New research on inherited herpesvirus may have implications for transplantation

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Up to half a million people in Britain today may not know it, but in their genetic material they carry a particular form of herpesvirus 6 inherited from a parent.

The study from the world-renowned Department of Genetics at the University of Leicester, is funded principally by the Medical Research Council (MRC), and published in the journal *Nucleic Acids Research*.

The research led by Dr Nicola Royle, Senior Lecturer in Genetics, has identified a mechanism by which the inherited herpesvirus 6 can escape from the chromosome and may be able to reactivate under certain conditions.

This research may have important implications for transplantation, as those seeking transplants are often immunosuppressed, and are more susceptible to viral reactivation. The implications of the study suggested screening donors for this inherited form of HHV-6 could help doctors make more informed decisions about which donors to use.

The research in Dr Royle's laboratory focuses on telomeres, structures at the ends of chromosomes that have a protective role. When a telomere becomes short or is damaged it can trigger cellular senescence or result in genetic changes; consequently telomeres have roles in ageing and cancer. The inherited herpesvirus 6 (CI-HHV-6) is found in a telomere and so the questions Dr Royle has been addressing are: what is the virus doing there and does it affect telomere function?

There are many human herpesviruses and most can enter latency following infection, during which they persist in a small subset of cells lifelong. For example, the primary infection of HHV-3 causes chickenpox in children but following latency it can reactivate and cause shingles.

The 1% of us that inherit CI-HHV-6 in a telomere have a high copy number of this virus (one copy per cell of the whole body) but it is not known if this is a form of latency.

The Leicester study found that in people with CI-HHV-6, the viral genome is intact (has all of the genes required to reactivate). They showed that the telomere with the virus is unstable - prone to sudden deletions resulting in a very short telomere that may cause further instability. This facilitates release of the viral genome. Dr Royle proposes that the virus uses normal telomere processes to escape from the chromosome and that this may represents the first step towards viral reactivation.

Dr Royle said the research may have important implications in a transplant setting because those seeking transplants are immunosuppressed, in order to stop their bodies rejecting the donor's organ. If the donor is one of the half a million people with CI-HHV-6 there may be a risk to the organ recipient or an impact on the transplanted organ, either through viral reactivation or through the effect on the telomere. Until further research is conducted to determine whether or not there is an increased risk, it may be prudent to screen organ donors for the inherited form of HHV-6.

Future research in Dr Royle's laboratory will seek to determine how often the HHV-6 escapes from the telomere and what controls this. Researchers also seek to understand how telomere shortening due to age could influence the rate of HHV-6 release from the chromosome. It is

predicted that this could increase the risk reactivation.

Provided by University of Leicester