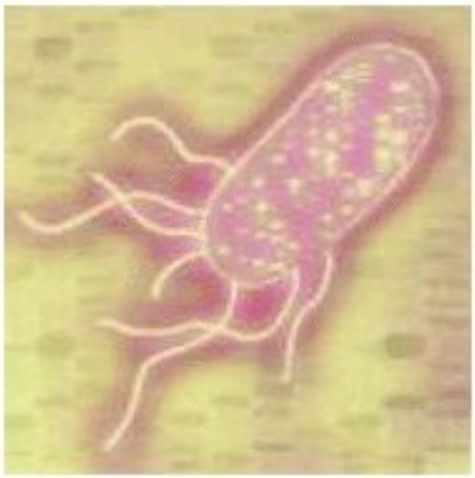
Abstracts



ERA-NET PathoGenoMics

PARTNERING WORKSHOP

January 21, 2008,
Hotel Serhs Campus
Vila Universitària (Campus UAB),
CERDANYOLA DEL VALLÈS,
Barcelona, Spain

Applied pathogenomics: Prevention, diagnosis, treatment and monitoring of infectious diseases

www.pathogenomics-era.net

LIST OF ABSTRACTS

(In the order of the programme of the workshop)

ORAL PRESENTATIONS

To be placed on: www.pathogenomics-era.net	
Name	Tanja Kostic
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Address	A-2444, Seibersdorf
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E-mail	tanja.kostic@arcs.ac.at
Representation:	research
Thematic area of interest	diagnostics (microbial diagnostic microarrays)
Title of the presentation	ARC microbial diagnostic microarrays for environmental and food analysis
Partners (name/country) of the planned proposal (if known):	

Short abstract (max. half page):

Microbial diagnostic microarrays are molecular tools used for simultaneous identification of microorganisms in food, clinical and environmental samples. The main advantages of MDMs are high throughput, parallelism and miniaturization of the detection system. Furthermore, both high specificity and high sensitivity of the detection can be achieved. Different microarray systems including microarrays based on short or long oligonucleotide probes, sequence-specific end-labelling of probes (SSELO) or approaches based on whole genome differences have been applied in our laboratory. These different approaches exhibit certain advantages and limitations and are suitable for different applications. In addition, depending in the application, various marker genes have been used for probe design including pathogenicity-related markers, housekeeping genes as well as key genes involved in environmental processes. In some cases, whole genome approaches (Diversity Arrays) have been applied as no suitable marker genes to be used for probe design could be identified.

Microbial diagnostic microarrays developed at our institute target environmental bacteria as well as human pathogens. All known (either by cultivation or by cultivation-independent analysis) methane oxidizing bacteria ca be easily identified by a microarray, which is based on sequence differences within the *pmoA* gene encoding the key enzyme methane monooxygenase. In the field of human pathogen detection, one of our developments is able to detect and identify common waterborne pathogens and indicator organisms. This microarray is based on the combination of a unique labeling method (SSELO), a novel concept of competitive oligonucleotides and the *gyrB* gene as phylogenetic marker resulting in high specificity and sensitivity. Other ARC microarrays have been developed for the typing of food pathogens rather than for their detection. The ARC Salmonella Serotyping Array is able to distinguish more than 40 *S. enterica* serotypes prevalent in Europe and has the potential to replace classical serotyping. It is based on specific short oligonucleotides, which target two housekeeping genes (*gyrB, atpD*) and two flagellin genes (*fliC, fljB*). The development of additional microarray-based typing methods in on-going.

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Representation:	Research / Industry
Thematic area of interest	Bioinformatics. Computational drug design.
Title of the presentation	In-silico drug design.
Partners (name/country) of the planned proposal (if known):	

Short abstract (max. half page):

BIOMOL-INFORMATICS has expertise in the application of the three-dimensional structures of protein target molecules in structure-based drug design. The company is specialist in in-silico analysis and prediction of new drugs activity on 3D models of proteins and in molecular dynamics techniques applied to docking of compounds.

BIOMOL-INFORMATICS can offer services in the generation of high-quality three dimensional models for essential proteins, prediction of protein-protein interactions and rationale design of disturbants of protein-protein interaction.

BIOMOL-INFORMATICS can build in-silico screening assays specifically tailored for proteins of interest in the development of new anti-pathogen drugs.

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Representation:	Industry
Thematic area of interest	Bacteria in-situ; microcolonies; microcultures and mRNA amplification for Genome-wide bacterial gene expression by microarrays & RT-qPCR
Title of the presentation	**Nanosamples for genome-wide bacterial gene expression studies** **Selective amplification of prokaryotic mRNAs – without any enrichment step**
Partners (name/country) of the planned proposal (if known): not yet known	

Short abstract (max. half page):

Prokaryotic mRNAs do not have a universal 3'-terminal sequence, like the polyA-tail in eukaryotic mRNAs. Therefore, oligo-dT priming enables universal and mRNA-specific priming for eukaryotes but the lack of an equivalent method has hampered prokaryotic gene expression studies: The use of random primers enables universal analysis of mRNAs, but in general, large amounts of total RNA (>10 µg) are required and cDNA products include large amounts of rRNAs (>90% of total RNA).

Although the well established mRNA amplification technologies for eukaryotic microarray studies were adapted for prokaryotic RNAs (Ambion.com: TechNotes 11(5) *Perform Microarray Analysis with Limited Bacterial RNA*) this approach requires an initial rRNA removal step which is tedious, species-specific (thus not universally applicable) and error-prone, especially due to the further combination with an enzymatic polyA-tailing reaction.

Furthermore, the complex procedure requires a minimum of 500 ng total RNA (>5.000.000 cells, based on 0.1 pg RNA per *E.coli* cell).

AmpTec has developed a novel priming strategy with "TR*inucleotide* primers".

The TR*inucleotide* primers result in **specificity for prokaryotic mRNAs** (species-independent selection against rRNAs), combined with 3'-preferential priming without requiring a universal 3'-sequence.

Results are shown for a model experiment, differential gene expression as heat-shock response in *E. coli*. We compared microarray data obtained with large samples (50 µg total RNA) and conventional cDNA labelling versus nano-samples (50 ng total RNA) and TR*inucleotide*-based mRNA amplifications with subsequent hybridisation on microarrays (fluorescent labelling) and Affymetrix GeneChips (biotin labelling). High concordance and data quality was observed, with minimal presence of rRNA sequences (< 2%).

