

## Blood groups and rabbit control?

Stiffen the sinews, summon up the blood

William Shakespeare, *King Henry V*, Act 3

While researchers in Australia and New Zealand were largely preoccupied with unravelling the field epidemiology of rabbit haemorrhagic disease and the benefits of having fewer rabbits, work was under way in Europe to find out more about the interactions between the virus and rabbits.

As previously described, Professor Luis Leon-Vizcaino in Murcia in south-eastern Spain was well aware that the virus causing *la enfermedad hemorrágica virica* made his red blood cells clump together when tiny volumes of them were carefully mixed in ELISA plate wells with serum from infected rabbits. Indeed, that understanding had been enough to design simple tests to detect virus in rabbit tissues and to measure the antibodies in rabbits that survived RHDV infection. However, it was French researchers in Nantes led by Dr Jacques Le Pendu who looked more closely into the matter and asked why this was so. Dr Nathalie Ruvoën-Clouet, a member of Le Pendu's team, soon came up with an explanation. She showed that RHDV attached to histo-blood group antigens or HBGAs and that, in rabbits, these antigens are located on the surface of cells that line the intestine and respiratory tract (Ruvoën-Clouet *et al.* 2000). Attaching to HBGAs helps the virus to enter the rabbit, in what is very much the first step of many. Other unique parts of the virus coat are needed to allow the virus to finally attach to the rabbit's liver cells and gain entry.

Most people would be familiar with the equivalent HBGAs in humans. They occur on our red blood cells and define our blood group as A, B or O, and they must be carefully considered for any incompatibility before transfusions are given. There is enough similarity between human HBGAs and virus binding sites in rabbits for the virus particles in the laboratory test to act almost like a weak glue to bring carefully prepared human blood cells together and cause them to clump.

With this new information, two riddles were apparently solved. Not only was there an explanation as to why human blood cells proved useful in initial tests for RHDV but there was also an understanding that the virus attached to the surface of rabbit mucosal cells in what appeared to be an important first step in the infection process.

Histo-blood group antigens are proteins with three sugar molecules attached to one end, forming what is called a trisaccharide terminal. RHDV binds to one of these sugars and this helps it adhere to cells on the rabbit's intestinal wall. In young rabbits, the protein precursors of the antigens are present in the tissues but they are few, and it takes time for them to mature and gain their full complement of sugars or become 'fully glycosylated'. This was once thought to partly explain why young rabbits are less prone to acute RHDV infection than older