Engineered platelets could meet demand and mend a broken heart

Platelets are the workhorses for haemostasis. They are activated during vessel injury to form a haemostatic plug and release a myriad of granules – essential to the process of clotting and facilitating tissue repair.

In clinical instances such as major trauma or leukaemia, platelets must be transfused and the NHS relies on blood donations from the public to fulfil this need. Unfortunately, demand can often outstrip supply. Additionally, donor platelets can arouse the vigilant immune system of the recipient to attack these ‘foreign’ platelets, leading to life-threatening bleeding complications.

Dr Cedric Ghevaert, A BHF-funded scientist and consultant haematologist at Addenbrooke’s hospital, has managed to overcome these obstacles and produce immunologically inert platelets using stem cells.

Pluripotent stem cells – which have endless differentiating potential – have been engineered by Dr Ghevaert to become the platelet-producing mother cells megakaryocytes. He and his group have used a technique known as gene editing to remove and manipulate any genes that may provoke the immune system, thereby engineering a megakaryocyte that secretes platelets which can go undetected by the immune system. Furthermore, his platelets are engineered to release Factor VII (FVII), a potent coagulant protein. Currently, it can be given synthetically (NovoSeven), but usually has to be given in high amounts to patients which leads to the risk of emboli development and subsequent stroke or myocardial infarction (MI). Dr Ghevaert’s engineered megakaryocytes and platelets have addressed this with gene editing. He and his lab have been able to produce platelets that contain therapeutic levels of specific clotting factors, including FVII, which can be released at the site of a wound without the risk of aberrant clotting.

Dr Ghevaert has formed a collaboration with Dr Kourosh Saeb-Parsy, a consultant transplant surgeon at Addenbrooke’s hospital, in an effort to prove that the engineered platelets are non-immunogenic in mouse transfusion models.

In an effort to promote the production of platelets from magakaryocytes, Dr Ghevaert is collaborating with Drs Ruth Cameron and Serena Best in the department of Material Science to manufacture a collagen ‘sponge’. The porous structure effectively traps the megakaryocytes to a desired site and allow the effective release of the platelets into a collection bag.

The function of platelets as a delivery system is also something Dr Ghevaert is currently exploring to help treat damaged heart muscle. His group are engineering megakaryocytes and platelets through gene editing to carry and release specific growth factors: proteins that would promote the repair of injured heart tissue following a MI. “The idea here is that the platelets provide an energy boost to the cells to promote repair” explains Dr Ghevaert. “A bit like giving builders some strong tea; it will help them work better and faster”. To test this analogy, Dr Ghevaert is in collaboration with Dr Thomas Krieg at the Cambridge Cardiovascular network, using a mouse model of MI. They are currently delivering these bespoke platelets to see if they will target and help improve repair of infarcted heart muscle.

The results so far show great promise and Dr Ghevaert believes that these bespoke platelets will be trialled in humans soon: “We are currently working on translating gene editing of blood cells at a clinical grade: making them suitable for human trials in the next 3-4 years”. It appears that genetically modified platelets may not only be readily available to stop bleeding, they could also mend a broken heart.

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