ERA-NET PathoGenoMics Dec 2008

NEWSLETTER -4

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chose 13 projects to be funded under the frame of the second multinational joint call. The three-year funding is expected to begin in February 2009

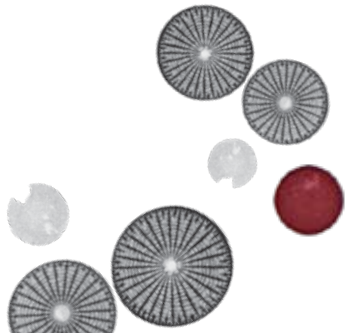
A glimpse at the projects…

Genome wide screening of the human pathogen Neisseria meningitidis for proteins enhancing serum resistance and evaluation of their vaccine potential

Project Coordinator: Ulrich Vogel ,Germany uvogel@hygiene.uni-wuerzburg.de

Project partners: Seppo Meri | Muhamed-Kheir Taha | Jan Poolman

Neisseria meningitidis (meningococcus) continues to be a major health threat by causing septicemia and meningitis with a case fatality rate of ~10%. A major line of immune defence against meningococci is the serum complement system, but certain serogroups are able to evade the immune response, leading to a limited strain coverage of current vaccines. 4 research groups from 3 countries undertook to develop novel vaccines that will generate antibodies capable of blocking bacterial factors involved in immune escape. To this end, a systematic genomic approach is proposed, in order to uncover complement regulatory molecules in meningococci.



PathoGenoMics PhD Award 2009

Information | Application:
www.pathogenomics-era.net
Deadline for Proposal Submission:
28th Febuary 2009

The PathoGenoMics PhD Award is an initiative of the ERA-NET PathoGenoMics patner countries to recognize the three most remarkable PhD theses in the PathoGenoMics field (Genome-based research on human-pathogenic bacteria and fungi) finished on 2008.

Award Endowment: 2000€

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Functional genomics of host-pathogen interactions using high-throughput screenings: a novel approach towards identifying therapeutic/prophylactic targets

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Project partners: Philippe Sansonetti | Thomas F. Meyer | Thomas Rudel | Carmen Buchrieser | Joerg Poetzsch

The progress of infections is the joint outcome of both pathogen and host-related features. This project, comprising 6 research groups from 3 countries, aims to identify novel pathogen determinants targeting crucial host functions, using genomic, bioinformatics and high-throughput screening methods. The group will focus on 5 important human pathogens: *M. tuberculosis, L. pneumophila, H. pylori, N. gonorrhoeae and K. pneumoniae.* The project complements ongoing work in the RNAi-Net, which focuses on the host side. This research program is expected to lead to the development of innovative therapies based on the modulation of the host-pathogen interface.

Pathogenomic approach to explore the use of bacterial interference as alternative treatment of recurrent urinary tract infections

Project Coordinator: Ulrich Dobrindt, Germany ulrich.dobrindt@mail.uni-wuerzburg.de

Project partners: Jörg Hacker | Timo Korhonen |Levente Emõdy | Istvan Wittmann
Eliora Ron | Catharina Svanborg; Björn Wullt

There is a strong need for alternatives to current antibiotic treatment, such as "bacterial interference", vaccination and new drugs. This project brings together 6 research groups from 4 countries to understand the molecular basis of asymptomatic bacteriuria (ABU) and to apply genomic approaches to exploit ABU *E.coli* isolates for "bacterial interference" to combat recurrent UTI. The acquired data will also provide additional information on bacterial traits that are associated with symptomatic infection, thus helping to identify new vaccine or drug targets for combating UTI. The geno- and phenotypic stability of isolate 83972 will be studied allowing its further improvement for bacterial interference.

ADHRES-Signature Project

Project Coordinator: Sophie de Bentzmann, France bentzman@ibsm.cnrs-mrs.fr

Project partners: Patrick Plésiat | Juan Luis Ramos| Isabel Sá-Correia | Soeren Molin
Catherine Nguyen | Matilde Fernández

Targeting bacterial virulence rather than survival may offer a reduced selection pressure for drug-resistant mutations. The most common virulence trait is a bacterial community called biofilm, which is highly resistant to antibiotic treatment and host defences. *P. aeruginosa, P. putida and B. cepacia* complex are particularly problematic, since they constantly exist as biofilm. The goal of this consortium, of 7 research groups from 4 countries, is to identify a core set of genes involved in biofilm and antimicrobial resistance important in in vivo infectious situation and relevant to clinical pathogenicity. Such a gene list is patentable, and amenable to screening by chips or any other technique for mRNA detection.

