What is this research about?
Canadian Blood Services’ researchers have been exploring new ways to fool the immune system. Why? The hope is to provide blood to patients for whom a match cannot be found.

Blood cells, like all other cells and tissues, have proteins and sugars on their surface that can act as antigens. Antigens help the immune system distinguish “self” from “foreign.” Encountering antigens not found on the body’s own cells signals the immune system to produce antibodies against the antigen and attack the cells.

Blood type is based on antigens on the surface of red blood cells. There are two major blood group systems: ABO (blood types A, B, AB and O) and Rh (positive or negative). These are important in transfusion and recipients are given compatible products based on their ABO and Rh blood type. If incompatible blood is transfused, the immune reaction can destroy the transfused cells and the recipient can become very ill. ABO and Rh are not the only red blood cell antigen groups. In fact, over 30 other blood groups systems have been identified so far. Patients who receive many transfusions can become sensitive to other red blood cell antigens (called alloimmunization). These patients need a closer match than just ABO positive or negative and finding matching blood can be a challenge. An alternative solution for these patients is to fool the immune system by masking or immunocamouflaging non-ABO red blood cell antigens so that they cannot be detected.

What did the researchers do?
Polyethylene glycol (PEG) is a polymer that has been safely used for over 30 years in a variety of drugs and therapies. For example, it is used to prolong the action of small protein-based medicines and is being investigated for many other medical uses. One of these novel uses is to mask antigens on cells and tissues so they are not detected by the immune system. This immunocamouflage masks antigens without affecting the function of red blood cells or their survival in the body, as shown in an animal model. In this study, the researchers compared PEG to an alternative polymer called PEOZ. Although PEG is widely used, a small number of studies have indicated a potential for patient reactions with PEG. PEOZ is believed to be less likely to cause patient reactions. The researchers looked at the shape and function of red blood cells coated with PEG or PEOZ to see if there were any changes. How well the polymers could prevent recognition of red blood cells by the immune system was also tested.

What did the researchers find?
PEOZ and PEG have different structures, but in many other ways they are similar. Both are quite simple polymers, they are cheap, easy to make and safe, with low toxicity. Overall, not many differences in the function of red blood cells coated with either PEG or PEOZ were seen. One of the few differences was in a measure called morphology, which describes red blood cell shape. A change in the shape of red blood cells can be a sign that the cells are damaged. PEOZ had less effect on red blood cell shape than PEG, suggesting that PEOZ may cause less damage to red blood cells. Both polymers had a similar ability to mask red blood cell antigens.
The researchers then tested how well PEOZ- and PEG-treated red blood cells could escape detection by the immune system. To do this they used a laboratory-based test to see if the immune system would react to the red blood cells after a transfusion. This test showed that PEG is better at camouflaging red blood cells than PEOZ. When red blood cells were coated with PEG they were not recognized by the immune system. When coated with PEOZ, the red blood cells were more likely to be recognized by the immune system. However, using PEOZ may still be suitable for patients who are sensitive to PEG. This study also allowed the researchers to better understand how PEG and PEOZ work to camouflage red blood cells. They discovered that mixing red blood cells with these polymers masks red blood cells directly by binding to specific antigens, but also indirectly, providing general camouflage for the cell surface.

How can you use this research?
For the majority of patients who need a transfusion, compatible blood can be found. However, for patients who have chronic illnesses and need continuous transfusion therapy, it can become very difficult to find compatible blood. If the donor and recipient have the same ethnic background a match is more likely. Therefore, blood banks around the world often work together to try to get the right blood to patients who desperately need it. Still, matches cannot always be found. Immunocamouflage is a potential solution to this issue. With immunocamouflage, incompatible blood can be transformed into compatible blood, and the immune system can be tricked. This technique is still at the testing stage in the laboratory, and has yet to be used in a patient. However, its potential for compassionate use in cases where a patient’s need is dire and a match cannot be found has been recognized by Health Canada. Continuing research into immunocamouflage of red blood cells and other cells and tissues will help understand and develop the many potential applications of this approach in transfusion and transplantation medicine.

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