

Crucell

Technologies

May 2010

Crucell's innovative approach has not only led to a broad range of successful vaccines and promising pipeline products, it has also inspired the development of an array of patented technologies to support that portfolio. We have five core proprietary technology platforms.

PER.C6[®] technology

Crucell's PER.C6[®] cell line is derived from a single, human cell, immortalized using recombinant DNA technology. As a result, PER.C6[®] cells can replicate indefinitely, making them uniquely flexible and ideally placed to meet the rising volume demands and stringent safety requirements of today's biopharmaceutical industry.

In areas where we do not aim to develop our own products, Crucell licenses the technology, leading to a number of companies and organizations around the world opting to use our PER.C6[®] technology platform. Potential customers not only need our know-how, but our PER.C6[®] cells, which are only available from us under agreement. This combination ensures PER.C6[®] is the best protected human cell technology in the world.

Since 2008, we have collaborated with DSM Biologics and together we license PER.C6[®] for proteins and antibodies and invest in further innovation of the technology. We feel there is still tremendous potential to reduce the production costs of monoclonal antibodies whilst increasing yield, leading to more affordable treatments for patients.

We also believe that antibody and other protein products based on PER.C6[®] technology may demonstrate enhanced biological properties, rendering them potentially more effective.

AdVac[®] technology

Crucell has been a key player in the development of adenoviral-based vaccines for more than six years. This has led to the availability of proprietary AdVac[®] vectors, constructed from adenoviruses not usually found in humans, such as Ad35. AdVac[®] vectors can be engineered to contain small genetic fragments of various viruses, parasites and bacteria, allowing the development of a wide variety of novel vaccines. While no adenovirus-based recombinant vaccines are currently on the market, AdVac[®]-based vaccines for tuberculosis (TB), malaria, Ebola and Marburg, and HIV are in (pre) clinical trials.

27 g/L

Record-level titer achieved at harvest for an antibody product using PER.C6[®] human cell line technology.



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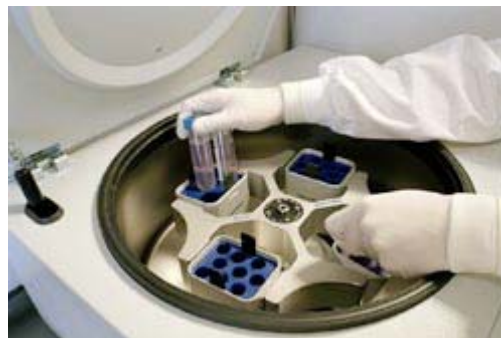
In contrast to commonly used adenoviral vectors, AdVac[®] technology can circumvent pre-existing immunity offering accurate dose control of vaccines. AdVac[®] vectors can be produced on the PER.C6[®] cell line, which supports the cost-effective production of industrial-scale quantities of vaccines.

MAbstract[®] technology

Our MAbstract[®] technology selects antibodies for possible therapeutic use and discovers novel drug targets using whole cells, tissues or infectious agents. It has been used to isolate antibodies for numerous diseases which can then be directly reformatted into antibodies for production using our PER.C6[®] technology. We believe MAbstract[®] has a number of potential advantages over other technologies on the market. For example, it uses a subtraction method of selection not available when generating human antibodies with other technologies and it does not have an inherent limitation on antibody specificity. Fully human antibodies also have an excellent safety profile.

STAR[®] technology

We acquired STAR[®] technology in 2004 and it has proved invaluable for increasing production of recombinant antibodies and therapeutic proteins on mammalian cell lines. One of its strong advantages is that the well-established mammalian cell banks used in STAR[®] technology eliminate the need for specially engineered mammalian cells. This also allows for rapid, stable mammalian cell clone generation, which



typically produces five to ten times more antibody or other therapeutic proteins compared to cell clones generated without STAR[®].

Virosomal technology

One of the challenges in vaccine development is creating products with defined antigens of high purity that can efficiently induce a protective immune response. To solve this, many antigen preparations resort to adjuvants to enhance the body's immune response. The most commonly used are aluminum salt derivatives, which are known to cause adverse reactions, for example, irritation and inflammation at the injection site. Our virosomal technology offers a tool for developing novel, predominantly synthetic vaccines for infectious and chronic diseases. These vaccines offer additional benefits because they are effective even in immune-suppressed patients and infants.

Virosomals are completely biodegradable and the technology is used in the manufacture of several of Crucell's registered products where it has an excellent safety record.



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