sncRNAomics - High throughput comparative sncRNAome analysis in major Gram-positive human pathogenic bacteria: functional characterisation by a systems biology approach and peptide nucleic acid drug design

Project Coordinator: Torsten Hain, Germany Torsten.Hain@mikrobio.med.uni-giessen.de

Project partners: Maja Rupnik | Axel Hartke | Bernd Kreikemeyer | Susanne Engelmann | Sonja Vorwerk | Thomas Hartsch

Novel anti-infectives are of high priority for global health care. Small non-coding RNAs (sncRNAs) in bacteria are an emerging class of new gene expression regulators, but their role in colonisation and pathogenicity is largely unknown. The consortium brings together 7 research groups from 3 countries, thus combining novel high-throughput sncRNA screening methods, whole-genome transcriptomics and proteomics and bioinformatics coupled with molecular characterization methods to provide new data regarding sncRNAs in major high-risk Gram-positive microbes (e.g. *Staphylococcus, Streptococcus, Enterococcus, Clostridium* and *Listeria*). Potential new drugs and diagnostic biomarkers will be validated using tissue-culture and subsequently in in-vivo models.

Transcriptional networks controlling virulence in filamentous fungal pathogens (TRANSPAT)

Project Coordinator: Antonio Di Pietro, Spain ge2dipia@uco.es

Project partners: Hubertus Haas | Gerhard Braus | Sven Krappmann | Ana Conesa | Roland Beffa

Invasive fungal infections in immunocompromised patients are on the rise, in particular of filamentous species (moulds). Still, little is understood about the ability of filamentous fungi to survive in the hostile environment of mammalian blood. Even less is understood about their clinical resistance to antifungal agents. TRANSPAT, comprising 6 research groups from 4 countries, aims to integrate genetic, genomic and bioinformatic tools to uncover clinically relevant transcriptional networks in fungi, exploiting the complete genome sequences and mutant collections of *A. fumigatus and F. oxysporum*. This approach will identify gene sets showing altered expression during invasive infection and/or exposure to antifungals.

The cell wall as a target to improve antifungal therapy against Invasive Aspergillosis

Project Coordinator: Axel A. Brakhage, Germany Axel.Brakhage@hki-jena.de

Project partners: Jean-Paul Latgé | Emilia Mellado Terrado | Fernando Pelaez | Dominique Costantini

Aspergillus fumigatus infections have dramatically increased worldwide. Due to the limited number and efficacy of antifungal drugs, the mortality from Invasive Aspergillosis (IA) is very high. The cell wall of A. fumigatus is a major drug target. This project aims at elucidating the relationship between signal transduction cascades and cell wall biosynthesis in *A. fumigatus*, leading also to the identification of drug-resistance mechanisms. Functional genomic analyses, large-scale mutant libraries and genetic reporter systems will be the key methodologies, employed by 5 research groups from 3 countries. The tools generated may lead to new, more efficient drugs.

Pathogenomics of increased Clostridium difficile virulence

Project Coordinator: Maja Rupnik, Slovenia maja.rupnik@zzv-mb.si

Project partners: Bruno Dupuy | Frederic Barbut | Adriano O. Henriques | Alexander Indra | Wolfgang Liebl

Clostridium difficile is increasingly associated with infections in hospitals and in the community, and hypervirulent types are emerging. Six research groups from 5 countries undertook this project, aiming to use genomic approaches to study *C. difficile* types with increased virulence and to analyze the presence of known and new virulence factors, regulation of their expression and genomic heterogeneity. The expected results will be valuable for recognizing, monitoring and diagnosing virulent types, improved prevention, and better treatment.

Transcriptome-based monitoring and eradication of chronic Chlamydial infection - ChlamyTrans

Project Coordinator: Matthias Maass, Austria m.maass@salk.at

Project partners: Kamil Önder | Mirja Puolakkainen | Dezso Peter Virok | Johann Bauer | Martha Böttcher

ChlamyTrans is a consortium of two commercial and four academic partners to study the pathogenomics of chronic Chlamydia infection. Genital *Chlamydia trachomatis* infection is the leading sexually transmitted disease and *Chlamydia pneumoniae* is a frequent cause of respiratory infection and linked to atherosclerosis in genetically susceptible individuals. The key for the chlamydial pathobiology is the ability of the pathogen to enter a non-replicative antibiotic-resistant state due to reprogramming of the host cell metabolism. The objective of ChlamyTrans is to use two complementary genome-wide transcriptomics approaches to produce commercially exploitable products for monitoring, treating and ultimately preventing chronic chlamydial infections.

