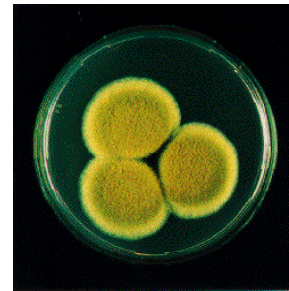


## Fungal Expression of Monoclonal Antibodies

Novozymes A/S and Neugenes<sup>1</sup> have formed a partnership for the evaluation of monoclonal antibody expression in fungal hosts. This partnership combines the advantages of efficient microbial expression with the ability to ensure correct translation and folding of the Monoclonal antibody molecule (MAB). The technology is based on expression in a heterokaryon fungal system and represents a unique and proprietary platform. In the future, this technology will potentially provide an inexpensive and robust alternative for large scale recombinant production of antibodies and other complex heterologous proteins.

**The Novozymes- Neugenes partnership represents a unique constellation centred on the following capabilities:**

- **Proprietary access to fungal MAb expression technology**
- **Extensive experience in development and production of recombinant proteins**
- **Experience with cGMP manufacturing of proteins**
- **Faster scale for microbial systems**



*Aspergillus oryzae*

### Business opportunity

For antibody producers, in particular, and large pharmaceutical companies, in general, the attractiveness of this partnership rests on several strong selling points, including:

- Proprietary IPR position which is free from dominating IP
- Reduced capital investments and production cost through use of proven and efficient fungal production systems
- Scalability and flexibility – A stable and robust production process that offers flexibility in optimization and development of production processes.

### Proprietary IP position

Utilizing Neugenes' MAb expression technology embodied in US Patent 5,643,745 we can offer the only known alternative technology to that owned by Genentech under US Patent 6,331,415.

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<sup>1</sup> [www.novozymes.com](http://www.novozymes.com); [www.neugenes.com](http://www.neugenes.com)

Through Neugenes' heterokaryon cell technology, the client is given proprietary protection. This platform is further complemented by Novozymes' long standing experience with large scale fermentation of enzymes and complex multimeric proteins.

### **Significantly reduced cost**

The ability to provide cost effective production alternatives is becoming increasingly important as Mabs are one of the most important classes of therapeutics under development. Compared to established mammalian cell culture production systems, fungal expression systems hold the potential for significant cost savings. This cost reduction will come from reduced capital investments, yield benefits and lower operating costs in production.

### **Effective, high volume production**

Today's average mammalian cell-line harvest is < 1 gram/liter produced during a 3-4 weeks batch cycle. In comparison, fungal fermentation holds the potential for yields exceeding several grams pr. liter during a 10 day batch cycle.

Furthermore development times are significantly reduced for fungal production hosts (typically 6-12 months compared with 18-24 months for mammalian hosts). In a fiercely competitive environment the speed to clinic is a top priority for success.

### **Proof of Concept Established**

Proof of concept has been demonstrated for this technology and Novozymes and Neugenes are currently evaluating expression of two therapeutic antibodies under commercial development by third parties. Initial expression results for these proteins have been shown to yield correctly folded and active material.

Novozymes has further initiated research collaboration with a University partner for evaluation of technology that will allow for in-vivo modification of fungal glycosylation patterns thereby addressing questions concerning post-translation modifications.

The partnership is currently looking for additional partners who have an interest in securing access to future MAb manufacturing capacity and technology to expand our application of this platform. Further information on this opportunity can be obtained from the following contacts:

Mr. W. Dorsey Stuart, Ph.D.  
CEO

Neugenes Corp.  
871 Industrial Road, Suite J  
San Carlos, California 94070  
Tel: +1 650 508 9672  
Fax: +1 650 508 9171  
[dstuart@neugenes.com](mailto:dstuart@neugenes.com)

Mr. Hans Ole Klingenberg  
Manager, Business Development

Novozymes  
1445 Drew Avenue  
Davis, CA 95616  
Tel: +1 530 750 5760  
Fax: +1 530 758 0317  
[haok@novozymes.com](mailto:haok@novozymes.com)

## **About Novozymes**

Novozymes is the world leader in research, development and production of enzymes for industrial applications. The company was created in November 2000, following a de-merger from Novo Nordisk A/S and has a history dating back to 1925. With 40 years of experience in biotechnology, we have developed a strong platform for discovery, diversity generation, optimization and production of microbial proteins and peptides.

Novozymes has made a strategic decision to expand its activities into new business areas. While maintaining our strength in the industrial enzyme marketplace, we are seeking to leverage our proprietary technologies for discovery, optimization and production of biopharmaceuticals and other biotechnology products.

Novozymes currently produces more than 600 products based on recombinant proteins and had a turnover in excess of \$ 850 million in 2002. We maintain sustained double digit growth and spend more than 10% of our sales on R&D.

## **About Neugenesis**

Neugenesis is a privately held biotechnology company, located in San Carlos, CA, focused on leveraging fundamental research employing the filamentous fungi, *Neurospora crassa*, into commercial biotechnology applications, incl. production of MABs.

Neugenesis was founded in Hawaii a decade ago by W. Dorsey Stuart, Ph.D. and other key individuals. Neugenesis' technologies are based on original academic research performed at the University of Hawaii School of Medicine and University of Kansas Medical Center in the USA, Leeds University in the UK, and Flinders University in South Australia. Neugenesis has supported basic complementary research accomplished at those locations.

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