



GTP Technology introduces improvements in continuous fermentation processes with *L. lactis*

Enhancements to induced expression and an improved constitutive promoter open way for increased use of *L. lactis* in biologic, diagnostic, and cosmetic applications

Toulouse, France, July 20, 2010-- Genes-To-Proteins Technology S.A. (GTP), a contract research organization specialized in protein engineering, announces today that it now offers significant improvements in continuous fermentation processes with *Lactococcus lactis*, a promising gene expression host. The improvements to the host deliver a number of benefits for biologic, diagnostic and cosmetic applications.

The company, which has now completed more than 800 projects for customers in the life sciences industries, has introduced enhancements to induced expression and developed a constitutive promoter for continuous fermentation processes in *L. lactis*. In so doing, it has overcome most of the difficulty of balancing translation/secretion in *L. lactis*

The inducible promoters used with *L. lactis* give the sometimes desirable control over the gene expression but also come with some disadvantages, such as overload of the secretion system, an unstable host and having to deal with the inducer itself. The new constitutive inducers being introduced by GTP are more stable. Stability is essential to process optimization and continuous fermentation. Since the rate limiting secretion is optimum in exponential growth phase, and this phase being sustainable in continuous fermentation, the system is finally significantly better suited for production.

GTP's innovation, originally developed in conjunction with academia, covers novel DNA sequences that function as promoters, expression vectors containing such sequences, and host cells transformed with these vectors, in particular lactic acid bacteria such as *L. lactis*. The invention also allows use of these promoters for the production of heterologous proteins, in particular therapeutic or vaccine-related proteins. The company has filed patents covering the technology.

The company has an ongoing innovation program and, amongst its current projects, is an investigation into promising approaches to biomass increase together with an industrial partner.

Choice of the expression system

The choice of the expression system is a key decision in the Gene-To-Protein process. GTP offers ten distinct systems and advises clients as to the best system for each project. Most genetic studies have focused on cells from mammals or birds, or prokaryotic cells such as bacteria, in particular *E. coli*. However, given the special features of these cells (the possibility of obtaining glycosylated or non-glycosylated proteins, presence of an oncogenic virus, limited yield, etc.), the industrial application of these new production methods is still limited, particularly by problems relating to the efficacy or safety of gene expression in these recombinant microorganisms.



Lactic acid bacteria are predominantly used in the agri-food industry today. The diversity of heterologous proteins that can be expressed in lactic acid bacteria combined with the harmlessness of these strains makes them particularly attractive for the production of recombinant proteins with therapeutic or vaccine-related goals.

***L. lactis* specificity: advantages & limits**

For gene expression, *L. lactis* presents important and interesting features for the production of biologic, diagnostic, food or cosmetic. These include: no endotoxins, straightforward downstream purification, linear scale-up, protease-free supernatant (option) and tight gene regulation.

GTP/INRA co-authored an article published May 2010 in Microbial Cell Factories giving more information on a functional inducible system. The "Production and purification of staphylococcal nuclease in *Lactococcus lactis* using a new expression-secretion system and a pH-regulated mini-reactor". It is accessible [here](#).

About GTP Technology – <http://www.gtptech.com/>

Genes-To-Proteins Technology S.A. is a French Contract Research Company providing custom recombinant protein production services. Applications include human health, agri-food and life-science tools. Capabilities include process creation and optimization with a variety of expressions systems (*bacteria*, yeast, insect & mammalian cells) and capacity up to tens of grams.

Founded in 2000, this company based in Toulouse has completed over 800 projects to date.

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