Pichia pastoris Protein Expression

Services for protein expression - accelerating time to market

VTU technology

VTU Technology is a leading contract research and development company, providing services for the fast track generation for high performance, industrial protein production strains and economically viable protein production processes for pharmaceutical companies and any other protein manufacturer. The company applies its exclusive cutting-edge ***Pichia pastoris*** **protein expression platform** and offers **expertise and services**, which span the entire range from gene or sequence to highly productive expression strains and processes from lab to pilot scale, in minimum time.

Technological Features

- Fine-tuning of expression using our **proprietary AOX1 promoter library**
- **High speed expression strain development** yielding unparalleled production levels (20 g/L peak expression)
- Co-expression of auxiliary proteins for **maximization of protein expression**
- **High-throughput microscale cultivation and screening** for highest-yield clones at unrivaled speed
- **VTU`s 2nd generation methanol-free AOX1-promoter variants** allow for effective methanol-free expression
- **Optimized procedures** for exploiting the full potential of *Pichia pastoris*

Track record for VTU´s *Pichia pastoris* toolbox

2 to > 10 g/L secreted with up to 90% purity

- Serum proteins
- Fabs
- Ab derived fragments
- Fusion proteins
- Cytokines
- Scaffold proteins
- Enzymes
- Your target protein

Our Specialized Services

- Gene design and cloning
- Development of customized high performance expression strains at unrivaled speed
- Validation of screening results (1L-fermentations)
- Process optimization and development
- Small scale production of non-GMP material
- Scale-up and GMP manufacturing through collaboration with Boehringer Ingelheim
- Sound technology transfer to our customers supporting regulatory filings

Your Advantages

- Valid and scalable results in minimum time
- Short and flexible project timelines with customized project design
- Full documentation to support your regulatory filings
- Uncompromising confidentiality
- FTO certified documented technology platform

Unique Promoter Library for Tunable Optimum Protein Expression

Solution – Fine Tuning and Co-expression

Our proprietary **promoter library of synthetic AOX1 variants** spans a wide range of activities and expression characteristics which allows an ideal match of promoter properties and specific requirements for **efficient expression** of a given target protein.
Furthermore, this particular technology is perfectly suited to construct efficient expression strains by **co-expression** of auxiliary proteins routinely used at VTU. Simultaneous transformation using a range of promoter variants and helper proteins, and applying selection pressure that will favour either low or high copy numbers, allows VTU´s skilled team to identify the most suitable combination (Figure 1). This exclusive library of synthetic promoters is complemented by in-house host strains and plasmids thus enabling the full exploitation of *Pichia pastoris*.

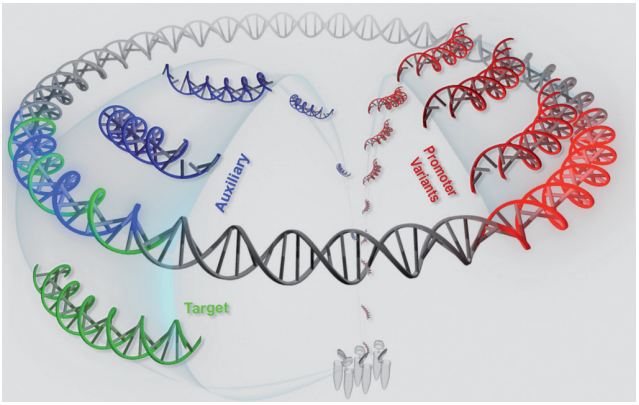

Figure 1: VTU´s pool approach allows to find the optimum combination of promoter variants, gene copy number and helper protein for a given target

Key to Sucess - High-Throughput Micro-cultivation and Screening

Our researchers screen up to **25,000 *Pichia* clones per week** for expression titer in fully equipped **state-of-the-art laboratories.** Past experience has shown that by screening thousands of clones we routinely see significant improvements in recombinant protein expression titer, **up to 10 fold.** This capability in conjunction with our proprietary ***Pichia* AOX1 promoter library** gives us unparalleled ability to tune gene expression and rapidly isolate high productivity clones.
The most promising candidates are subsequently taken directly into fermentation in a set of paralleled 1L-bioreactors to confirm the effective productivity of the expression strains.

AOX1 – Controlled Methanol-free Protein Expression

VTU´s 1st generation methanol-induced promoter variants – known as the strongest and most effective yeast promoters – exhibit unparalleled production levels. This unmatched technology platform is now complemented by **novel 2nd generation AOX1 promoter variants** allowing for methanol-free expression thus providing our customers high performance expression strains no longer dependent on methanol induction. These new promoter variants show significantly increased recombinant protein production in comparison with constitutive expression, at the same time retaining the advantage of a late metabolic burden caused by recombinant overexpression, thus outperforming PGAP as the conventional alternative for methanol-free expression in Pichia pastoris (Figure 2).
VTU´s methanol-free high performance protein expression strains are highly favorable for large scale production of heterologous proteins through elimination of efforts and costs associated with methanol handling.

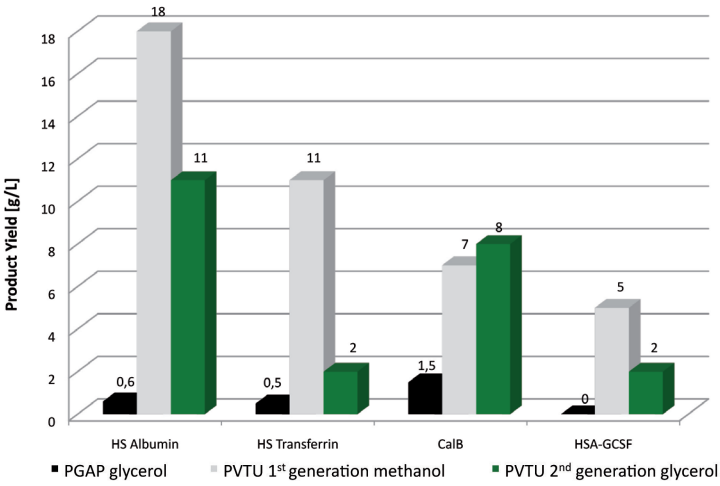

Figure 2: Comparison of protein expression driven by PGAP, VTU´s 1st generation methanol-driven PAOX1 and VTU´s 2nd generation methanol-free PAOX1

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