What is this research about?
Platelets are normally thought to be the primary cellular mediators of hemostasis and can encounter a variety of inflammatory processes. For years, however, data has been accumulating that platelets may not only be exposed to inflammation but may also work to mediate it directly. For example, platelets contain and secrete several biological mediators that have no obvious role in hemostasis but significantly affect local innate immune responses by, for example, attracting neutrophils to sites of inflammation. In addition, platelets may directly regulate adaptive humoral immune responses by the expression and secretion of molecules such as CD40/CD40L. Platelets also avidly bind to microorganisms by expressing Toll-like receptors (TLR). It appears now that platelets may act as circulating sentinel cells that encounter blood borne infectious products for presentation and activation of innate immune responses.

What did the researchers do?
Toll-like receptors (TLR) are molecules primarily expressed on innate immune cells such as dendritic cells and are critical for the host to recognize infectious microorganisms. In 2004, Dr. Semple's laboratory discovered that mouse platelets express TLR and went on to show expression of TLR on human platelets. There followed an intense race to understand why clotting cell like platelets would express some of the most important immune molecules known. In 2006, Semple’s group and Dr. Kubes’ group in Calgary published papers within months of each other. These papers showed that platelet expression of TLR4 was responsible for gram negative (LPS)-induced thrombocytopenia, a condition that is commonly observed in septic patients in the ICU. Since then, over 100 papers have been published showing a) that platelet TLR expression allows platelets to interact with a wide variety of cells during infections; and b) that these interactions allow the platelet to directly activate or suppress inflammatory responses.

What did the researchers find?
The work on platelet TLR has implications for a number of clinical conditions affected by infections and also has implications for platelet products, particularly, those that may have bacterial contamination. On the one hand, beneficially, platelets have been shown to have potent anti-bacterial effects via TLR/bacterial binding and the secretion of potent bactericidal agents like thrombocidins that kill bacteria. However, some bacteria may bind to platelet via TLR interactions and perhaps mask bacteria from detection and/or promote bacterial growth. In addition, bacterial activation of platelets may increase the risk of thrombotic events in vivo.

How can you use this research?

In brief...
Platelets appear to bind foreign microorganisms circulating in the blood to trigger an immune response.
Further work is required to understand how platelets interact with infectious agents and either inhibit or promote bacterial growth. In addition, the role of platelets in modulating immunity is an active avenue of research as we may be able to develop novel platelet-derived therapies to prevent unwanted inflammatory adverse reactions.

About the research lead author: Dr. John Semple is a Senior Scientist and Head of Transfusion Medicine Research at the Keenan Research Centre of the Li Ka Shing Knowledge Institute at St Michael’s Hospital, Toronto, Canada. He is also a Professor in the Departments of Pharmacology, Medicine and Laboratory Medicine and Pathobiology at the University of Toronto and an Adjunct Scientist with Canadian Blood Services. His research interests include, among others, animal models of platelet autoimmunity related to ITP, platelet-bacteria interactions and Transfusion Related Acute Lung Injury (TRALI).

This Research Unit is derived from the following publications:

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