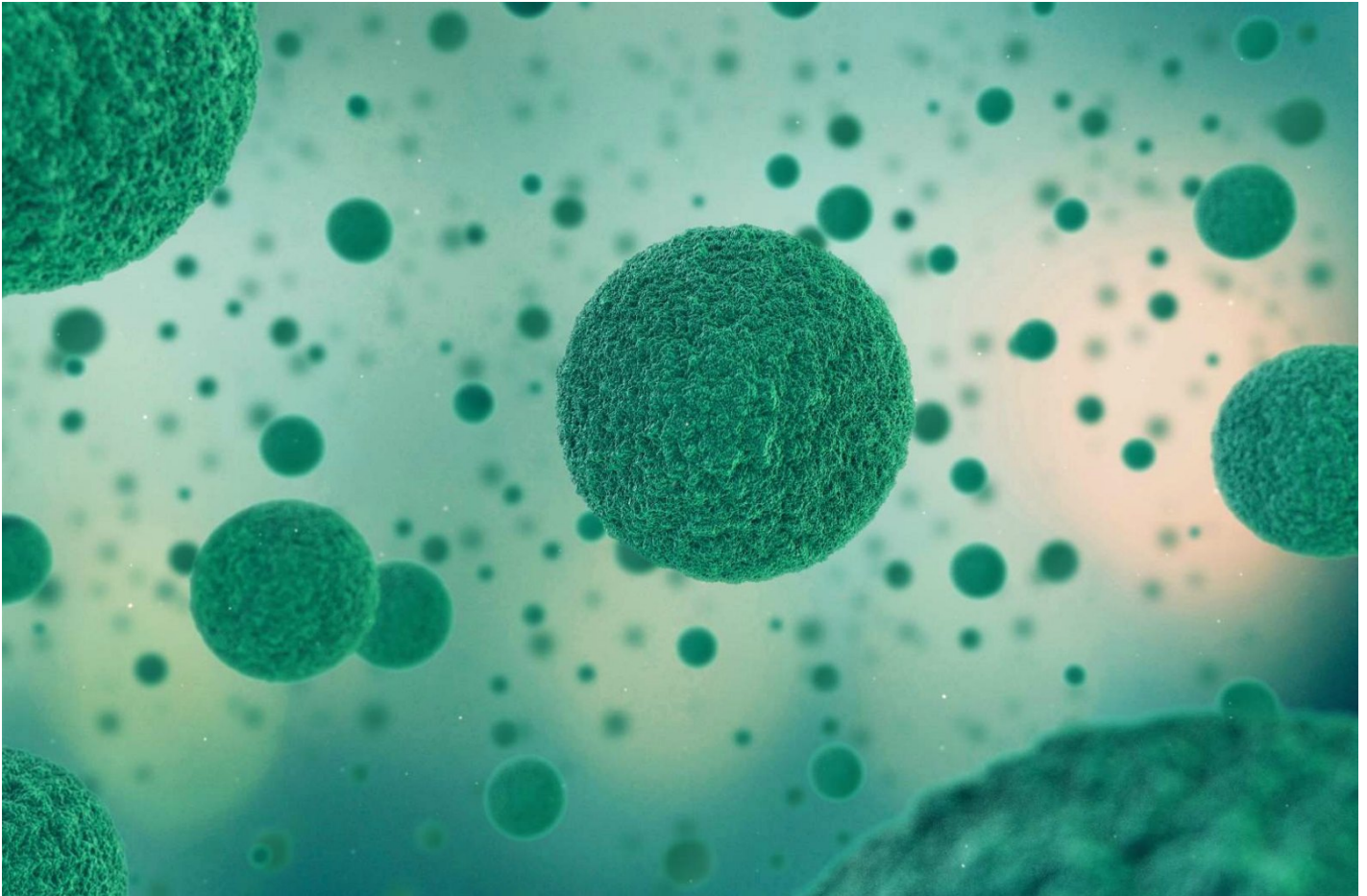


# Revolutionary Cell Technology Helps Fight Deadly Diseases

Leiden University



It was a first for science when research in The Netherlands led to the development of PER.C6 technology, which uses human cells to produce vaccines for combating infectious diseases like the flu, AIDS, and the West Nile and Ebola viruses.

In late 2006, the United Nations and the World Health Organization released a report stating that AIDS had claimed 2.9 million lives during the year, and that since 1981, more than 25 million people have died of the disease.

AIDS and other life-threatening illnesses are now being targeted by companies who have licensed the groundbreaking PERC.6 technology, first developed in the early 1990s at Leiden University, in Leiden, The Netherlands. Subsequently, Crucell, the company founded by the technology's co-inventor, is now a sizable worldwide player in developing and producing vaccines.

The combination of scientist, inventor, business leader and company founder is not common. But those familiar with Domenico (Dinko) Valerio, Ph.D., previously a gene therapy professor and biomedical scientist at Leiden University, as well as Crucell's former president and CEO, know he's a world apart when it comes to thinking outside the box.

