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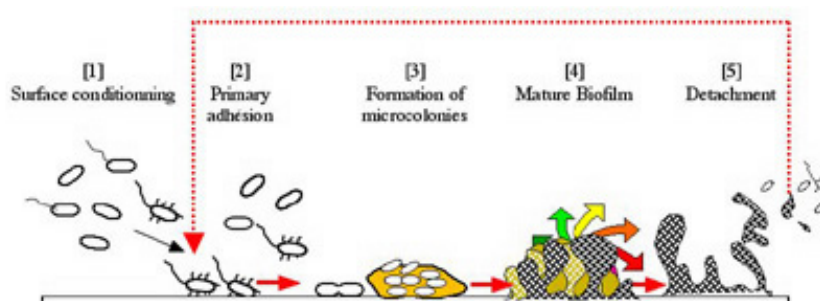
## Abstract

Surface attached, matrix-enclosed communities are called **biofilms**. In medical and industrial settings, biofilms are often detrimental and display distinct phenotypes compared to free-swimming bacteria. Using genetic and genomic tools combined with a fermenter-based experimental model, our goal is to identify essential bacterial cellular factor and physiological pathways involved in the process of biofilm formation. These approaches may lead to a better understanding of the biofilm biology as well as to strategies to control pathogenic biofilms.

## Annual Report

### Bacterial biofilm formation

Most of what has been learned about bacterial physiology derived from pure, free-floating bacterial laboratory cultures where bacteria adopt a planktonic lifestyle. However, from clear-running water to dental plaques, it is now recognized that in most ecosystems, microorganisms predominate as surface attached, matrix-enclosed communities called **biofilms**. In medical and industrial settings, biofilms are often detrimental due to physiological particularities of biofilm-bacterial physiology as compared to their well-studied planktonic, free-swimming equivalent. Using genetic and genomic tools, our goal is the identification of the essential cellular factors involved in the process of biofilm formation (see Fig.1).



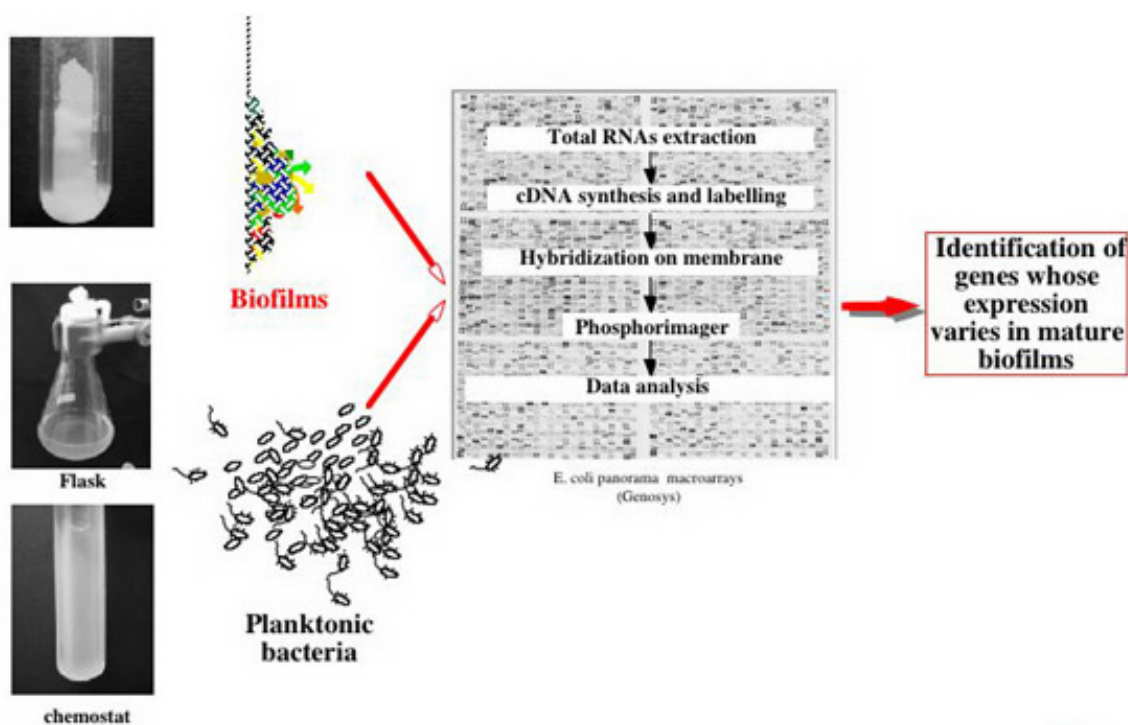
### I. Functional profiling of mature biofilm formation in *Escherichia coli*: critical role of envelope stress responses [ Christophe Beloin, Patricia Latour-Lambert, Agnes Roux]

