# Microbial Functional Genomics: Pulling Together a Variety of Approaches and Concepts

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## Abstract

With the human and mouse genome sequences behind us, whole microbial genome sequencing has become the most active area in genomics today. As easy targets have been worked on first, the microbes under scrutiny today are frequently uncharacterized and difficult to grow and isolate. In those cases, genome sequences often constitute the first and only reliable information about the microorganism to which they belong. It also becoming the rule that no experiments (genetics, transformation, mutagenesis) are directly possible on the microorganism. For better characterized microbes, the competition in the field pushes us to get interested in "anonymous genes" for which no functional clues have be gained from routine sequence analysis.

"Exploratory genomics" is the term we have coined to define the activity of our laboratory, mainly devoted to the analysis of gene and genome sequences we know nothing about. The two laboratory branches -experimental and bioinformatics- work in close collaboration to elucidate the functions of genes of fundamentals, biomedical or biotechnological interest.

I will present an overview of the variety of approaches that are required -and developed - in the wet laboratory (e.g. high throughput protein production and characterization, 3-D structure determination and analysis, incomplete factorial experimental design, etc.) as well as - in silico - (parallel computing for whole genome comparison, target prioritization, LIMS, TCoffee for multiple sequence/structure alignment, PhydBac for phylogenomics, etc.) to generate testable hypothesis, from which rational experiments can be designed, performed, and their results understood. Examples will be drawn from our experience with fastidious microorganisms such as *Rickettsia conorii*, *Tropheryma whipplei*, mimivirus, as well as with *Escherichia coli* genes of unknown function in search of new antibiotic targets). These combined approaches are now being extended to the functional genomics of potential bioterrorism agents (e.g. *Francisella tularensis*, *Chlamydia psittaci*, *Bacillus anthracis*, etc.) that very few laboratories in the world will be allowed to manipulate and experiment with.

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