Innate immune responses to Streptococcus pneumoniae and S. pyogenes

Project Coordinator: Pavel Kovarik, Austria kovarik@univie.ac.at

Project partners: Emmanuelle Charpentier | Ilkka Julkunen | Sylvia Knapp | Claire Poyart | Estzter Nagy

Pharmacological modulation of pathogen recognition is a promising, approach to adjust the strength of immune responses. In this project, the recognition of *Streptococcus pneumonia and Streptococcus pyogenes* by the host innate immune cells will be studied on a whole-genome scale. These bacteria are still a major health concern and are also acquiring widespread resistance to antibiotics. The clinical manifestations of these pathogens are highly variable, partly due to differential recognition of the pathogens by the innate immune system. The project, jointly carried out by 5 academical research groups and one biotech company from 3 countries, will identify novel players in streptococcal diseases and develop strategies leading to modulation of the host's immune response.

Pathogen-host metabolomics and interactomics (Pathomics)

Project Coordinator: Thomas Rattei, Germany t.rattei@wzw.tum.de

Project partners: Johannes Hegemann | Romé Voulhoux | Agathe Subtil | Matthias Horn
Jan Rupp | Ana Conesa Cegarra

Bacterial protein secretion is a key mechanism underlying infection, pathogenesis and modulation of the host cells. In this project, novel biomarkers and drug target candidates will be developed for the diagnosis and therapy of *Pseudomonas aeruginosa* and Chlamydiae infection. Both pathogens secrete effector proteins into their host cells, and share a high prevalence of infection and disease, limited diagnostics and unspecific therapy. This project benefits from the combined efforts of 7 research groups from 4 countries, and will contribute considerably to the therapeutic efforts targeting these pathogens by developing novel diagnostic strategies and biomarkers and identifying drug target candidates.

METAGUT: Development, prevention and early diagnostic detection of Clostridium difficile-associated colitis – an interdisciplinary network

Project Coordinator: Stephan Johannes Ott, Germany s.ott@mucosa.de

Project partners: Vítor Martins dos Santos | Manuel Ferrer | Andres Moya |Laya Pedrola |
Bernhard Ronacher | Miguel Godinho

Pseudomembranous colitis is an infectious disease of the human colon, mostly caused by *Clostridium difficile*. A major aetiology of pseudomembranous colitis is the use of broad-spectrum antibiotics, which lead to an altered intestinal microflora and to activation or overgrowth of *C. difficile*. The goal of the project network, comprising 7 research groups from 4 countries, is to characterize the composition and metabolic/functional status of intestinal microflora from the non-diseased stage towards *C. difficile*-associated pseudomembranous colitis in the human system, thereby enhancing our understanding of this disease and paving the road for the early diagnosis and effective prevention and intervention strategies.

Identification of hot spots of divergence and rapidly changing genes within Shiga toxin producing Escherichia coli

Project Coordinator: Alexander Mellmann, Germany mellmann@uni-muenster.de

Project partners: Dorothea Orth | Nicolas Barnich |Eduard Torrents

Identification of hot spots of divergence and rapidly changing genes within Shiga toxin-producing *Escherichia coli* is the predominant nonpathogenic facultative flora of the human intestine. Some *E. coli* strains have acquired specific virulence factors, allowing them to cause a broad spectrum of human diseases. This project, which represents a multi-disciplinary collaboration of four research groups from Austria , France , Germany and Spain, will focus on Shiga toxin-producing *E. coli* (STEC) and on Adherent-Invasive *E. coli* (AIEC), two intestinal pathogenic subgroups of *E. coli.* The results of this project will lead to a new understanding of basic principles of pathogenesis, to improvement of diagnosis and typing, and to establishing of new preventive and therapeutic approaches.

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The ERA-NET *PathoGenoMics* is funded by the European Commission to strengthen transnational co-operations and co-ordination of national genome-based research programmes on human-pathogenic microorganisms.

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Award Endowment:

2.000€

Information/Application: see
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Projektträger Jülich Forschungszentrum Jülich GmbH
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ACADEMY OF FINLAND
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ANR Agence Nationale de la Recherche
ministère éducation nationale enseignement supérieur recherche
ministère délégué à la recherche
FCT Fundação para a Ciência e a Tecnologia
MINISTÉRIO DA CIÊNCIA, TECNOLOGIA E ENSINO SUPERIOR
MINISTERIO DE CIENCIA E INNOVACIÓN
FWF Der Wissenschaftsfonds.
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