

# SYNTHETIC GENES FOR YEAST EXPRESSION

## *Fields of Application /*

- High yield recombinant protein production
- Stable and safe antigen production of e.g. malaria or SARS genes
- Knock-out and knock-in mutant construction
- Two hybrid and one hybrid screens
- Metabolic pathway optimization

## *The Problem /*

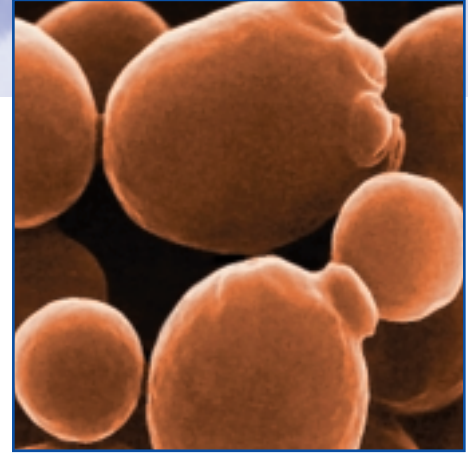
Improvements in yeast expression systems, coupled with the development of yeast surface display and refinements in two-hybrid methodology, are expanding the role of yeasts in the process of understanding and engineering eukaryotic proteins. Especially the methylotrophic yeasts *Hansenula polymorpha* and *Pichia pastoris* have been developed as **effective production systems for recombinant proteins**, offering economy, ease of manipulation, the ability to perform complex post-translational modifications and high expression levels. Moreover, genetics of *Saccharomyces cerevisiae* and *Schizosaccharomyces pombe* are very well understood and have become

a powerful tool in basic science to understand the molecular biology of eucaryotic cells.

However, yeast systems have presented certain problems when used for the commercial-scale production of recombinant proteins.

These include issues of **product yield and quality**, such as production of wrongly processed forms of the desired protein product.

Many of the encountered problems are related to the fact that yeasts prefer several synonymous codons above others. Synonymous codon usage has co-adapted with tRNA pools to enhance the efficiency of protein synthesis (reviewed in Akashi 2001). Differences in cellular concentrations or codon-anticodon stability can lead to translation inefficiencies both within and among synonymous families. Thus **codon usage of highly expressed genes** shows a higher correlation with tRNA abundance, a greater degree of third base pyrimidine bias, and a lesser tendency to the A+T richness which is characteristic of the yeast genome. Moreover, the recombination systems in yeasts are **highly active**, restricting the number of genes which can be propagated to yeast to sequences with no direct repeats or concatamers.



## *The Technical Solution/Our Service /*

- Codon optimization
- G/C content adaptation
- Inhibition of internal splicing and premature polyadenylation
- Prevention of creation of stable RNA secondary structures
- Avoidance of direct DNA repeats and thereby recombination events
- Finding the most efficient signal peptide / gene combination

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# SYNTHETIC GENES FOR YEAST EXPRESSION

## Your Success /

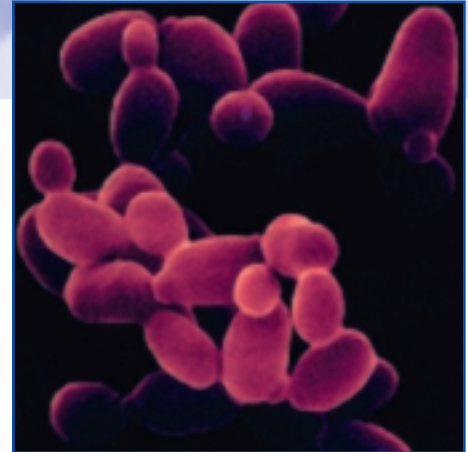
Today, many researchers benefit from synthetic genes **for increased heterologous protein production in yeast**. GENEART has so far successfully completed the synthesis of genes designed for heterologous expression in:

- *Saccharomyces cerevisiae*
- *Schizosaccharomyces pombe*
- *Pichia pastoris*
- *Pichia angusta (Hansenula polymorpha)*

In many cases a dramatic increase in protein production has been reported, which regularly has **exceeded wild type driven gene expression by a factor of 2 to 3 and in some cases even by a factor of 10 or more**. Taking the costs of protein production into account and by freeing up resources from highly trained scientists, **synthetic genes are very cost effective tools** in modern molecular biology. Moreover, we have been able to increase genetic stability of transgene expression from no detectable expression to **high and stable protein production**. As a consequence for many scientists, codon adaptation and gene optimization rapidly have become the system of choice for heterologous gene expression in yeast.

By relying on rationally designed synthetic genes, recent advances have been made in the quality of recombinant proteins in fermenter culture and in the quality of the protein product, namely **improved secretion signals and glycosylation patterns**.

GENEART's partner with a strong expertise in yeast expression, our unique **GeneOptimizer™** bioinformatic know-how and our fast and highly reliable GeneAssembler DNA construction service offer you access to high performance yeast producers, allowing maximum expression without the need of natural templates.



## References /

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