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World's first study of bionic 'assassins' to wipe out HIV

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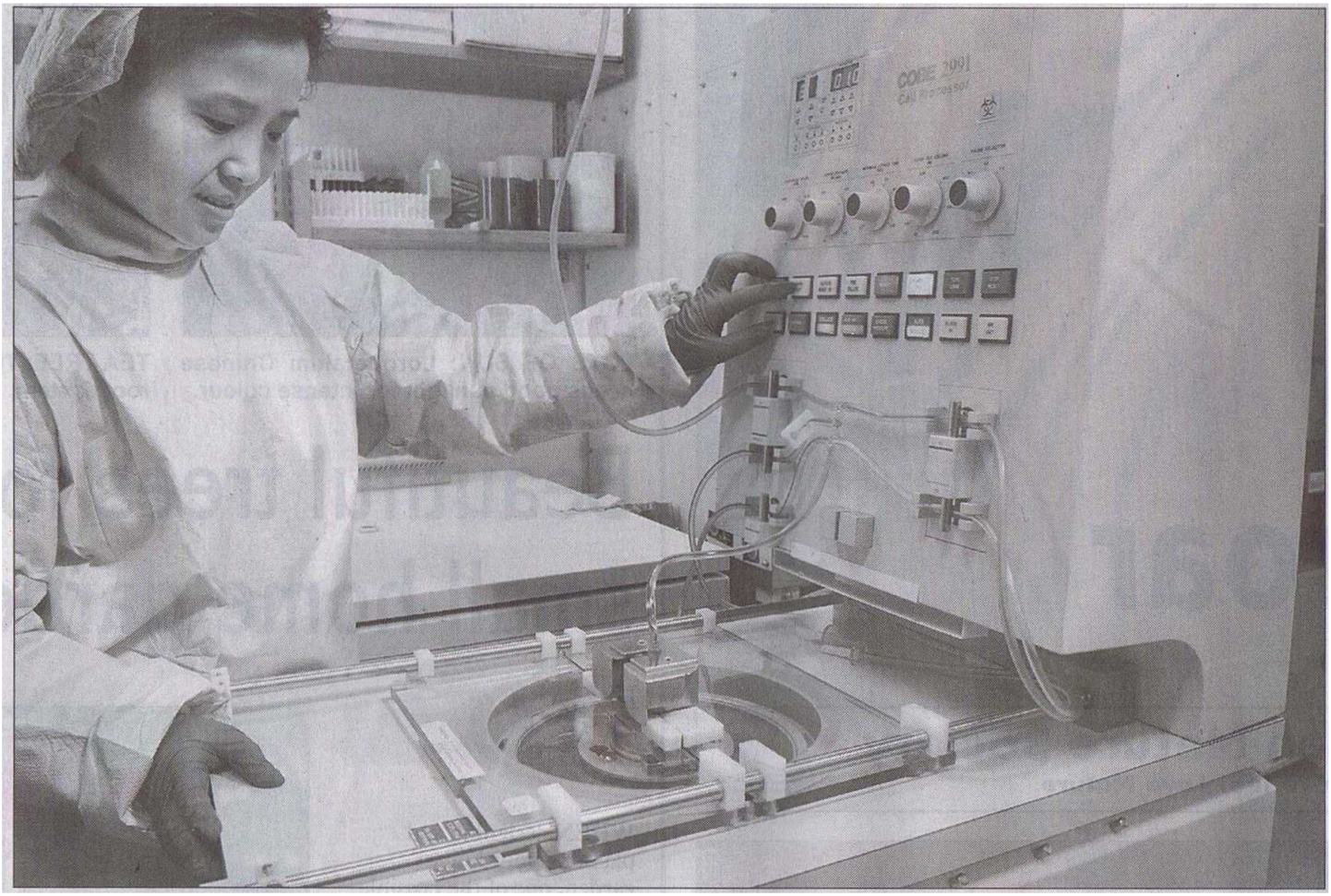
— Dr Bent Jakobsen, Adaptimmune's chief scientific officer



IMPROVING A 'KILLER': Scientists at Oxford University spin-out company Adaptimmune are working to improve the protective ability of "killer" T-cells to recognise infected cells, especially in people with HIV. – LPS photo courtesy of Adaptimmune UK

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LONDON: A great step forward has been taken to treat HIV infection. A company that can engineer immune cells to see through HIV's many disguises and act as "bionic assassins" is taking this technology from the laboratory into clinical trials with HIV patients.