The technology is directly applicable to even smaller samples (appr. 5 ng total RNA) and further extension to pico-samples is possible: appr. 50 pg total RNA or appr. 500 cells, based on 0.1 pg RNA per *E.coli* cell. Techniques for manipulation of these small cell numbers and appropriate RNA isolation methods have to be developed to fully explore the potential of this amplification technology.

To be placed on: www.pathogenomics-era.net	
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Representation:	Research; diagnostic assay development for clinics
Thematic area of interest	Development of microarrays for medical diagnostics, microbe sequencing
Title of the presentation	Comprehensive microarray platform at the Austrian Research Centers serving the development of assays for medical diagnostics
Partners (name/country) of the planned proposal (if known):	

Short abstract (max. half page):

There has been a dramatic rise in the use of microarrays for biological and biomedical research over the last few years since these new tools allow to analyse thousands of genes or proteins simultaneously leading to a better understanding of their function and biological interplay.
The Molecular Diagnostics Unit of the Austrian Research Centers (ARC) can refer to 5 years of microarray experience including both microarray design and production as well as assay development. Our portfolio, focusing on medical diagnostics, comprises not only oligonucleotide-based DNA microarrays for genotyping as well as for gene expression - and DNA methylation analyses, but also protein arrays. Examples of current in-house developments including microarrays for infectious disease and cancer diagnostics will be presented to show the broadness of our applications and to explore how ARC's expertise could be of use for ERA-NET PathoGenoMics project proposals.
The Molecular Diagnostics Unit of the Austrian Research Centers is further planning to establish a new generation sequencing facility which should also be beneficial for the objectives of the PathoGenoMics consortium.

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Representation:	Industry
Thematic area of interest	High throughput bioreactors and IT infrastructure for collaborative research projects (enabling technologies)
Title of the presentation	*A generic information model for biological data integration and analysis*
Partners (name/country) of the planned proposal (if known):	

Short abstract (max. half page):

Evolving measurement technologies provide large amounts of biomedical data from different information domains at an increasing speed. Often, research uses multiple data domains simultaneously and has a specific need for highly dimensional data on dynamic processes. Therefore, sophisticated experiment control and data management needs arise.

Medicel develops software and a bioreactor system for research purposes. Medicel Integrator is a software research infrastructure designed for managing biological research projects and for storing, processing and integration of biological data. Medicel Explorer is a system with 15 parallel bioreactors with individual controls for the design and execution of complex cell cultivation experiments. It allows fast automated sampling for further measurements using off-line technologies. It can be used as a front end to Medicel Integrator through its in-line measurement instruments.

A central piece of the Integrator is its integrated data warehouse. We have developed a unified information model for integration of biological data from multiple information domains and address data management issues that arise thereof. This unified information model is based on general systems theory and has a broad biological knowledge representation power. We discuss how it supports long term integration and precise description (modeling) of primary and derived data from public data sources alongside with data from the research organisation and from collaborators.

In this presentation we will introduce our research hardware and integrative collaborative research software. We offer these two platforms and our know-how to participants of the pathogenomics-eranet project.

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Representation: Choose suitable(s): Research / Clinics / Industry	Research
Thematic area of interest	Bacterial Virulence
Title of the presentation	Relationship between Metabolism and Virulence in certain bacterial pathogens

Partners (name/country) of the planned proposal (if known): Alexandra FRIEDRICH, Germany; Jörg STÜLKE, Germany; Muhamed-Kheir TAHA, France; Sylvie NESSLER, France; Ignacio MORIYON, Spain; Jean-Jacques LETESSON, Belgium.

Short abstract (max. half page):

The virulence of bacteria is frequently affected by the availablity of carbon sources. For example, the uptake of a rapidly metabolizable carbon source (glucose, fructose, cellobiose) by the firmicute *Listeria monocytogenes* inhibits the activity of PrfA, a transcription activator for the major virulence genes of this organbism, by a yet unknown mechanism. In addition, to be operative PrfA requires a functional phosphotransferase system (PTS), the main carbohydrate uptake and phosphorylation system in bacteria. Pathogenic proteobacteria and symbionts frequently contain an incomplete PTS (the membrane component is lacking). This system cannot transport sugars, but carries out only regulatory functions. The PTS genes are frequently located in an operon together with genes affecting the virulence of these organisms. Indeed, we found that inactivation of genes encoding PTS proteins prevents the synthesis of the components of a type IV secretion system necessary for the virulence of *Brucella melitensis*. Similar mutations introduced into *Neisseria meningitidis* have an influence on the synthesis of capsular polysaccharides and on cell adhesion as well as on the survival rate in a mouse model. The effects of the PTS components on bacterial virulence seem to be related to the phosphorylation state of the PTS proteins, which is governed by glycolytic intermediates, ATP and the PEP/pyruvate ration in bacterial cells. In addition, inactivation of a PTS-related, metabolite controlled protein kinase in *Mycoplasma pneumoniae* prevents the cytotoxic effect of this organism on HeLa cells.

During the project we plan to propose we will try to unravel the detailed molecular mechanisms underlying these phenomena in Listeria, Neisseria, Brucellae and Mycoplasmae and to identify potential targets for new antimicrobial agents. The PTS proteins seem to be most suitable for this approach, because this system is unique for bacteria.

In addition to searching for other academic partners willing to join us in these research activities, mainly in the clinical area, we are also searching for industrial partners.

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Representation:		Research
Thematic area of interest	Bacterial virulence, metabolism and diagnosis	
Title of the presentation	Relationship between carbon metabolism and virulence in intracellular pathogens: developing a combined growth medium-DNA typing tool applicable to the direct diagnosis and identification of *Brucella*.	
Partners (name/country) of the planned proposal (if known): Josef DEUTSCHER, France; Alexandra FRIEDRICH, Germany; Jörg STÜLKE; Germany, Muhamed-Kheir TAHA, France, Sylvie NESSLER, France		

Short abstract (max. half page):

Objectives:

- To perform a microarray analysis of gene expression to identify candidates involved in virulence/host adaptations, including metabolic pathways.
- To study the effect of C sources and substrates reported to accelerate *Brucella* growth in *Brucella* metabolism and to design an improved growth medium.
- To develop a molecular typing tool for the direct identification of species and biotypes in growth media.

To identify shifts related to metabolic adaptations likely to occur in the host or described as promoting *Brucella* growth, we will compare gene expression in exponential and stationary phase of *Brucella* wild type grown in a defined DMEM as well as in minimal media with glucose or glutamate-lactate as carbon sources supplemented or not with inositol or erythritol. Likewise, we will carry on with the studies of gene expression in the two-component regulatory system *bvrR/bvrS* mutants. In these studies, we will take advantage of the *Brucella* microarray constructed by us as a result of previous projects.

