Biotechnological applications of lactic acid bacteria

SENIOR SCIENTISTS:

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Research Field and Subjects

A multidisciplinary range of genomics/post-genomics, biochemical, and biophysical approaches are used to study the function of genes that are involved in carbon metabolism, in cell wall biosynthesis, and in the mechanisms of stress response of different LAB species (*Lactobacillus plantarum, Lactococcus lactis and Streptococcus thermophilus*).

Applications are in the following biotechnological areas:

1. Live mucosal vaccine vectors.

Strains of *Lactobacillus plantarum* are engineered to produce and deliver antigens to the nasal, vaginal or intestinal mucosa, using the mouse as an experimental system (in collaboration with Institut Pasteur-Lille). Mutants defective in the biosynthesis of the cell wall are constructed to enhance the local immune response, and to prevent uncontrolled release of the genetically modified microorganisms into the environment.

2. Second-generation probiotics.

Strains of *Lactobacillus plantarum* are engineered to be used as dietary adjuncts to deliver/remove compounds with a beneficial/detrimental effect on human health, in particular production of low-calory sugars or ammonium removal.

3. Metabolic engineering of dairy starters.

Dairy starters are engineered to produce yoghurt, cheese, buttermilk with improved health and organoleptic properties, in particular through the re-routing of the pyruvate flux towards the production of lactate isomers, aroma (diacetyl, acetaldehyde, acetate) and natural sweeteners (polyols, alanine). Futhermore, LAB offers strong perpectives in their use as cell factory for metabolite production.

4. Genomics and post-genomics.

The complete sequence and the analysis of the genome of *Streptococcus thermophilus* (yoghurt starter and sole non-pathogenic *streptococcus*) has been established. DNA microarrays are currently being used for global transcriptomic analyses.

Products and Services

- Gene knockout in LAB
- Heterologous expression in LAB
- Genome assembly and annotation
- Bioinformatics tools for DNA microarrays design and managment
- Small scale fermentation facilities and analysis of fermentation products

Main Equipment

- Small scale fermentors
- HPLC

Representative References

- HOLS P., M. KLEEREBEZEM, A.N. SCHANCK, T. FERAIN, J. HUGENHOLTZ, J. DELCOUR and W.M. de VOS (**1999**) Conversion of *Lactococcus lactis* from homolactic to homoalanine fermentation through metabolic engineering. Nature Biotechnology 17, 588-592.
- DELCOUR J., T. FERAIN, M. DEGHORAIN, E. PALUMBO and P. HOLS (**1999**) The biosynthesis and functionality of the cell-wall of lactic acid bacteria. Antonie van Leeuwenhoek 76, 159-184.
- DERZELLE S., HALLET B., FRANCIS K.P., FERAIN T., DELCOUR J. and HOLS P. (**2000**) Changes in cspL, cspP, and cspC mRNA abundance as a function of cold shock and growth phase in *Lactobacillus plantarum*. J. Bacteriol. 182, 5105-5113.
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- DERZELLE, S., B. HALLET, T. FERAIN, J. DELCOUR AND P. HOLS (**2003**) Improved adaptation to cold-shock, stationary-phase, or freezing stresses in *Lactobacillus plantarum* overproducing cold-shock proteins. Appl. Environ. Microbiol. 69, 4285-4290.

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Patents

- P.HOLS, M. KLEEREBEZEM, J HUGENHOLTZ, T. FERAIN, O. KUIPERS, J. DELCOUR AND W.M. DE VOS (**1999**) Process for the production of alanine by recombinant microorganisms, Patent Nr. W01999NL9900021/EP19990900710.
- C.GRANGETTE, A. MERCENIER, J. DELCOUR AND P. HOLS (**2002**) Cell wall mutants for delivery of biologically active compounds, Patent Nr. EP02447119.5.

Awards

- Food Ingredients Research Award (Paris, 1999, NIZO food research/UCL, M. kleerebezem and P. Hols) on "Efficient 'in-situ' production of L-Alanine sweetener in dairy food products"

Partnership

- Members of *Institut des Sciences de la Vie* (ISV) research group
- Participant in three EU-RTD projects (Labdel, Deprohealth, Nutracells)
- Participant in two *Région Wallonne* projects
- (First Europe-Dadmas, Waleo-Encefala)
- European collaborations with WCFS (Ede, Nl), INRA (Jouy en Josas, Fr), IPL (Lille, Fr)
- Eurogentec (DNA microarrays)

STAFF

Total: 12

KEY WORDS FOR R&D

dairy products, yoghurt, cheese
genomics, genome, microarrays
heterologous expression
intestinal delivery
lactic acid bacteria, LAB
Lactobacillus
Lactococcus
metabolic engineering
mucosal vaccines
probiotics
Streptococcus

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