The 3D model shows how the viral protein piggybacks onto the molecular machinery components inside human cells, promoting virus replication and spread of infection through the body.

"When you look at the image, it's like a backpack on an elephant: the small compact fragment of viral protein fits nicely on the back of the human protein," said Dr Golovanov.

By studying the images along with biochemical experiments using the human version of the cellular protein, the team has uncovered the mechanism by which the viral and cellular proteins work together to guide the viral genetic material out of the cell's nucleus. Once there, the genetic material can be utilised to make proteins that are used as building blocks for new viruses. The researchers have also confirmed that this relationship between the two proteins exists for related herpes viruses that infect monkeys.

Dr Golovanov continued, "Our discovery gives us a whole step more detail on how herpes viruses use the human cell to survive and replicate. This opens up the possibilities for asking new questions about how to prevent or treat the diseases they cause."

Professor Janet Allen, BBSRC Director of Research, said "This new research gives us an important piece of the jigsaw for how a particular viral infection works on a molecular level, which is great news. Understanding the relationship between a human, animal or plant – the host – and the organisms that cause disease – pathogens – is a fundamental step toward successful strategies to minimise the impact of infection. To study host-pathogen relationships we have to look in detail at the smallest scale of molecules – as this study does – and also right through to the largest scale of how diseases work in whole systems – a crop disease in the context of a whole area of agricultural land, for example. BBSRC's broad portfolio of research into host-pathogen relationships facilitates this well."

550 MILLION YEARS AGO RISE IN OXYGEN DROVE EVOLUTION OF ANIMAL LIFE

Researchers funded by the Biotechnology and Biological Sciences Research Council (BBSRC) at the University of Oxford have uncovered a clue that may help to explain why the earliest evidence of complex multicellular animal life appears around 550 million years ago, when atmospheric oxygen levels on the planet rose sharply from 3% to their modern day level of 21%.

The team, led by Professor Chris Schofield, has found that humans share a method of sensing oxygen with the world's simplest known living animal – *Trichoplax adhaerens* – suggesting the method has been around since the first animals emerged around 550 million years ago.

This discovery, published on 17 December in the January 2011 edition of EMBO Reports, throws light on how humans sense oxygen and how oxygen levels drove the very earliest stages of animal evolution.

Professor Schofield said "It's absolutely necessary for any multicellular organism to have a sufficient supply of oxygen to almost every cell and so the atmospheric rise in oxygen made it possible for multicellular organisms to exist.

"But there was still a very different physiological challenge for these organisms than for the more evolutionarily ancient single-celled organisms such as bacteria. Being multicelluar means oxygen has to get to cells not on the surface of the organism. We think this is what drove the ancestors of *Trichoplax adhaerens* to develop a system to sense a lack of oxygen in any cell and then do something about it."

The oxygen sensing process enables animals to survive better at low oxygen levels, or 'hypoxia'. In humans this system responds to hypoxia, such as is caused by high altitudes or physical exertion, and is very important for the prevention of stroke and heart attacks as well as some types of cancer.

Trichoplax adhaerens is a tiny seawater organism that lacks any organs and has only five types of cells, giving it the appearance of an amoeba. By analysing how *Trichoplax* reacts to a lack of oxygen, Oxford researcher Dr Christoph Loenarz found that it uses the same mechanism as humans – in fact, when the key enzyme from Trichoplax was put it in a human cell, it worked just as well as the human enzyme usually would.

They also looked at the genomes of several other species and found that this mechanism is present in multi-cellular animals, but not in the single-celled organisms that were the precursors of animals, suggesting that the mechanism evolved at the same time as the earliest multicellular animals.

Defects in the most important human oxygen sensing enzyme can cause polycythemia – an increase in red blood cells. The work could also open up new approaches to develop therapies for this disorder.

Professor Douglas Kell, Chief Executive, BBSRC said "Understanding how animals – and ultimately humans – evolved is essential to our ability to pick apart the workings of our cells. Knowledge of normal biological processes underpins new developments that can improve quality of life for everyone. The more skilful we become in studying the evolution of some of our most essential cell biology, the better our chances of ensuring long term health and well being to match the increase in average lifespan in the UK and beyond."