Optimal combination of the growth medium components will be determined by checkerboard using a high throughput Bioscreen system which enables the simultaneous comparison of strains and media (C sources and supplements) combinations as well as the automatic calculation of the lag and generation times and final growth yields.

The complete sequence of the genomes of *B. melitensis, B. suis*, *B. abortus* and *B. ovis* will be used to search regions of DNA sequence variability that might be useful as markers for identification and differentiation. Specific multiplex PCR assays will be developed to discriminate between all biovars of *B. melitensis*, *B. abortus*, and *B. suis*. These new tests will be combined with our multiplex Bruce-ladder PCR assay, which discriminates *brucellae* species, into a new test that would also discriminate all *Brucella* biovars not only upon isolation in pure culture but also directly in the new media. These PCR protocols will be transferred to a real time PCR platform.

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Representation: Choose suitable(s): Research / Clinics / Industry		Research
Thematic area of interest	Microbial pathogenesis	
Title of the presentation	Subversion of host cell functions by bacterial respiratory pathogens	
Partners (name/country) of the planned proposal (if known):		

Short abstract (max. half page):

Subversion of host cell physiology by bacterial pathogens is essential for a successful progression of the infection. Pathogens display a repertoire of specific and often sophisticated virulence factors in order to modulate host cell functions in their own benefit, generating the unbalance of the host fine tuned inflammatory status. The outcome of the host-pathogen interplay will be highly modulated by the host innate immunity, represented by a broad range of host defences (secretion of antimicrobial peptides, recruitment of neutrophils, secretion of inflammatory cytokines…). Host immune status itself can be modulated by a number of factors such as age, diet/drinking/smoking habits, genetic alterations, long-term medication, and others.

In the laboratory we are using as a model organism the respiratory pathogen non-typable *Haemophilus influenza* (NTHi). Our ongoing projects aim to: (i) understand the strategies developed by NTHi to subvert the lung epithelium/alveolar macrophages host cell machinery in order to achieve survival and persistance/replication; (ii) delineate the role of NTHi lipoologosaccharide and adhesion factors to the dynamics of host-pathogen interaction; (iii) define host cell responses (at a genomic scale) derived from NTHi infection and the effect of a range of physiological alterations in such host responses.

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Representation:		Research / Clinics
Thematic area of interest	Host-Pathogen interaction of Gram-negative bacteria	
Title of the presentation	**Molecular pathogenesis in *Aeromonas***	
Partners (name/country) of the planned proposal (if known): we are looking for partners or to be included in a project		

Short abstract (max. half page):
Genomic and proteomic analyses of molecules/structures able to determine *Aeromonas* virulence. Studies with mutant characterization of molecules like LPS and outer-membrane proteins (especially with iron capturing systems). Genetic and molecular characterization of *Aeromonas* induced surface structures like lateral flagella (basic for adhesion and invasion) and capsules. Mutant isolation, mainly avirulent, in genes obtained after genomic subtraction between *Aeromonas* virulent and avirulent strains, with special focus on type III secretion system described by us in *Aeromonas* for the first time. Characterization of the toxins secreted by this system always related to bacterial pathogens. Genetic and molecular determination of genes related to biofilm formation using an IVET (in vivo expression technology) system. Identification of virulent genes in two different infectious models (fish and mice) using STM (site-tagged mutagenesis) linked to microarrays. Finally, use of genes (free DNA vaccines) and molecules/structures (cell-free vaccines) fundamentals for *Aeromonas* virulence as immunoprophilactics.

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Representation:		Research
Thematic area of interest	*Salmonella* interaction with host cells	
Title of the presentation	Type III secretion systems in *Salmonella enterica*	
Partners (name/country) of the planned proposal (if known):		

Short abstract (max. half page):

Type III secretion systems (T3SS) enable pathogenic Gram-negative bacteria to secrete and inject (translocate) pathogenicity proteins (effectors) into the cytosol of eukaryotic host cells. Injection of effectors into the cytosol of animal or plant cells initiates a biochemical cross-talk between pathogen and host. The effectors often interfere with eukaryotic signal transduction pathways. In this way they establish niches for colonization and avoid the host defense response. *Salmonella enterica* is a bacterial species belonging to the Enterobacteriaceae family. Some *Salmonella* serovars cause a broad spectrum of diseases including gastroenteritis, bacteremia and typhoid fever, depending on the serovars and the animal species infected. Salmonellae contain two T3SS encoded by two pathogenicity islands termed SPI-1 and SPI-2. The system encoded by SPI-1 is necessary for invasion of epithelial cells and for the initial penetration of the intestinal mucosa. The T3SS encoded by SPI-2 is activated following entry of bacteria into eukaryotic cells, facilitates bacterial multiplication and is essential for the systemic stages of infection. We are interested in improving our knowledge of *Salmonella*–host interaction through the identification and functional study of T3SS effectors of this pathogen. Specific objectives are: 1) Analysis of the function of the interaction of known effectors with mammalian proteins during *Salmonella* infections. We are performing two-hybrid screening in yeast to find these interactions. 2) Study of the regulation of *srf* genes, the secretion and translocation of the Srf proteins and their role in virulence. These proteins are T3SS candidate effectors because SsrB, the SPI-2 regulator, regulates their expression. 3) Identification of new *Salmonella* T3SS effectors. We are exploring the possibility of performing a screen on a library of translational fusions between *Salmonella* chromosomal genes and a fragment of the calmodulin-dependent adenylate cyclase gene derived from *Bordetella pertussis* (*cyaA*').

Although our group is of recent creation, we have a background in the study of *Salmonella* genetics and virulence (see J. Bacteriol. 2007, 188:7963-7965; Microbiology 2005, 151:579-588; J. Microbiol. Methods 2004, 56:83-91) and a previous background in the study of signal transduction in mammalian cells (see, for instance, Nat. Genet. 2002, 32:306-311; Oncogene 2000, 19:403-409; J. Biol. Chem. 1998, 273:1634-1639), two necessary components to the study of pathogen-host cell interactions. We are very much interested in making contacts and establish productive collaborations with other groups involved in this field of research.