Biofilm formation corresponds to a major switch in bacterial lifestyle that is thought to affect the expression of multiple genes and operons. We used DNA macro-arrays to study the wide scale effects of biofilm formation at the genomic and transcriptional levels, by comparing the expression profile of *E. coli* biofilm compared to agitated laboratory planktonic culture conditions (see Fig.2).

We showed that bacterial biofilm differentially expressed genes corresponding to unknown genes, stress and envelope stress responses, energy production and envelope biogenesis functions amounting up to 10% of the *E. coli* genome. We used gene disruption as a fundamental tool to substantiate and validate the biological content of our analysis and showed that over a third out of the 60 most highly biofilm-induced genes are required for the formation of mature biofilm. Hence, this approach experimentally assigned new biofilm-related function to 21 genes. We provide evidences for the high and consistent expression of stress envelope response genes in mature *E. coli* biofilms and demonstrate that the partial expression of elements of the *cpx* pathway (*cpxP*, *spy*) is a general feature of biofilm gene expression in *E. coli*. These results constitutes the first comprehensive analysis of the global transcriptional response triggered in *E. coli* biofilms and provide insights into the biofilm physiological signature. (Beloin, C. *et al.*, submitted).

## II. Molecular analysis of biofilm formation by pathogenic yeast *Candida albicans* et *Candida glabrata*

In a Pasteur collaborative project (Programme Transversal de Recherche-PTR) with Christophe d'Enfert's groupe (Unité Postulante Biologie et Pathogénicité Fongique) and Françoise Dromer's lab (Unité Postulante de Mycologie Moléculaire), we developed a continuous flow culture system allowing the production and study of *Candida albicans* biofilms. This model is currently used to investigate gene expression in *Candida* biofilms using macro and micro-arrays.



## III. Regulation of biofilm formation in *Staphylococcus aureus*

Collaboration with Inigo Lasà laboratory, University of Navarra, Spain.

Within a close collaboration with Inigo Lasà's laboratory, we investigated the role of SarA, a central regulatory element that controls the production of *S. aureus* virulence factors. We showed that SarA is essential for *S. aureus* biofilm development in particular through the activation of polysaccharide intercellular adhesin (PIA/PNAG) production encoded by the *ica* operon. (Valle, J, *et al.*, submitted)

## IV. Development of rapid gene inactivating methods in Gram-negative bacteria.

Our laboratory developed, with others (see e.g. Datchenko *et al.*, PNAS 2000), a rapid PCR-based method to inactivate target genes in *E. coli* (Chaverroche *et al.*, Nucl. Acid. Research, 2000). In collaboration with E. Carniel's group, (Unité de Bactériologie Moléculaire et Médicale, Laboratoire des *Yersinias*), we adapted this method that now allows the rapid disruption of genes in the bacterial genera *Yersinia*, *Serratia*, *Salmonella* et *Shigella* (cf <http://www.pasteur.fr/recherche/unites/Ggb/methodes.ang.html>). (Derbise *et al.*, submitted). (Rossi *et al.*, submitted), (Solano *et al.*, *Mol. Microbiol*, 2002).

**Photo 1** : Bacterial biofilm formation : a model

**Photo 2** : Expression profiling of planktonic versus biofilm bacteria : strategy.

**Keywords**: Biofilm, DNA-arrays, candida albicans, Escherichia coli

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