While the world's biopharmaceuticals labs were producing vaccines from animal cells, Valerio was working at Leiden University on a revolutionary technology that would change the way vaccines are made.

During the 1980s, when it was less common to combine disciplines, Valerio found a way to combine his drive to be a good scientist with a drive to be a good business leader.

## **Invention Makes Waves**

Valerio, whose work as the co-inventor of PER.C6 technology, a human cell platform, is credited with making the unique production process of vaccine products available to industry. PER.C6, which uses a human cell line, forever changed the face of antibody and vaccine products.

“Up until the development of PER.C6, animal cells, like fertilized chicken eggs used to produce flu vaccine, and hamster cells used in rheumatoid arthritis medicine, were the only types of cells used to make vaccines.

The driving force behind Valerio's work was his interest in responding to the need for vaccines for all people.

“Not only was animal cell vaccine production limiting, it also didn't address the need for new vaccine types that can only be produced on human cells,” he explains.

In 1993, Valerio had started a biotechnology company called IntroGene. As an entrepreneur and scientist, he set out to do what no one had done before — to develop an alternative vaccine-manufacturing technology using human cells.

While scientists had considered the development of a technology using human cells, the obstacles against commercializing it were huge.

“Human cells had never been used because of the difficulty growing a large enough number for commercial purposes,” says Valerio. “PER.C6 technology is very different. It uses healthy cells in a controlled environment that allows the cells to divide and multiply in indefinite numbers.”

In 1994, Valerio worked together with scientists in the lab of Alex van der Eb, a professor of tumor virology, who had pioneered the concept of gene transfer into mammalian cells.

“He created one of the first human cell lines,” says Valerio, who views his former professor also as a mentor. “I was interested in this work because I wanted to make products that required human cell lines. There was nothing appropriate for manufacture at the time in terms of safety, scalability and availability.”

Once the scientists saw that viruses propagated well on PerC.6, their work took a new direction.

Three years later, IntroGene had successfully launched PER.C6. By 1999, IntroGene was positioned to move into new fields, developing vaccines and producing antibodies from its human cell line.

## **Building Crucell**

In 2000, IntroGene's purchase of the company U-Bisys led to the creation of Crucell, and Valerio became its president and CEO. The company's goal was to develop and market a range of vaccines and antibodies for use in fighting infectious diseases.

Valerio points out the successful building of Crucell, a NASDAQ and Euronext-listed company, came about in part

because Leiden is ideally suited for collaborative biomedical research.

“They have a reputation of being a world-class research institution, and there was then a willingness to take advantage of commercial opportunities,” says Valerio.

“It’s one thing to have superb technology at academic centers; it’s another thing to put that technology to commercial use.”

It was a decisive moment in 2000 when a team of Crucell researchers and scientists recruited by Valerio recognized that the base ingredient of the gene therapy they were working on could be used to make a vaccine that would prevent an infection with viruses.

“We moved from gene therapy to developing PerC.6 into a vaccine manufacturing platform,” says Valerio, who also notes it was the same year that he took the company public.

Merck & Co. recognized that the cell line that Valerio had developed had a critical component needed for the AIDS vaccine. Valerio also was interested in using the cell line to develop his own company’s products.

“The cell line is broadly applicable,” he says.

Of the many products that today are being generated on PER.C6 several are now being tested in humans. These include vaccines for influenza, West Nile and Ebola viruses and tuberculosis.

Paul van Grevenstein, formerly a managing director at Leiden University Medical Center (LUMC) and responsible for all technology transfer at LUMC, agrees that Leiden has an outstanding biomedical research base. Van Grevenstein, who now heads an international tech transfer consulting firm, handled the negotiations with IntroGene/Crucell.

“We negotiated two main agreements,” he explains. “One, which was called the master agreement, dealt with the spinning out from the university, and another, a few years later, dealt with the ultimate assignment of Leiden’s share in the then still early stage PERC.6 technology.”

When discussing the factors that helped the creation of Crucell, van Grevenstein notes that the management of Leiden University in those days was supportive of the technology transfer possibility of Valerio’s discoveries. One other important factor, he notes, is that founder Valerio is also adept at surrounding himself with exceptional people and that he dares taking calculated risks.

“One of the elements of this tech transfer story is that at some stage, Dinko changed the company’s emphasis from a gene therapy track to a business model using the PERC.6 technology,” he says. “That took foresight and courage.

“Valerio was very clear about the steps he wanted to take to grow the company,” van Grevenstein continues. “Tech transfer is at its best when it is done for the creation of value, taking the technology to the next step through collaborative research.”

Crucell has grown quickly over the last decade and is now the largest independent vaccine company in the world. In 2004 Valerio stepped down as CEO and founded a new company together with international venture capital veteran Michiel de Haan, called Aescap Venture Management in Amsterdam. In this venture capital company Valerio has what he calls a “second career” by selecting, investing and coaching companies to become the Crucell of the future.

Meanwhile, Crucell’s development of vaccines continues, and the success story that put the company on the world stage over a decade ago continues to make great strides in developing vaccines that eradicate infectious diseases

worldwide.

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