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Representation: Choose suitable(s): / Clinics / Industry		Research
Thematic area of interest	Intracellular bacteria	
Title of the presentation	Genes responsible for intracellular survival in mycobacteria and chlamydiae	
Partners (name/country) of the planned proposal (if known):		

Short abstract (max. half page):

Our research interests focus on the genetic mechanisms utilized by mycobacteria and chlamydiae to promote their intracellular survival and reactivation within the eukaryotic host cell. Mycobacteria require the regulated expression of a set of genes to maintain a persistent infection. We would like to study some of the genes important for intracellular survival and reactivation of mycobacteria and *Chlamydophila pneumoniae*. Their products could be possible targets for drug development. Among others, special emphasis will be dedicated to the role of RNase E in the regulation of RNA metabolism, SmpB and trans-translation and in general the connection of bacterial metabolism and pathogenecity.

This is basic research with cloning, expression, purification and optionally characterisation of proteins, which can serve as potential drug targets, either because they are virulence factors, or conserved regulatory proteins, essential for cell viability. With the methods for molecular engineering we are able to create recombinant *Escherichia coli*, *M. bovis* BCG or *M. smegmatis* cells to study the impact of our target protein on intracellular survival or even to develop vaccine candidates for TB.

We would gladly cooperate with pharmaceutical, bioinformatics companies to participate in projects leading to the development of antibacterial drugs or vaccines, especially against *M. tuberculosis*.

On the other hand we keenly offer our facilities to research groups or companies with differing ideas, which are seeking for academic groups with this kind of background.

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Representation:	Clinics and research
Thematic area of interest	Prosthetic joint infections
Title of the presentation	Detection of prosthetic joint infection in septic and aseptic loosening
Partners (name/country) of the planned proposal (if known):	

Short abstract (max. half page):

Implantation of orthopedic prostheses is now a common practice everywhere. For the enormous number of surgical procedures involving implantation of invasive foreign biomaterials, even if nowadays rare, complications such as infections and early aseptic loosening have a huge impact on morbidity, mortality and medical costs. True differentiation between early aseptic and septic loosening can be extremely difficult if not impossible in many cases.

The isolation of the offending organism is sometimes difficult, despite improved technologies and new methods. Treatment strategy is therefore often speculative and not well defined. For all this reasons improved diagnostic and treatment tools clearly are warranted.

A well-designed and carefully conducted study will include all patients undergoing removal or exchange of a knee or hip prosthesis for septic or aseptic loosening in a period of two years (1.1.2009 to 31.12.2010 presumably 300+ cases?) We will compare the results of different methods used for the microbiologic diagnosis; culturing of samples of periprosthetic tissue and culturing of samples obtained from the explanted prostheses bath using a short, low-energy ultrasound.

In addition we would like to define a new method for differentiation between septic and aseptic loosening during surgical intervention including specific calorimetric techniques on the samples obtained from the sonicate of explanted prostheses.

With comparison of standard and new microbiologic and calorimetric techniques we would like to determine a method to help answer during surgical intervention when aseptic loosening is truly aseptic and not actually a variant of a low-grade septic one. Exact answer to this question eventually guides different but already well defined treatment strategies.

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Representation: *Choose suitable(s):*	Research
Thematic area of interest	Prosthetic joint infections - biomaterials
Title of the presentation	Susceptibility for infection of conventional orthopedic implants
Partners (name/country) of the planned proposal (if known):	

Short abstract (max. half page):

Implantation of orthopedic prostheses is now a common practice everywhere. For the enormous number of surgical procedures involving implantation of invasive foreign biomaterials, even if rare, complications such as infections have a huge impact in terms of morbidity, mortality and medical costs.

The susceptibility of various materials used in orthopedic surgery to infection with bacteria is still rather unknown. All current strategies to determine the infection rate assume that the interface between biomaterial surface and surrounding tissue represents the setting where bacterial contamination develops into an established and clinically relevant infection. It is this interface thus the appropriate ground for the susceptibility studies.

In a well-designed and carefully conducted study we will try to define a new protocol for in vitro and in vivo testing of different biomaterials used in orthopedic surgery such as: commercially pure titanium, titanium alloy, Co-Cr alloy, and polyethylene regarding bacterial infection susceptibility (St. aureus …..).

Firstly we will modify a well-known method for in vitro seeding and detaching bacteria from glass beads to be appropriate for beads of interested biomaterials. Then we will proceed with use of different methods such as: standard culturing, sonication, calorimetric techniques, PCR, for improved bacterial detachment from infected biomaterials, the microbiologic diagnosis and determination of the bacterial quantity to determine the in vitro propensity of bacteria to colonize different biomaterials.

Secondly an animal model modification for bacterial foreign body infection will be instituted using reduced size plates and balls produced from the same orthopedic biomaterials as for the in vitro part and of the same quality of the real implantable devices. By implanting one plate and two balls of a biomaterial of interest under the skin of a mouse, on each side on the back and proceeding with standardized inoculation to induce a device related infection we will standardize the study animal model. Following implantation we will observe mice for 7 to 10 days, and then after killing them we will extract the material and the surrounding tissue. With the already mentioned in vitro protocol for bacterial infection diagnosis and analyses and some additional histological and material testing we will tray to determine the in vivo predisposition of bacteria to colonize the biomaterial. All the other substances will then be tested in the same fashion searching for the differences.

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Representation: Choose suitable(s): Research / Clinics / Industry	Research
Thematic area of interest	Fungal infections
Title of the presentation	Emergence and evolution of denture-related stomatitis: role of the oral microbial community.

Partners (name/country) of the planned proposal (if known):

Short abstract (max. half page):
Denture-related stomatitis (DRS) is an inflammatory process involving the palatal mucosa when it is covered by total or partial dentures, with prevalence values ranging from 24 to 60%. Aetiological factors in DRS include the trauma caused by an ill-fitting denture, lack of oral and prosthesis hygiene and a favourable environment for proliferation of microorganisms. The infective factors are essentially associated with the presence of an increased number of *Candida* spp, mainly *C. albicans* although it has also been connected with bacteria from the oral cavity. Given the complexity of the oral microbiota it is quite unrealistic to assume that a single organism, rather then a consortium or community, is responsible for the emergence and evolution of the pathology. Our overall objective is to study possible associations and interactions of *C. albicans* and bacteria in the emergence/development of DRS.

