



2006 European Life Sciences and Pharmaceuticals Of The Year Award
Analyst: Sangeetha Prabakar
Technology Innovation OTY Award: Mologen AG

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**2006 Frost & Sullivan Technology Innovation
Of The Year Award**

F R O S T  S U L L I V A N

Award Description

Frost & Sullivan's Technology Innovation Award is bestowed upon a company (or individual) that has carried out new research, which has resulted in innovation(s) that have or are expected to bring significant contributions to the industry in terms of adoption, change, and competitive posture. This award recognizes the quality and depth of a company's research and development program as well as the vision and risk-taking that enabled it to undertake such an endeavor.

Research Methodology

To choose the award recipient, Frost & Sullivan's analyst team tracks innovation in key hi-tech markets. The selection process includes primary participant interviews and extensive primary and secondary research via the bottom-up approach. The analyst team shortlists candidates on the basis of a set of qualitative and quantitative measurements. The analysts also consider the pace of research and technology innovation, and the significance or potential relevance of the innovation to the overall industry. The ultimate award recipient is chosen after a thorough evaluation of this research.

Measurement Criteria

In addition to the methodology described above, there are specific criteria used to determine the final rankings. The recipient of this award has excelled based on one or more of the following criteria:

- Significance of the innovation(s) in the industry, and across industries (if applicable)
- Potential of the products of innovation(s) to become industry standard(s)
- Competitive advantage of innovation vis-à-vis other related innovations
- Impact (or potential impact) of innovation(s) on company or industry mind share and/or company bottom line
- Breadth of intellectual property related to the innovation(s), that is, patents, scientific publications, papers in peer-reviewed journals.

Award Recipient – Mologen AG, Germany

Frost & Sullivan's 2006 Technology Innovation Of The Year Award in vector technologies for gene therapy and genetic vaccination is conferred upon MOLOGEN AG of Germany in recognition of the company's development of the Minimalistic Immunogenically Defined Gene Expression (MIDGE®) vector technology. This technology represents an innovative molecular tool that helps in the safe and effective transfer of genetic information into somatic cells, and will thus facilitate the battle against difficult-to-treat human diseases.

In principle, the gene therapy of several life-threatening diseases including cancer involves treating or preventing them by the transfer of the correct or correcting genetic information into the affected body cells. One of the key problems in gene therapy and genetic vaccination is finding a suitable gene carrier (a vector) to transfer the gene into target cells, and subsequently provides sufficient levels of expression. Moreover, a vector to be useful in human gene therapy needs to address many more parameters such as tissue specificity, small size but huge DNA carrying capacity, non-vector-immunogenicity, simple manufacture procedures, combined to a high stability under a broad range of storage conditions.

Traditionally, such vectors are either modified viruses, often derived from pathogenic viruses, or recombinant bacterial plasmids. All of these have several disadvantages, such as anti-vector immunogenicity, limited transport capacities, poor or no tissue specificity or a considerable content of unwanted respectively unneeded DNA sequences. Some vectors do not work in nondividing cells. Others require a complex and cost-driving manufacturing procedure. Moreover, viral vectors usually also express viral proteins, which in some cases have led to dangerous and even deadly immunological effects. If, to be functional, the transported genes need to integrate into the host (target) cell genome, viral vectors have recently been reported to cause leukemia and may promote the development of other kinds of cancer. Hence, the lack of an

efficient vector with the desired qualities is a major challenge for the research- and medical applications of genetic information.

The MIDGE technology could help overcome such efficacy and safety challenges. Designed by Mologen researchers, MIDGE vectors are non-viral expression constructs that are characterized by their unique features, particularly by their high safety. MIDGE vectors are made in a two-step process in which the expression cassette is cut out of a suitable plasmid. The resulting fragment of double-stranded DNA, containing the required sequences only, is then sealed by hairpin DNA oligonucleotides at both ends, which results in a linear, covalently closed molecule much smaller than the size of plasmids. As MIDGE vectors contain only the expression cassette (promoter, coding sequence, and terminator/poly-A-site), they are able to address the above-mentioned limitations of conventional vectors. Not surprisingly, MIDGE vectors are now being designed for use in both prophylactic and therapeutic vaccination.

One of the main advantages of the MIDGE technology is the potential to attach other molecules to the ends of the vector and thereby add new functionalities. Such molecules could be, for example, ligands of a receptor, allowing for cell-specific application of MIDGE, or functional molecules to facilitate the escape of the DNA from degradation by endosomes. All of these strategies result in a specific and efficient expression of the therapeutic protein or antigen.

The manufacturing process of MIDGE vectors is relatively simple: In a one-reaction-container, a two-step procedure using well-established methods of molecular biology, followed by simple concentration and purification steps. Production and quality control procedures are standardized and apply to each MIDGE vector regardless of the gene encoded.

MIDGE vectors appear to be non-toxic even if overdosed. They do not generate anti-vector immune reactions. Most importantly, integration into the host cell genome is neither required for MIDGE function, nor has it been observed experimentally.

Clearly, MIDGE vectors have the potential to substitute bacterial plasmid DNA and viral vectors in the field of gene therapy and DNA vaccination, setting new standards in safety and efficacy.

In conclusion, MOLOGEN is creatively using its MIDGE vector technology platform for the development of novel gene therapies against cancer and vaccines against infectious diseases for which there are unmet needs. Taking this into consideration, Frost & Sullivan confers upon MOLOGEN the Award for Technology Innovation.