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Making mountains out of molehills: how stem cells become platelets

You have 100,000 km of plumbing (blood vessels) in your body. What then keeps them from leaking? This essential work is carried out by tiny cells called platelets, which are able to form a plug to stop bleeding after blood vessel damage.

Platelets have a volume 10 times smaller than a red blood cell, curiously they are produced from giant cells called megakaryocytes (MKs). These MKs are generated from haematopoietic (blood) stem cells (HSCs) in the bone marrow and in the lungs. In fact, HSCs give rise to all the different cellular components of blood such as white and red blood cells. For the HSCs to produce MKs and platelets the activity of a specific protein called thrombopoietin or TPO is needed. TPO sends a signal through a particular receptor on the cell surface and this triggers changes that push the cells to become MKs and platelets rather than, say, red or white blood cells.

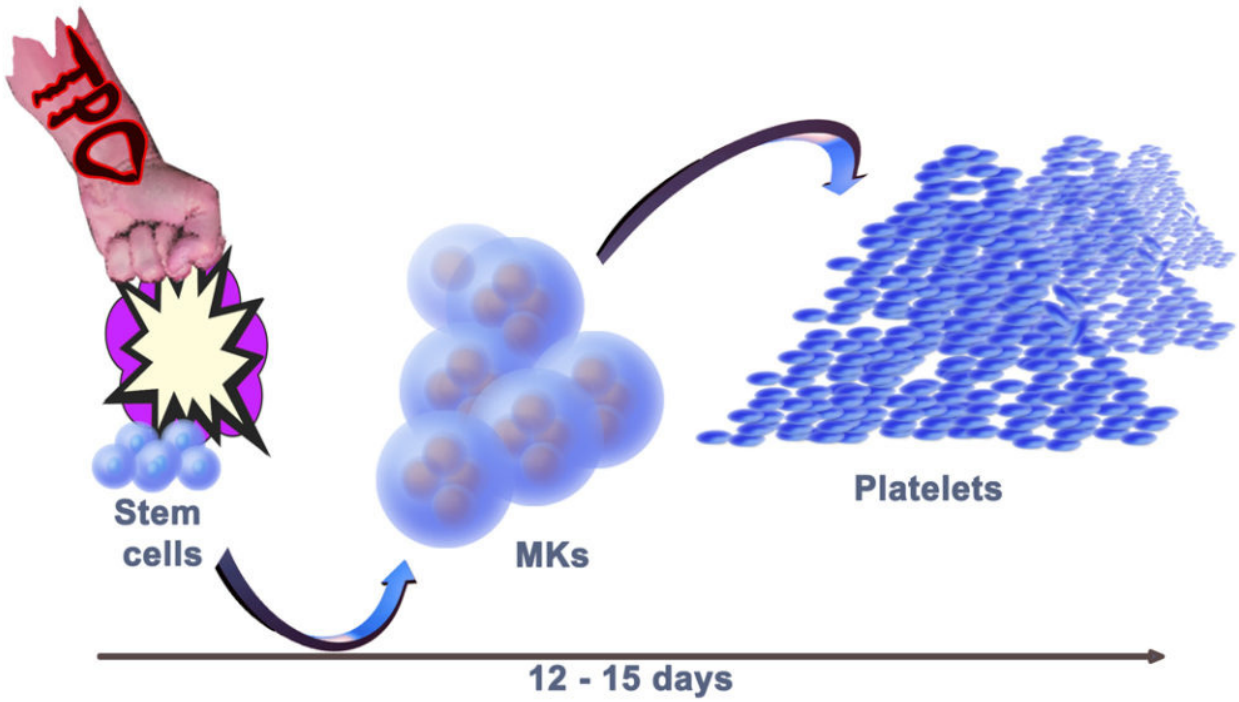

Fig. 1. Heamatopoietic stem cells purified from cord blood or bone marrow samples are stimulated by thrombopoietin (TPO) in culture to differentiate into mature megakaryocytes (MKs). Mks then release functional platelets into the culture medium. Each stem cell can generate up to 420 platelets.

There are diseases, known as thrombocytopenias, characterized by abnormally low platelet numbers in the circulation. The reasons that lead to these diseases are varied, and include immunological problems, genetic conditions, certain medications, infections, cancer and blood transfusions. Low platelet counts can cause internal bleeding (eg, in the intestines or the brain) and in severe cases result in death. Treatment for thrombocytopenia depends on the cause, the status of the patient and other specific needs. One of these

treatments is platelet transfusion, using platelets isolated from blood donors. This treatment is effective in the short term, however many patients become refractory to platelet transfusion and this is a serious clinical issue. This happens, for instance, in patients that need ongoing transfusions due to thrombocytopenia induced by chemotherapy. Many of these patients develop antibodies that destroy the transfused platelets and the patients remain in danger of serious bleeding. Finding compatible or matching platelets is not always feasible.

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Publication

Megakaryocyte Differentiation and Platelet Formation from Human Cord Blood-derived CD34+ Cells.
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