ERA-NET PathoGenoMics Jan 2011

NEWSLETTER -8

Hungary Finland Spain Germany Israel France Austria Portugal Slovenia Latvia

PathoGenoMics PhD Award 2011

Information | Application:
www.pathogenomics-era.net
Deadline for Proposal Submission:
28th Febuary 2011

The PathoGenoMics PhD Award is an initiative of the ERA-NET PathoGenoMics partner countries to recognize three outstanding PhD theses in the PathoGenoMics field (Genome based research on human-pathogenic bacteria and fungi) completed during 2010.

Award Endowment: 2000€

Award presentation will take place during the 4th FEMS congress, Geneva, June 2011

ERA-NET PathoGenoMics

chose 9 projects to be funded under the frame of the third multinational joint call. The three-year funding is expected to begin in March 2011

A glimpse at the projects...

Analysis of the cellular mechanisms underlying the early response of the host to stress induced by *Listeria* infection / LISTRESS (*Listeria*-induced cellular stress during infection)

Project Coordinator: Trinad Chakraborty / Torsten Hain
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Project partners: Pascale Cossart FR, Marc Lecuit FR, Jürgen Wehland, Lothar Jänsch DE, Francisco García-del Portillo ES, Didier Cabanes PT, Yair Aharonowitz, Anat A. Herskovits IL

This project aims to analyse the role of the *Listeria* factors that induce post-translational modifications and organelle remodelling in order to overcome host recognition and response. Bacterial ligands as well as their intracellular pattern recognition receptors (PRRs) will be identified using functional genomic strategies, 3D- and 2-photon imaging technologies, and clinical material from patients with inflammatory bowel disease harbouring mutations in predisposition loci. Interacting targets and downstream events leading to the induction of cell autonomous defences and innate immune signalling pathways will also be pursued, and interactions between *Listeria* effector ligands and host proteins will be mapped.

Invasive aspergillosis: Biomarkers for prevention, diagnosis and treatment response (aspBIOmics)

Project coordinator: Hermann Einsele
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Project partners: Axel Brakhage DE, Jean Paul Latgé FR, Alain Troesch FR, Cornelia Lass-Floerl AT, Manuel Jurado Chacon ES

Invasive aspergillosis (IA) infection-associated mortality incidence is growing and increasingly affecting a broader range of patient groups. A major problem in the management of IA is the poor diagnosis. This consortium proposes to develop and evaluate an efficient diagnostic platform for IA, based on a battery of in vitro assays for a comprehensive multimodality analysis, combining the detection of *Aspergillus* elements (RNA, polysaccharides, proteins), host factors including cytokine profiles and host genetic susceptibility. This strategy also has the potential to identify patients who are at a high risk of IA infection and to monitor treatment progression.

Human fungal pathogens under oxygen stress: adaptive mechanisms to hypoxia and reactive oxygen species and their consequences for host interaction and therapy / OXYstress

Project coordinator: Joachim F. Ernst
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Project partners: Jesus Pla ES, Axel Brakhage DE, Enrique Herrero ES, Cornelia Lass-Flörl AT, Christian Leggewie DE

The proposal is based on the fact that invasive pathogens frequently interact with the human host in niches low in oxygen, often associated with increased levels of reactive oxygen species (ROS) and carbon dioxide. During systemic infections, pathogens often encounter and adapt to numerous hypoxic niches within tissues, organs and cells. The proposal unites an international panel of experts to clarify and exploit the molecular mechanisms of fungal responses and host interactions under oxygen stress in vitro and in experimental models of infection. In particular, differences between host-pathogen interactions under hypoxia and normoxia will be established. The study includes the development of novel fluorescent reporters for hypoxic infections, and the identification of both diagnostic biomarkers and novel targets for antifungal drugs.

Helicobacter pylori diversity in pathogenesis, antibiotic resistance, and evasion from natural and vaccine-induced immune responses (HELDIVPAT)

Project coordinator: Sebastian Suerbaum
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Project partners: Ivo G. Boneca FR, José Carlos Machado PT, Christine Josenhans DE, Rainer Haas DE, Peter Malfertheiner DE

Helicobacter pylori chronically infects more than one half of the world's human population, causing chronic gastritis and complications such as peptic ulcer disease and malignancies. Treatment is undermined by a rising rate of antibiotic resistance, lack of vaccine and significant genetic diversity and variability. The HELDIVPAT project, building on the results of a previous ERA-NET PathoGenoMics funded project, HELDIVNET, will explore how the genetic diversity of *H. pylori* is connected to pathogenesis, its ability to evade immune responses and resistance to antibiotics. The consortium partners have access to unique resources, including a novel strain collection from a vaccine trial and a globally representative collection of MLST-characterized *H. pylori* strains.

