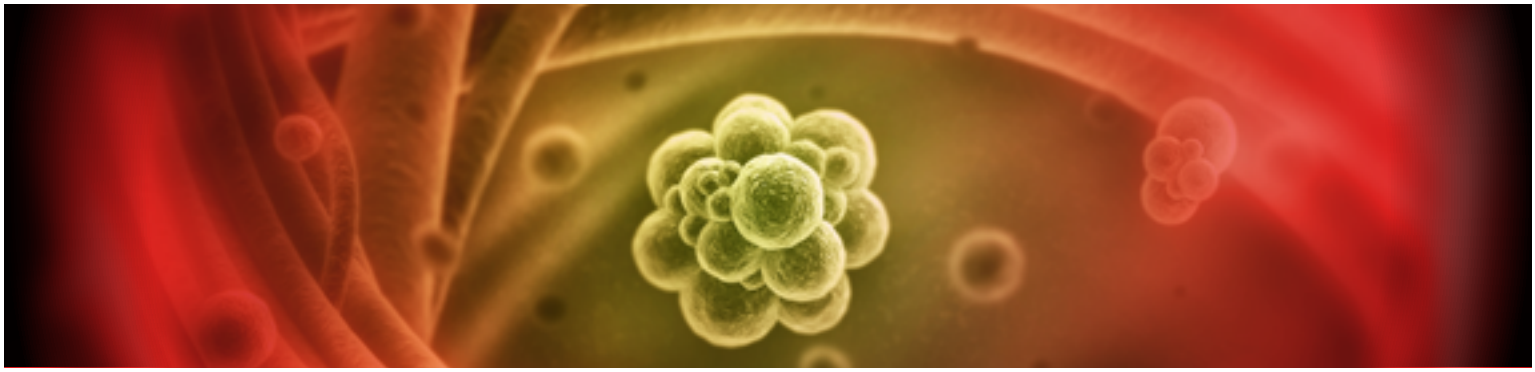

Infect-ERA
February 2014

NEWSLETTER2

Second Infect-ERA Call for Research Projects

The Infect-ERA program, which aims to coordinate European funding for human infectious disease research, published its second joint call for transnational research projects on human infectious diseases. The collaborative projects should favorably include researchers from the academic, clinical and/or industrial sectors. A portion of the funding will be reserved to support projects of **young scientist** consortia. Proposal submission follows a two- step process. Pre-proposals must be submitted by April 02, 2014, and full proposals by August 04, 2014. Projects are expected to start at the end of 2014 / beginning of 2015.

The submitting consortia should comprise **3-6 partners**, with no more than 2 partners per country. For further details, see:
http://www.infect-era.eu/2nd-call-2014

The coordinated funding of multinational research projects in infectious diseases is a primary feature of the Infect ERA program. It is anticipated that four annual calls for transnational joint research projects will be launched during the lifetime of the ERA-NET (2013-2016). The first was published in January 2013, resulting in the submission of 42 proposals.

Seeking partners to build a joint proposal? Visit
http://www.infect-era.eu/public-partners

Seeking training opportunities for your students or post-docs? Visit the Infect-ERA sister initiatives training catalogue
http://www.infect-era.eu/training

Looking for a job? Seeking to recruit personnel skilled in the field of Infectious Diseases? Visit the Infect-ERA Job Opportunities Bulletin Board:
http://www.linkedin.com/groups/Job-Opportunities-Bulletin-Board-4995046.S.579874902178688614?qid=71ec4043-e83c-40bf-8be5-0e67ee55deac&trk=groups_most_popular-0-b-ttl&goback=%2Egmp_4995046

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Following the first call, eight projects were selected for funding:

Krappmann Sven

partner countries:

Germany Austria

Israel

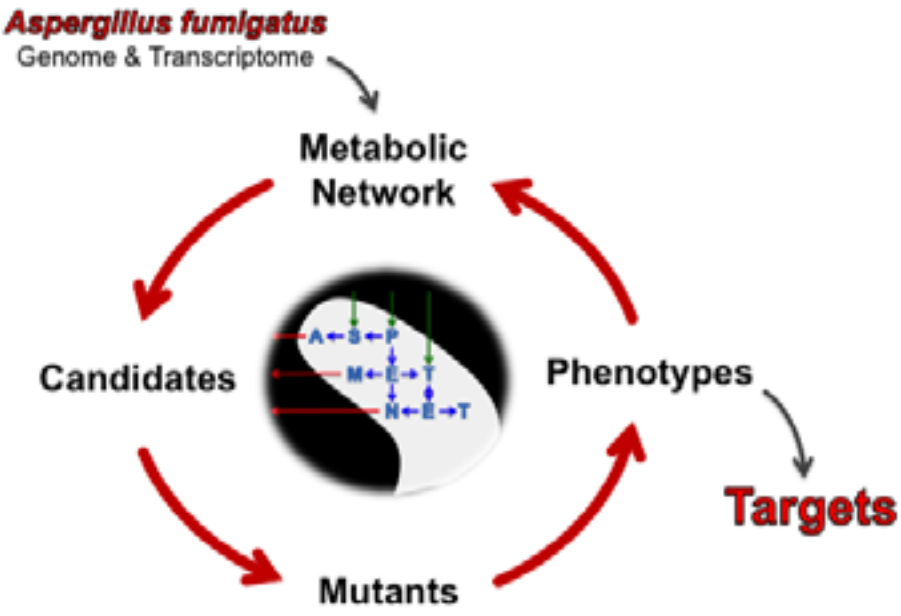
Systematic identification of antifungal drug targets by a metabolic network approach (AspMetNet)

