunter, RW & Hers, I, 2014, '[Protein kinase C and P2Y12 take center stage in thrombin-mediated activation of mammalian target of rapamycin complex 1 in human platelets](#)'. *Journal of Thrombosis and Haemostasis*, vol 12., pp. 748-60
- van den Bosch, MTJ, Poole, AW & Hers, I, 2014, '[Cytohesin-2 phosphorylation by protein kinase C relieves the constitutive suppression of platelet dense granule secretion by ADP-ribosylation factor 6](#)'. *Journal of Thrombosis and Haemostasis*, vol 12., pp. 726-35
- Moore, SF, Hunter, RW, Harper, MT, Savage, JS, Siddiq, S, Westbury, SK, Poole, AW, Mumford, AD & Hers, I, 2013, '[Dysfunction of the PI3 kinase/Rap1/integrin \$\alpha\$ IIb \$\beta\$ 3 pathway underlies ex vivo platelet hypoactivity in essential thrombocythemia](#)'. *Blood*, vol 121., pp. 1209-19
- Moore, SF, van den Bosch, MTJ, Hunter, RW, Sakamoto, K, Poole, AW & Hers, I, 2013, '[Dual Regulation of Glycogen Synthase Kinase 3 \(GSK3\) \$\alpha\$ /beta by Protein Kinase C \(PKC\) \$\alpha\$ and Akt Promotes Thrombin-mediated Integrin \$\alpha\$ \(IIb\) \$\beta\$ \(3\) Activation and Granule Secretion in Platelets](#)'. *Journal of Biological Chemistry*, vol 288., pp. 3918-3928

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Recent publications

- Moore, S, Smith, NR, Blair, TA, Durrant, TN & Hers, I, 2019, '[Critical roles for the phosphatidylinositide 3-kinase isoforms p110 \$\beta\$ and p110 \$\gamma\$ in thrombopoietin-mediated priming of platelet function](#)'. *Scientific Reports*, vol 9.
- Blair, TA, Moore, SF, Walsh, TG, Hutchinson, JL, Durrant, TN, Anderson, KE, Poole, AW & Hers, I, 2018, '[Phosphoinositide 3-kinase p110 \$\alpha\$ negatively regulates thrombopoietin-mediated platelet activation and thrombus formation](#)'. *Cellular Signalling*, vol 50., pp. 111-120
- Agbani, E, Williams, C, Li, Y, van den Bosch, M, Moore, S, Mauroux, A, Hodgson, L, Verkman, AS, Hers, I & Poole, A, 2018, '[Aquaporin-1 Regulates Platelet Procoagulant Membrane Dynamics and In Vivo Thrombosis](#)'. *JCI Insight*, vol 3.
- Battram, A, Durrant, T, Agbani, E, Heesom, K, Paul, DS, Piatt, R, Poole, A, Cullen, P, Bergmeier, W, Moore, S & Hers, I, 2017, '[The Phosphatidylinositol 3,4,5-trisphosphate \(PI\(3,4,5\)P3\)-binder Rasa3 Regulates Phosphoinositide 3-kinase \(PI 3-kinase\)-dependent Integrin \$\alpha\$ IIb \$\beta\$ 3 Outside-in Signaling](#)'. *Journal of Biological Chemistry*, vol 292., pp. 1691-1704
- Agbani, E, Williams, C, Hers, I & Poole, A, 2017, '[Membrane Ballooning in Aggregated Platelets is Synchronised and Mediates a Surge in Microvesiculation: Synchronised ballooning and microvesiculation](#)'. *Scientific Reports*, vol 7.

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