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Representation:	Research / Clinics / Industry
Thematic area of interest	Diagnostics
Title of the presentation	Enhancement of pathogen detection in molecular clinical diagnosis and applied testing by targeted nucleic acid isolation
Partners (name/country) of the planned proposal (if known): not yet	

Short abstract (max. half page):

In nucleic acid-based analysis of pathogens a variety of factors can compromise the results. Among them are PCR-inhibiting substances co-eluted during the nucleic acid isolation procedure. Further, in complex biological samples such as blood, punctates, liquor and food a high proportion of non-target (human, animal) to target nucleic acids exists. During PCR reactions primers can bind to non-target nucleic acids, thereby reducing sensitivity and specificity of the assay. Molzym has developed and commercialised an IP-based procedure, MolYsis, for the selective enrichment of pathogen cells (bacteria, fungi) and subsequent isolation of nucleic acids from blood and other body fluids. As a result the analytical sensitivity of a universal rDNA qPCR detection assay can be increased by up to 20,000 fold. Molzym is seeking for partnership in the field of development of new analytical approaches taking advantage of the innovative pre-analytical procedure. Applications could be clinical diagnosis or applied testing in food and pharma industries. Because of its modular nature MolYsis can be combined with any downstream pathogen detection and monitoring system. Among them could be hybridisation assays, DNA or RNA-based array technologies or mass spectrometry.

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Representation:	Industry
Thematic area of interest	New drug discovery methods
Title of the presentation	Positive selection of protein translation inhibitors
Partners (name/country) of the planned proposal (if known): Manuel Santos, Portugal	

Short abstract (max. half page):

Omnia Molecular is a biotechnology company dedicated to the discovery of new anti-infective compounds. Omnia is developing proprietary technology designed to accelerate the process of lead discovery, allowing larger numbers of compounds to be screened and speeding up the process of taking selected hits to clinical trials.

Omnia is focused on multi-drug resistant bacterial and fungal pathogens. We are interested in the identification of compatible partners that can benefit from our expertise and collaborate with us in the development of our projects.

In this presentation we will introduce our company, discuss our scientific program, and present our first preliminary results in the identification of new families of anti-infectives.

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Representation:	Research
Thematic area of interest	Molecular basis of the infectious diseases
Title of the presentation	Study of the fluoroquinolone targets in *Streptococcus pneumoniae*: regulation of *gyrA* expression and interspecific transfer of resistance.

Partners (name/country) of the planned proposal (if known):

Short abstract (max. half page):

Streptococcus pneumoniae is an important human pathogen and a major cause of pneumonia, meningitis, otitis media and sepsis. This broad pathogenic potential reflects its ability to adapt to different habitats within the human host. The emergence of resistance to antimicrobial agents commonly used for the treatment of pneumococcal diseases, has highlighted the need for novel antimicrobial agents directed at new targets. DNA topoisomerase IV (topo IV) and DNA gyrase (gyrase) are the molecular targets of Fluoroquinolones (Fqs). These enzymes belong to the type II topoisomerases which function by passing one DNA double helix through another, using a transient double-strand break. Gyrase is an A_2B_2 complex encoded by *gyrA* and *gyrB* genes and catalizes ATP-dependent negative supercoiling of DNA and is involved in DNA replication, recombination and transcription; topo IV, a C_2E_2 complex encoded by *parC* and *parE* genes, is essential in chromosome partitioning. Both enzymes affect supercoiling, which is altered by a number of external stimuli, growth phase and the infection process. Regulation of *gyrA* expression is dependent on the DNA supercoiling as its transcription is activated when DNA is relaxed through inhibition of DNA gyrase activity by Novobiocin. Moreover, a bending motif in *gyrA* promoter region acts as a transcriptional inhibitor.

Besides mutations in gyrase and topoIV, fluoroquinolone-resistance in pneumococcus is acquired by horizontal transfer. By this mechanism, *via* recombination, pneumococal strains can interchange genetic material with the viridans group streptococci (VGS) yielding hybrid genomes. These interchanges take place in the oropharinx where the VGS are commensals as pneumococci can be. Some fluoroquinolone-resistant pneumococcal strains have mosaic structures in those genes coding for the topoIV and the gyrase. Moreover, it has been detected the presence of an *ant*-like gene in the intergenic *parE-parC* region interchanged. The *ant*-like gene is absent from *S. pneumoniae* strains whereas is present in the intergenic *parE-parC* region of viridans group streptococci. As the VGS share the same mechanism of resistance to Fqs than pneumococcus and the prevalence to this antimicrobial is higher than values found in pneumococcus, the VGS could represent a reservoir of resistance to this group of antibiotics.

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Representation:	Research
Thematic area of interest	Bioinformatics, Structural Biology, Tropical Diseases
Title of the presentation	Genome-wide characterization of structural determinants of the evolution of Mycobacterium tuberculosis drug resistance.

Partners (name/country) of the planned proposal (if known):
Matthias Wilmanns, EMBL-Hamburg (Germany) and Stefan Niemann, CMB-Borstel(Germany)

Short abstract (max. half page):

Marc A. Marti-Renom1, Stefan Niemann2, Matthias Wilmanns3
1Structural Genomics Unit. Bioinformatics Department, Prince Felipe Research Center, Valencia, Spain, 2Molecular Mycobacteriology Group, NRC for Mycobacteria, Research Center Borstel, Borstel, Germany, 3EMBL Hamburg Unit, Hamburg, Germany.

With about 8 million individuals newly diseased and about 2 million deaths each year, tuberculosis (TB) is the deadliest bacterial infection worldwide. The problem is reinforced by the development of multi-drug resistant strains (MDR) and the increasing rates of dual infection with HIV. Gloomy as the numbers are, only an estimated 10% of the 2 billion infected individuals worldwide will actually develop TB disease in their lifetimes, pointing to a remarkable influence of host and pathogen genetic factors in modulating infection outcome.

The actual situation in drug resistance "hot spots" is increasingly influenced by the emergence and clonal expansion of highly transmissible MDR strains strongly arguing for a bacterial evolution towards a hyper virulent phenotype. The application of ultra-high throughput genome sequencing approaches has allowed us to trace microevolution in MDR strains and to identify the genomic variations in MDR outbreak strains. However, the large amount of genetic variation determined (>100 single nucleotide polymorphisms, SNPs) renders interpretation of the results difficult and demonstrates the need for new tools allowing to identify those genetic variants that have a functional implication and might be involved in the network of genes modulating disease associated capacities of clinical isolates e.g. compensating for drug resistance phenotypes.

In our presentation we will outline our research in the context of the goal of this proposal, which is to combine computational and experimental approaches to characterize the evolutionary and structural changes affecting response variation to treatment against MTB. To achieve such aim we propose to develop and apply computational tools for the prediction of functional implications of experimentally characterized SNPs. Such predictions will be then used to guide functional and structural experiments to characterize the determinants of multi-drug resistance in MTB.