Impact of mobile genetic elements and horizontal gene transfer on bacteria-host adaptation: a genomic view (MobileGenomics)

Project coordinator: Buchrieser Carmen
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Project partners: Philippe Glaser FR, Ulrich Dobrindt DE, Sören Schubert DE, Joachim Reidl AT, Tamara Smokvina FR

This project aims to study horizontal gene transfer (HGT) and mobile genetic elements (MGE) in the human gut environment and in the upper and lower respiratory tracts. Commensals, probiotics and important opportunistic bacterial pathogens are present in both niches. The study will analyze niche-specific representatives of these three classes. The aims of this project are to increase basic knowledge on genome variability, on the mechanism leading to this variability and on the impact it has on host adaptation, colonization and virulence. The research is expected to impact our understanding on niche adaptation, bacterial survival in harsh conditions, colonization and virulence acquisition related to MGE and HGT, and to help decipher the impact of antibiotics and screen for more efficient probiotics and vaccines.

Global analysis of antisense regulatory mechanisms in *Staphylococcus aureus* / ARMSA

Project coordinator: Iñigo Lasa
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Project partners: Pascale Romby FR, Francois Vandenesh, Tom Geissmann FR, Susana Domingues PT, José R. Penadés ES

This research project is dedicated to exploring the effects of antisense RNA transcription on gene expression in *Staphylococcus aureus*, a leading cause of nosocomial and community acquired infections. The project will determine the transcriptome map of *S. aureus* using tiling arrays and deep sequencing strategies to identify overlapping transcription. The resulting map will be used to analyze the stability of overlapping transcripts; the effect of active replication of pathogenicity islands (PI) or phages on the bacterial transcriptome; and antisense mediated gene regulation in bacterial populations and at single cell level. Mutants deficient in particular antisense transcripts or in proteins involved in antisense mediated gene regulation will be assayed. This work is also anticipated to provide novel *S. aureus* targets for antibiotics.

Characterisation of host cell pathways altered by effectors of *Brucella*, *Chlamydia*, and *Coxiella*: identification of novel therapeutic targets / CELLPATH

Project coordinator: Luís Jaime MOTA
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Project partners: João Paulo Gomes PT, Anja Lührmann DE, Carmen Plasencia ES, Isabel Rodríguez Escudero ES, Suzana Salcedo FR

The purpose of this project is to characterise the molecular and cellular function of effector proteins from *Brucella spp., Chlamydia trachomatis*, and *Coxiella burnetii*, all relatively uncharacterised intracellular Gram-negative bacterial pathogens. The research will focus on the host cell signalling pathways targeted by effectors of *Brucella*, *Chlamydia*, and *Coxiella* and on the possible correlation of the mode of action of the effectors with their gene sequence variability and expression levels among different strains, including recent clinical isolates. The results may lead to novel therapeutic approaches, vaccines and diagnostics.

A genome-wide approach for characterizing the mode of action of novel compounds against tuberculosis (GeMoA)

Project coordinator: Marc A. Marti-Renom
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Project partners: Matthias Wilmanns DE, LLuís Ballell ES, Olivier Neyrolles FR, Brigitte Gicquel FR

Infection with *Mycobacterium tuberculosis* (Mtb), the causing agent of tuberculosis (TB) is best described as a dynamic balance between activation and suppression of host responses, orchestrated by complex interactions between multiple host and bacterial components. Therefore, single-target approaches for drug identification, have achieved limited success. The present project addresses this limitation by applying genome-wide approaches to characterize the mechanism of action of selected chemical compounds with activity against Mtb. This line of research can lead to unexplored new modes of action against Mtb and a series of potential targets and corresponding compounds to be further explored as treatment against TB.

Understanding colonisation and the transition to pathogenic dissemination by *Candida species*: towards early diagnostic and therapeutic approaches (CANDICOL)

Project coordinator: Attila Gacser
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Project partners: Christophe D'Enfert FR, Uwe Gros DE, Bernard Hube DE

The CANDICOL project aims to dissect the genetic and transcriptional underpinnings of the transition of the main pathogenic *Candida species* from commensalism to host dissemination. The project will identify and classify shared or distinguishing attributes of these species by establishing and optimizing research model systems, and studying fungal and host transcriptional patterns, genetic networks and fungal antigens associated with infections. Novel mutant strain collections will be developed and will help in identifying sets of fungal genes crucial for colonisation and dissemination. This research is important stepping stone in developing novel diagnostic tools for discriminating and predicting stages of fungal infection as well as identifying feasible targets for novel antifungal therapeutic.