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Genetic trail to Blood type

A long standing mystery of a rare blood type has been solved, says S.Ananthanarayanan.

That people who need blood, because of blood loss or for surgery, need the right kind of blood, was discovered only in 1901. Till then, blood transfusion sometimes helped patients recover, but often led to their death because their body rejected the blood they received and created serious illness. But after the discovery that all people fell into just four categories of blood type, the right blood type has been used and transfusion has saved countless lives.

In addition to these four blood groups, there are many other features that need to match, These are significant only in rare cases but persons who are affected need to find donors who have the same feature, or they need to store their own blood for planned surgery or emergencies. One such rare type, which was discovered in 1952, could not be identified by testing a blood sample – and a patient could no know she needed this type, and donors could not be identified for blood banks to stock this type of blood. The journal, ***EMBO Molecular Medicine*** , carries a report by ***Bryan Ballif*** of the University of Vermont and ***Lionel Arnaud*** of the French National Institute of Blood Transfusion, and their colleagues, that they have cracked the secret of this elusive and rare blood type, which would help those who need it know that they need it and also help identify donors.

Blood groups

Blood groups arise from surface features, called ***antigens***, of red blood corpuscles. The immune system in the body develops defenses, called ***antibodies,*** against alien substances, but not against its own blood cells, whose surface features it recognizes. The most important of these features lead to all blood falling into one of four groups, ***A, B, AB and O***. Blood of group A and group B have different features, while blood of group AB has both the features but blood of group O has no feature. Thus, persons with blood of group A, B or O need only that kind of blood, but persons of group AB can receive blood of both A and B and also of group O, which is not affected by any antibody. And blood of group O can be accepted by any person, as there are no surface features to invite attack.

Group		RECIPIENTS			
		A	B	AB	O
DONORS	A	Match	Clash	Match	Clash
	B	Clash	Match	Match	Clash
	AB	Clash	Clash	Match	Clash
	O	Match	Match	Match	Match

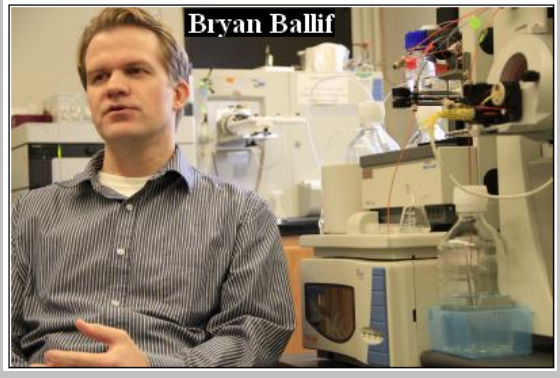
In addition to the blood group, there is a factor called the RH factor, which can be positive or negative. Persons who are **RH+ve** can receive **RH–ve** blood but not the other way. Persons with group A, B or O, with **RH–ve** thus need specific type of blood while persons with **A+ ve** can receive any blood. And blood of type **O–ve** is good for anybody.

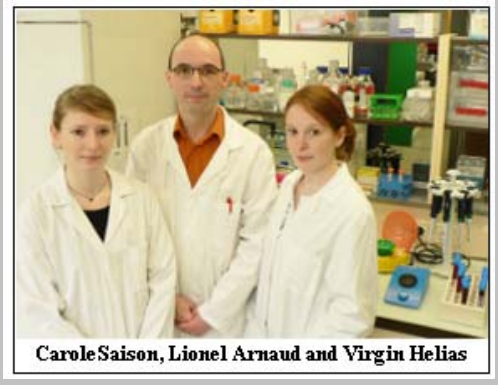
And there are further factors, there are 32 in all, that also need to match, but these are rare. Many of these factors also tend to occur in specific racial communities, for example, the **U-ve type** is found only with persons of African descent, while **Vel-ve** and **Lan-ve** is found only in light skinned races. As blood needs to be tested for these factors also, knowing a donor's race could save time while blood matching for a rate type, in an emergency.

Vel Negative

One such rare feature is the Vel negative – so named after the patient, a 66 year old lady patient of colon cancer, who was first discovered to have this kind of blood, in 1962. Reporting on her case, the French medical journal ***Revue D'Hématologie*** identified her as, simply, "Patient Vel." After a previous transfusion, Mrs. Vel had developed a potent antibody against some unknown molecule found on the red blood cells of most people in the world—but not found on her own red blood cells. What this compound has defied identification and from this case, a new blood type – ***'Vel negative'*** was named. Soon it was soon found that there were more similar cases, though rare, and it is estimated that about 1 in 2,500 persons in Europe or North America are Vel negative.

But for 60 years now, what molecular feature identifies this blood type has eluded detection. As a result, there is no systematic method to identify a person who is Vel negative - it turns out to be the case only when she repeatedly shows adverse reaction to transfusion. As the blood type is rare, and also difficult to detect, many patients succumb to transfusion in emergencies and even in the case of known Vel negative patients, it is difficult to identify blood donors or to create stocks of Vel negative blood products.




Carole Saison, Lionel Arnaud and Virgin Helias

The discovery of Ballif and Arnaud and their collaborators has put an end to the difficulty to detect Vel negative. Arnaud and coworkers in Paris first collected stocks of the rare Vel-negative antibody and used biochemical methods to partly isolate the mystery protein from the surface of human red blood cells. The work continued under Ballif in the

University of Vermont. Ballif and colleagues used facilities funded by the Vermont Genetic Network – a high resolution instrument that separates charged atomic or molecular fragments, to zero in on the mystery protein. “I had to fish through thousands of proteins,” Ballif says. The protein found is very small, as proteins go, and arises out of small part of the person’s DNA, and has been named ‘***Small Integral Membrane Protein, or SIMM 1***’. Next, Arnaud’s team in France tested seventy people known to be Vel-negative. In every case, they found a deletion—a tiny missing chunk of DNA—in the gene that instructs cells on how to manufacture SMIM1. This was the proof the scientists needed to show that the Vel-negative blood type is caused by a lack of the SMIM1 protein on a patient’s red blood cells.

The discovery of what causes certain people to be Vel negative provides us with a simple, DNA assay test for the blood type. "Identifying and making available rare blood types such as Vel-negative blood brings us closer to a goal of personalized medicine," says Ballif. “Even if you are that rare one person out of 2,500 that is Vel-negative, we now know how to rapidly type your blood and find blood for you—should you need a transfusion.”