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Representation:		Research
Thematic area of interest	Vaccine candidates, surface proteins, streptococci, proteomics	
Title of the presentation	New proteomic approaches for identifying vaccine candidates in pathogenic Gram-positive bacteria	
Partners (name/country) of the planned proposal (if known):		

Short abstract (max. half page):

Bacterial surface proteins play a fundamental role in the interaction between cell and its environment. They constitute a diverse group of molecules with important functions. Moreover, they are potential drug or vaccine targets. The post-genomic era offers exciting new opportunities for vaccine research, which are expected to shorten the time of vaccine discovery. The new genomic and proteomic technologies allow the search for new targets at a genome-wide level, but the enormous number of candidates identified can overwhelm the required *in vivo* validation process, leading to question the ultimate impact of these strategies on speeding up vaccine discovery. The specific area of research to which the proposal refers is the identification of a set of potential vaccine candidates against two pathogenic Gram-positive bacteria: the first species is *Streptococcus pneumoniae*, which is pathogen in humans, being the leading cause of infective pneumonia in children and adollescents. Pneumococcal infections have increased in frequency and severity in the last decade in the developed countries, and they are a major problem in developing countries. This resurgence has heightened public concern, largely because no totally effective vaccine is available, resistance to certain antibiotics has recently emerged, and pneumococcal infections can cause high morbidity and mortality. The other bacterium is S. suis, a swine pathogen causing different pathologies, which, in addition to originate economic losses, can cause zoonosis in people which are in close contact with infected animals.

In this proposal, a novel shotgun-proteomics based approach will be applied to identify streptococcal protein vaccine candidates, consisting of the surface digestion of live bacteria with proteases, the recovery of generated peptides and their separation and identification by two-dimensional chromatography coupled to tandem mass spectrometry (2-D LC/MS/MS). This will allow a fast identification of highly expressed and exposed proteins. The proteins identified will be validated to assess their *in vivo* accessibility to antibodies. Finally, protection assays on animal models will be carried out with the selected proteins.

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Representation: Choose suitable(s): Research / Clinics / Industry		Research / Clinics / Industry
Thematic area of interest	Gram-negative pathogens	
Title of the presentation	Lipopolysaccharides with design: a new way to obtain vaccines from E. coli cells	

Partners (name/country) of the planned proposal (if known): we are looking for partners or to be included in a project

Short abstract (max. half page):

According to the DNA sequence obtained from the *E. coli* K12 *waa* gene cluster (which codifies for the lipopolysaccharide (LPS)-core, and the use of genetic recombination in frame, we wish to obtain an *E. coli* K12 mutant with only the *waaA* gene (the only essential gene in *waa* which codifies for the Kdo transferase), which would allow us to obtain an E. coli K12 strain with only Kdo in their LPS. The construction of LPSs with design from this strain will be by introduction of the *waa* gene clusters from different Gram-negative bacteria. With the enteric bacteria, because all these genes are clustered in a single *waa* gene cluster with a single plasmid, like in *Klebsiella pneumoniae*, *Serratia marcescens*, *Proteus*, *Plesiomonas shigelloides*, and others, previously obtained in our research group and some of them already published. In other Gram-negative bacteria with an already known genome we will be able to detect *waa* genes (no always correctly assigned) and in some cases not in a single *waa* gene cluster, like for instance *Yersinia*, *Actinobacillus*, *Pasteurella*, *Haemophilus*, *Neisseria*, etc were two or more clusters could be detected. In these cases we would amplify the different *waa* gene clusters and using compatible plasmids we will introduce in the strain *E. coli* K12 with only *waaA*. Finally, we will study the immunoprotective ability of this mutant strain carrying the different *waa* gene cluster/s against experimental infections with the corresponding Gram-negative bacteria

POSTERS

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Representation: Choose suitable(s): Research / Clinics / Industry	Research
Thematic area of interest	DNA repair, virulence factors, divalent cations uptake
Title of the presentation	IDENTIFICATION OF NOVEL TARGETS FOR ANTIBACTERIAL COMPOUNDS DEVELOPMENT

Partners (name/country) of the planned proposal (if known):

Short abstract (max. half page):

The increase of bacteria resistance to chemotherapeutic agents is stimulating the search of new strategies to attack human and animal infections. One of them is the use of vaccines by using either attenuated mutants of pathogenic strains or immunogenic and antigenic outer membrane proteins, which generate specific host humoral response and protection against the bacterial infection. Another approach is the design of new antibacterial compounds based in cellular processes not explored so far as some aspects of the DNA metabolism such as DNA repair pathways. Identification of these novel targets can open future perspectives to develop new antibacterial compounds.

Our team has been working for more than 25 years about several aspects related with the DNA repair in bacterial cells, the study and identification of virulence factors, the design of animal bacterial vaccines and the study of immunogenic divalent cation-uptake proteins. Further, our works have been focused on different bacterial pathogens as *Salmonella enterica, Pasteurella multocida, Haemophilus parasuis, Streptococcus suis, Pseudomonas aeruginosa* and *Staphylococcus aureus*. As a consequence of all these studies, our group has an strong expertise in bacteria manipulation and selection, randomly or site-directed mutant construction and in *in vitro* techniques as quantitative PCR or RT-PCR, protein purification, electroforetical mobility assays, footprinting assays, unknown DNA binding proteins isolation, pulse field gel electrophoresis, DGGE, or arrays hybridization. Also we have carried out several *in vivo* procedures using different animal models, evaluating the virulence of bacterial strains as well as performing challenge experiments for protection study assays related with new vaccine development.

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Representation: *Choose suitable(s):* Research / Clinics / Industry		Research
Thematic area of interest	Model organisms, yeast, bacterial virulence factors	
Title of the presentation	Yeast as a tool to find and assess the function of bacterial virulence factors	
Partners (name/country) of the planned proposal (if known):		

Short abstract (max. half page):

The budding yeast *S. cerevisiae* is a well-known and easy to manipulate model eukaryotic organism that has gained importance in the latest years due to the broad availability of post-genomic tools. Given the conservation of signalling modules that regulate the cytoskeleton, trafficking and cell cycle between yeast and higher eukaryotes, our group in the University of Madrid has proposed this system for studying the function of bacterial virulence factors injected into host cells by Type III Secretion Systems (TTSS). We have successfully used this system to study *Salmonella* and enteropathogenic *E. coli* TTSS effectors that interfere with yeast GTPases and MAP kinase pathways [Rodríguez-Escudero *et al*. (2006) *Microbiology* 152:3437-52; Alemán *et al*., (2005) *Cell Microbiol*. 7:1432-46; Rodríguez-Escudero *et al*. (2005) *Microbiology* 151:2933-45; Rodríguez-Pachón *et al*., (2002) *J Biol Chem*. 277:27094-102]. "Humanized" yeasts, expressing human host targets of bacterial virulence factors coupled to yeast signalling pathways, can also be used to screen for novel virulence factors or to study the function of known virulence factors, as well as the interaction with their targets in an *in vivo* scenario. Given its technical simplicity as compared to classic *in vivo* cellular microbiology assays, this system could be used systematically on candidate virulence-related genes obtained from post-genomic analyses on pathogenic bacteria.

