Research Topic for the ParisTech/CSC PhD Program

Subfield: Molecular Microbiology

ParisTech School:AgroParisTech, Doctoral school ABIES

Title:Interplay between peptidoglycan and polysaccharide synthesis in *Lactococcus lactis*, a model Gram-positive ovococcus.

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Short description of possible research topics for a PhD

Lactococcus lactis cell wall (CW) polysaccharides (CWPS) are essential for CW homeostasis and cell division, since mutations in gene clusters encoding CWPS lead to strong defects ingrowth, cellmorphology and septation. In preliminary experiments, we have isolated suppressor mutants with improved growth and fitness. By whole chromosome sequencing, mutations were mapped inside a gene encoding a penicillin-binding protein (PBP) of the peptidoglycan (PG) biosynthesis pathway involved in PG polymerization, thus supporting the link between CWPS biosynthesis, PG biosynthesis and cell division. The objective of the PhD project is: 1) to isolate other suppressor mutants; 2) to characterize selected mutants by genetic studies and biochemical analysis of CW components (PG and CWPS); 3) to identify the molecular mechanisms underlying the suppressing phenotype of the mutants. The results obtained in this project are expected to provide novel insights in the regulatory networks that control CW synthesis and cell division in bacteria, which could provide the targets of novel antibiotics in pathogenic Gram-positiveovococci, such as streptococci.

Required background of the student: Bacterial genetics, molecular microbiology, biochemistry

A list of 5(max.) representative publications of the group: (Related to the research topic)

1. Sadovskaya, I., Vinogradov, E., Courtin, P., Armalyte, J., Meyrand, M., Giaouris, E., Palussière, S., Furlan, S., Péchoux, C., Ainsworth, S., Mahony, J., van Sinderen, D., Kulakauskas, S., Guérardel, Y., and Chapot- Chartier, M.-P. (2017) Another brick in the wall of *Lactococcuslactis*: an essential rhamnan polysaccharide trapped inside peptidoglycan. **MBio.** 12;8(5).
2. Chapot-Chartier, M. P., and Kulakauskas, S. (2014) Cell wall structure and function in lactic acid bacteria. **Microbial cell factories** 13 Suppl 1, S9
3. Ainsworth S, Sadovskaya I, Vinogradov E, Courtin P, Guerardel Y, Mahony J, Grard T, Cambillau C, Chapot-Chartier MP, van SinderenD. (2014) Differences in lactococcal cell wall polysaccharide structure are major determining factors in bacteriophage sensitivity. **MBio**. May 6;5(3).
4. Andre, G., Kulakauskas, S., Chapot-Chartier, M. P., Navet, B., Deghorain, M., Bernard, E., Hols, P., and Dufrene, Y. F. (2010) Imaging the nanoscale organization of peptidoglycan in living *Lactococcus lactis* cells. **Nat Commun** 1, 27
5. Chapot-Chartier, M. P., Vinogradov, E., Sadovskaya, I., Andre, G., Mistou, M. Y., Trieu-Cuot, P., Furlan, S., Bidnenko, E., Courtin, P., Pechoux, C., Hols, P., Dufrene, Y. F., and Kulakauskas, S. (2010) The cell surface of *Lactococcus lactis* is covered by a protective polysaccharide pellicle. **J.Biol.Chem.**285, 10464-10471