Hepatitis C 'switch' offers target for new drug research

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Scientists have discovered a 'switch' in the Hepatitis C virus which could be used as a target for new kinds of drug treatment.

Hepatitis C affects more than 170 million people worldwide, but current combination treatment is only effective against a limited range of this naturally highly variable virus.

However, according to new research by the University of Warwick, the newly discovered SL9266 'switch' is very highly conserved and present in all Hepatitis C viruses, meaning this offers a good starting point for further research into an across-the-board treatment.

This region represents a vulnerable spot for attacking and clearing the virus from the body as it controls a critical event in the earliest stages of the virus lifecycle.

It seems the switch modulates the mutually incompatible translation and replication processes that must occur for the virus to spread inside the body.

University of Warwick scientists at the School of Life Sciences and their collaborators in the Roslin Institute at the University of Edinburgh are now working with chemists to develop custom-designed drugs that target the switch and lock it in the 'off' position.

By locking the virus into a translation-only phase it cannot initiate

replication, a process critical for infecting other cells in the liver.

The immune response to the initially infected cell would contribute to the clearance of the virus from the body.

Despite the variability of the virus, the mechanism and function of this 'switch' is thought to be highly conserved, providing a means of targeting all Hepatitis C viruses.

Professor David Evans of the University of Warwick said: "Hepatitis C is a growing concern worldwide and is set to place a massive demand on the organ transplant system.

"We are already at the stage in many countries where the main need for liver transplants is due to liver damage caused by the Hepatitis C virus.

"Current medication is not effective in all cases, that's why it's vital that we continue to build on this early-stage research to focus drug development work on treatment which works across all Hepatitis C genotypes."

The research, funded by the UK Medical Research Council, is published in the journal *Nucleic Acids Research*.

The study is entitled A twist in the tail: SHAPE mapping of long-range interactions and structural rearrangements of RNA elements involved in HCV replication.

It is co-authored by Andrew Tuplin, Madeleine Struthers and David Evans of the University of Warwick and Peter Simmonds of the Roslin Institute, University of Edinburgh.

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