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Representation: Choose suitable(s): Research / Clinics / Industry	Research
Thematic area of interest	Extended-spectrum b-lactamase producing Gram negative pathogens
Title of the presentation	Trends and shifts in ESBL production in Klebsiella spp. in Hungary
Partners (name/country) of the planned proposal (if known):	

Short abstract (max. half page):

ESBL- producing klebsiella isolates were collected from all over Hungary between 2002 and 2006. Strains were tested for ESBL production and detected TEM, SHV and CTX-M type ESBL genes were sequenced. The clonal distribution was investigated by PFGE on all isolates and by MLST on selected strains. From 2002 to 2004 SHV-5 and SHV-2a proved the dominant enzymes in Hungary. Molecular typing techniques established that several epidemic plasmids were responsible for the dissemination of these ESBL genes. No clonal relationship could be established among various outbreak isolates. In contrast to previous observations CTX-M-15-producing Klebsiella pneumoniae emerged as the most prevalent ESBL-producing pathogen in the country in 2005. Most of the strains belonged to one of three large epidemic clones corresponding to sequence types 11, 15 and 147 respectively.

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Representation: Choose suitable(s): Research / Clinics / Industry		research
Thematic area of interest	*Yersinia enterocolitica* pathogenesis, gene regulation, DNA methylation	
Title of the presentation	Regulatory networks controlling virulence factor expression in *Yersinia enterocolitica*	

Partners (name/country) of the planned proposal (if known): Antonia Juarez (Spain), Josep Casadesus (Spain), Bianca Colonna (Italy), Lionello Bossi (France)

Short abstract (max. half page):

Bacteria are faced with constantly changing environments. These changes have to be sensed by the bacteria in order to adapt their lifestyle and behavior accordingly. This is not only true for bacteria in environmental habitats, but is especially important for pathogens after an infection of a host. A prerequisite for adaptation is that changes can rapidly and correctly be sensed by the bacteria and are translated into appropriate transcriptional responses.

We analyzed the regulation of the *hreP* gene of the enteropathogenic bacterium *Yersinia enterocolitica*. *hreP* is expressed specifically during an infection, but not under standard laboratory conditions, and is necessary for full virulence. By transposon mutagenesis we identified three regulators of *hreP* transcription that we called *pyp* (for *protein regulating expression of Yersinia hreP*). Each of these regulators acts independent of the others in activating *hreP* transcription; however, they are connected on transcriptional level, as two of the regulators activate each other's transcription. Further analyses indicate that the regulators not only control the transcription of *hreP*, but also the expression of other phenotypes associated with virulence. These include type-II protein secretion and type-IV pili. Genomic analysis indicates that the regulators are predominantly found in the genus *Yersinia*, and probably have been acquired horizontally. Interestingly, similar genes can be found on mobile genetic elements in some other enteropathogenic bacteria. Preliminary data suggests that global regulators like RovA and H-NS further modulate expression of the *pyp* genes.

In addition to the Pyp regulatory network we study the influence of DNA methylation on gene expression in *Y. enterocolitica*. Overproduction of the DNA adenine methyltransferase (DamOP) results in deregulation of virulence factor expression. The affected phenotypes include type-III secretion, motility, invasion into host cells, and LPS expression. On molecular level, this is in part mediated via proteolytic degradation by the ClpP proteasomal protease. As DamOP mainly results in changed phenotypes associated with the bacterial surface, this might reflect a general mechanism how *Y. enterocolitica* modulates the immune recognition by the host.

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Representation:		Industry
Thematic area of interest	Bacteria in-situ; microcolonies; microcultures and mRNA amplification for Genome-wide bacterial gene expression by microarrays & RT-qPCR	
Title of the presentation	**Nanosamples for genome-wide bacterial gene expression studies** **Selective amplification of prokaryotic mRNAs – without any enrichment step**	
SEE THE ABSTRACT UNDER 'ORAL PRESENTATIONS'		

To be placed on: www.pathogenomics-era.net		
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Representation:		Research
Thematic area of interest	Helicobacter	
Title of the presentation	**The role of genetic polymorphisms of NOD1 , TLR4, IL-8 and defensin genes in *Helicobacter pylori*-induced duodenal ulcer and gastritis**	
Partners (name/country) of the planned proposal (if known):		

Short abstract (max. half page):

The SNPs of genes and pattern recognition molecules were investigated by RFLP and ARMS reactions applying the DNA of patients with chronic gastritis and duodenal ulcers.

- NOD1 rather than TLR4 is of functional significance in sensing *H. pylori*
- AA genotype of NOD1 G796A polymorphism is a potential risk factor in *H. pylori*-induced duodenal ulcer
- The genetic determination of higher IL-8 production is important not only in ulcerative processes but also in chronic gastritis
- SNPs in human defensin beta1 gene are also risk factors for gastritis

Conclusion:

- Host factors, including intracellular pathogen receptors, IL-8 and defensinin production fluence *H.pylori*-induced mucosal damage

Further ,INTERNATIONAL. MULTICENTER studies, increasing the number of patients would be necessary to confirm these results. We are open to investigate DNA samples from different countries

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Thematic area of interest	Host-Pathogen interaction of Gram-negative bacteria	
Title of the presentation	**Molecular pathogenesis in *Aeromonas***	
SEE THE ABSTRACT UNDER 'ORAL PRESENTATIONS'		

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Representation:		Research / Clinics / Industry
Thematic area of interest	Gram-negative pathogens	
Title of the presentation	Lipopolysaccharides with design: a new way to obtain vaccines from E. coli cells	
SEE THE ABSTRACT UNDER 'ORAL PRESENTATIONS'		

NO PRESENTATION

To be placed on: www.pathogenomics-era.net	
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Representation: *Choose suitable(s): Research / Clinics / Industry*	Research and Clinics
Thematic area of interest	Diagnosis and vaccines of intracellular bacteria
Title of the presentation	
Partners (name/country) of the planned proposal (if known): Chantal de Chastellier/France	
Short abstract (max. half page): Our group research interest is focussed to intracellular bacteria innate and adaptive immunity using *Listeria monocytogenes* and *Mycobacterium ssp*. as model pathogens. Our purpose is to characterize common intracellular-derived virulence factors to both pathogens to use them in vaccine constructs and prove the hypothesis of multimeric vaccines, that is, vaccines effective for more than one intracellular pathogen. Our group is also interested in discovering cell factors involved in both pathogens cell biology and immunity to search for novel drugs to treat both infectious diseases: listeriosis and tuberculosis.	