The HIV pandemic has become one of the most serious challenges to human health. There is no cure and more than 33 million people are now living with the human immunodeficiency virus, rising by about another million every year.

This is the world's first study using patients' cells carrying an engineered T-cell receptor to treat HIV. Researchers at Oxford University spin-out company Adaptimmune seek to increase the power of the T-cell receptor on our T-cells, a type of blood cell that protects the body from infection, usually able to kill any attacking germs.

The mission is to take "adoptive T-cell therapy" to the next level by engineering T-cell receptor proteins that recognise cancerous or infected cells,as a means of "supercharging" the strength of patients' own T-cell defence responses.

Adaptimmune's clinical trials with its US partner, the highly respected University of Pennsylvania, could have important implications in the development of new treatments for HIV, potentially slowing - or even preventing - the onset of Aids (acquired immunodeficiency syndrome). Also, the process could be used to target and destroy cancerous and other infected cells.

The trials make use of the body's natural ability to recognise infected cells. When a virus infects cells, it hijacks the host cell machinery in order to replicate and spread infection.

These infected cells then expose small parts of the virus proteins on their surface, offering a "molecular fingerprint" (an epitope) for killer T-cells from our immune system to identify.

This triggers an immune response, eliminating the virus and any cells involved in its production. HIV not only replicates itself quickly on infection but also has the ability to mutate rapidly, swiftly disguising its "fingerprints" to allow it to hide from killer T-cells.

Researchers at Adaptimmune have spent a decade working on ways to improve the natural ability of the T-cell receptor (TCR) to recognise infected and cancerous cells; a process that has involved remaking the natural TCR protein and then modifying its ability to bind to the molecular fingerprints of the affected cells.

Remarkably, in 2008, with colleagues at Pennsylvania University, they engineered and tested a killer T-cell receptor that can recognise all the different disguises that HIV is known to have used to evade detection.

The scientists transferred this receptor to killer T-cells to create genetically engineered "bionic assassins" able to destroy HIV-infected cells in culture. Now, a year later, they are taking their unique technology into the clinic - for the first time, allowing them to test the power of super-potent immune cells against HIV in reality.

"The immune system uses T-cell receptors to find and trigger the elimination of infected cells," said Dr Bent Jakobsen, Adaptimmune's chief scientific officer. "HIV poses an intractable challenge because it has a phenomenal ability to escape detection through mutation while the immune system is not able to adapt its TCRs.

"Together with our colleagues at Pennsylvania we have previously shown that it is possible to engineer a T-cell receptor that detects the known spectrum of HIV escape mutants for this particular fingerprint and triggers a more potent immune response when transferred into a patient's cells," he added.

Current HIV treatment regimens are based on combinations of anti-retroviral drugs that, although successful in delaying the onset of Aids for several years, have serious side-effects and must be taken daily for life.

Drug resistance is also increasingly a problem. New, effective ways to control the disease therefore remain a priority, as well as the cost and availability of such drugs in poorer parts of the world where the pandemic is most acute.

If the trials confirm the safety and preliminary effectiveness of the engineered T-cell treatment for HIV, Adaptimmune plans to conduct a follow-on trial to confirm efficacy in a larger group of patients. In partnership with its colleagues at Pennsylvania it is also planning a first safety study of engineered T-cells targeted to cancer to start this year. — LPS