HIV's origin

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How the virus passed to humans

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HIV, the virus that causes AIDS, a disease that has killed some 25m people in the past quarter century, may be one of the most thoroughly investigated viruses ever. But there is still some uncertainty about its origin. Most researchers think it was passed from animals to humans in central Africa. But understanding more about how humans picked up the virus may possibly help in the search for effective treatment.

Those who are trying to discover more about the origin of HIV in humans tend to go looking in the forests in central Africa. Researchers may get up at dawn hoping to grab chimpanzee faeces that fall from the trees. Antibodies in such excrement have suggested that the virus jumped into humans from a Cameroonian population of chimps early in the last century. The virus probably made the leap at least twice more since. A separate group of chimps in Cameroon has infected a handful of locals with a nonpandemic version of HIV. Waste from wild gorillas suggests they are probably responsible for a third form of the virus.

An alternative strategy to poking around in the jungle is to ask why humans are susceptible to HIV in the first place. This approach may now be providing some useful answers. In a paper published in *Science* on Friday June 22nd, Michael Emerman of the Fred Hutchinson Cancer Research Centre, in Seattle, describes how he and his colleagues looked at a different virus (known by the catchy name, PtERV1) which was active about a million years after human lineage parted from the chimp one. It appears that ancient hominids successfully evolved immunity to that virus, but in doing so were somehow left defenceless against HIV.

To show this, Dr Emerman considered the details of a particular immune-system protein. All primates make "TRIM5alpha", which protects them from viruses in the same broad category as HIV. But each species makes a slightly altered version, making them immune to different combinations of such viruses. The type that rhesus macaques produce, for example, confers complete resistance to HIV; the sort made by baboons slows that virus's replication by 50-fold.

Dr Emerman first proved that the particular protein made by all humans causes them to be resistant to PtERV1. That makes sense because chimpanzee and gorilla genomes are littered with broken copies of this virus, yet the human genome is free of it. Demonstrating the fact, however, was difficult because the PtERV1 virus is long-extinct. Researchers had to pick through hundreds of different mutated versions of the virus genome found in chimp and gorilla DNA to work out what the intact virus genome probably would have looked like. Then they put part of that genome into a virus capable of reproducing only once, and used it to try to infect some cells. Cells with the particular human protein shrugged off this threat, but those without it were infected.

But Dr Emerman also stumbled upon a less obvious finding. He thought that by changing a critical patch of human TRIM5alpha protein, so that it was like the version made by early humans, he would render it ineffective against PtERV1. That all went to plan. But the same change also made human protein protective against HIV. As it turned out, every primate TRIM5alpha protein that he tested worked against either PtERV1 or HIV (or neither)—but never against both. Thus by evolving a defence against PtERV1, early humans left themselves wide open to the HIV pandemic 4m years later.

This finding will not lead directly to any new treatment for HIV. But it gives researchers another avenue to explore. So far they have concentrated on getting drugs to tackle enzymes that are needed for the replication of HIV. But as HIV grows increasingly resistant to those drugs new medicines may, just possibly, be created by turning this particular human protein into something more like that produced by monkeys. That could potentially be achieved for a wealthy few using an unproven technology called gene therapy. More practically, a molecule that either mimics the monkey protein, or that binds the monkey sort to the human protein, and so makes it able to recognise HIV, could show the way to future teatments.