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Representation:	Research
Thematic area of interest	Pseudomonas aeruginosa pathogenesis and biofilm formation
Title of the presentation	
Partners (name/country) of the planned proposal (if known): Jean Marc Ghigo	
Short abstract (max. half page): Pseudomonas aeruginosa, such as most microbes exist as surface associated communities called « biofilms ». The biofilm lifestyle is an efficient means for microorganisms to maintain a protected niche. In humans, establishment of the biofilm leads to chronic bacterial infection. Biofilms have been shown to display increased resistance to antibiotic treatment and are recalcitrant to eradication via the immune system. To spawn novel communities in new locations, microorganisms must successfully transit from the biofilm to the planktonic growth state. Whereas molecular knowledge on the biofilm formation process is now increasingly available, how bacterial cells detach is largely unknown. However, a productive field of investigation is likely to be the identification of molecular targets, which induce natural dispersion of the biofilm and make the released planktonic bacteria accessible to efficient therapeutic treatments. Our group will focus on identifying the key regulators that are involved in the perception of environmental cues that induce biofilm formation or dispersion and on the characterization of the molecular determinants that mechanically contribute to biofilm development and subsequent disruption.	

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Representation:	Research
Thematic area of interest	Microbial biofilms
Title of the presentation	
Partners (name/country) of the planned proposal (if known):	

Short abstract (max. half page):

The objectives of the studies undertaken in the laboratory are to identify bacterial factors involved in the formation of commensal and pathogenic *Escherichia coli* biofilms, with particular emphasis on biofilm-specific physiological properties and competitive bacterial interactions within mixed biofilms (see www.pasteur.fr/recherche/unites/Ggb).

We use of genetic, genomic and molecular biology approaches combined with different biofilm models, has enabled us: **(i)** to identify several bacterial factors promoting both initial surface contacts and bacterial-bacterial interactions during the tri-dimensional development of the biofilm; **(ii)** to study gene regulatory pathways involved in, or specifically associated with, biofilm formation; **(iii)** to investigate functions performed in the heterogeneous biofilm environment both in mono and multispecific contexts and **(iv)** to maintain several close collaborations in which similar questions have been addressed in other microorganisms such as *Salmonella enteritidis, Klebsiella pneumoniae, Staphylococcus aureus, Candida albicans* and *Candida glabrata.*

These approaches may lead to a better fundamental knowledge of this predominant bacterial lifestyle and help design biofilm control strategies.

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Representation:		Research
Thematic area of interest	Bacterial biofilms	
Title of the presentation		
Partners (name/country) of the planned proposal (if known):		

Short abstract (max. half page):

Biofilms are communities of microorganisms growing on a surface and enclosed in an exopolysaccharide matrix. Microbial biofilms are responsible for many nosocomial infections related with the use of implants (orthopaedic devices, urinary catheters, prosthetic heart valves). These interactions are characterized by their tendency towards chronicity and resistance to antibiotic treatment.

The main focus of our research is the study of biofilm formation process in two pathogenic bacteria: staphylococci and salmonella. We are interested in identifying the structural compounds of the biofilm matrix, the regulatory mechanisms controlling this bacterial lifestyle and the contribution of biofilm formation to the bacterial virulence, long-term survival in the environment and horizontal DNA transfer. The approaches that we use in our research projects are mainly based in our expertise in bacterial genetics and molecular biology that we try to combine with global proteomic, transcriptomic and genomic approaches.

In the last few years, our group has significantly contributed to the elucidation of several aspects of bacterial biofilm formation process, notably with (i) the identification of new family of surface proteins required for biofilm formation (Bap, biofilm associated protein); (ii) identification of cellulose as a major exopolysaccharide compound of the biofilm matrix of *S. enteritidis* together with the evaluation of the role of GGDEF proteins in regulation of cellulose biosynthesis; (iii) analysis of the role of global virulence regulators (sarA, σ^B, agr, two-component systems) of *Staphylococcus aureus* in the biofilm formation process; and (iv) genetic analysis of the mobility of patogenicity islands of *S. aureus*.

More information about the group activity (http://www.agrobiotecnologia.es/es/grp-biofilmsMicrobianos/index.htm)

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Representation: Choose suitable(s): Research / Clinics / Industry		Research/Industry
Thematic area of interest	Genomics, Genetics, Molecular Biology	
Title of the presentation		
Partners (name/country) of the planned proposal (if known):		

Short abstract (max. half page):

Sistemas Genómicos is an independent Company, leader in Genomics, Genetics and Molecular Biology. Our high technological level and great innovation capacity, with a human team of more than 60 professionals in Genomics areas, make us the leading company in Genomic Technology in Spain. Sistemas Genómicos offers a standard of excellence and quality, accredited by the most exigent international normative.

Our Research Division put at disposal of Scientific Community the whole technological capacity of our Company. The Research Division offers integral solutions in Genomics addressed to Academia and Research Centres.

Sistemas Genómicos relies on the public-private cooperation in research, development and innovation, in areas of strategic interest for our economy, through the creation of large research consortiums.

Our company actively seeks the establishment of strategic alliances to promote R+D+I projects in the areas of Genomics, Genetics and Molecular Biology.

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Representation:		Clinics
Thematic area of interest	Antimicrobial resistance; susceptibility testing and identification	
Title of the presentation	N.A.	
Partners (name/country) of the planned proposal (if known):		

Short abstract (max. half page):

Our group is interested in two main aspects:

1. Biochemical and genetic aspects of resistance to antimicrobial agents, with special emphasis in broad-spectrum beta-lactams and fluoroquinolones in gramnegative bacteria and glycopeptide and new compounds in grampositive bacteria. The group is also involved in molecular epidemiology of multiresistant noscomial pathogens.
2. Use of molecular methods for identification of bacteria of medical importance. Similarly, we are performing evaluations of commercial systems for identification and susceptibility testing of human pathogens, and in vitro studies of antimicrobial agents recently approved for clinical use (tigecycline, daptomycin,…).