Project coordinator: Krappmann Sven, University Hospital Erlangen, Germany

Partner countries: Austria, Germany, Israel

Project description:

Infections caused by fungi pose a prevalent threat to patients with a compromised immune system. Current antifungal drugs tend to have limited efficacy, and may be accompanied by severe side effects or emerging pathogen resistance. In the search for specific targets of antimycotic therapy, metabolic pathways have been widely neglected. AspMetNet will explore the primary metabolism of one of the main pathogenic fungal species, Aspergillus fumigatus, as an essential virulence determinant. The project will reconstruct the metabolic network by mining the *A. Fumigatus* genome and transcriptome data sets to identify biosynthetic pathways and forecast key reactions. Following candidate prioritization, gene targeting will culminate in the collection of mutant strains. Based on the data emerging from the characterisation of these mutant strains, the metabolic network model will be refined, yielding additional gene candidates. This candidate selection and testing approach can be applied to the analysis of other pathogenic fungi to identify promising targets for therapeutic intervention.



Chakraborty Trinad

partner countries:

Germany France

Portugal Israel

Subversive pro- and anti-inflammation trade-offs promote infection by Listeria monocytogenes (PROANTILIS)

Project coordinator: Chakraborty Trinad, Institute of Medical Microbiology Justus-Liebig University Giessen, Germany

Partner countries: Germany, France, Portugal, Israel

Project description:

Listeriosis is a leading cause of death from food-transmitted bacterial pathogens. It can cause infections in the blood stream and brain, and lead to abortion, neonatal infection and fetal death. The causative organism, Listeria monocytogenes (Lm), is a Gram-positive, environmentally ubiquitous bacterium that can breach intestinal, blood-brain and placental barriers. The clinical course of listeriosis has initially no specific symptoms until Lm reaches the central nervous system and/or the fetal-placental barrier. Thus Lm induces little inflammation in the host, either at the intestinal level or systemically. Proposing that anti-inflammatory responses mediated by bacterial factors are an essential component of Lm's disease-causing potential, the project seeks to identify and characterise the bacterial factors that cause the suppression of the clinical symptoms of listeriosis.

Knapp Sylvia

partner countries:

Austria Germany

Sweden France

Dissecting the bacterial recognition machinery in human cells using haploid genetics and CRISPR-mediated genome engineering (Haplo-Infect)

Project coordinator: Knapp Sylvia, Medical University of Vienna & CeMM - Research Center for Molecular Medicine of the Austrian Academy of Sciences, Austria

Partner countries: Austria, Germany, Sweden, France

Project description:

In the absence of novel antibiotics on the clinical horizon, the rise in multidrug- resistant bacterial infections constitutes a global threat. Adjuvant immunotherapy is a promising strategy for combating infections without triggering drug resistance. For adjuvant immunotherapy to work, protective immune responses must be scaled to the level of infectious threats, thus allowing for efficient pathogen clearance while minimizing inflammation-induced tissue damage. Haplo-Infect will conduct genome-wide screening using haploid human immune cells. The genes will be disrupted using gene trap mutagenesis (i.e. generating knock-out cell clones). By subjecting mutagenised cell pools to a selection scheme, mutants with desired phenotypes will be enriched and identified by sequencing. We will then verify the functional relevance of these molecules by testing individual cell clones from the human gene trap mutant collection and by exploring RNA-programmable Cas9-mediated genome editing.

Jean Dubuisson

partner countries:

France

Denmark

Romania

Identification of host factors involved in Hepatitis C Virus assembly and characterization of their potential role in vivo (HCV-ASSEMBLY)

Project coordinator: Jean Dubuisson, Center for Infection, Institut Pasteur of Lille, University Lille Nord de France, Lille, France

Partner countries: Romania, Denmark, France

Project description:

The Hepatitis C virus (HCV) virus infects the liver, leading in the majority of cases to liver diseases. Despite recent advances in the knowledge of the interaction between HCV and its host, the understanding of how new viral particles are assembled within infected cells is still poor. The objective of HCV-ASSEMBLY is to identify cellular factors involved in this process by using a genome-wide screen based on small interfering RNAs. The integration of the data generated will enable the identification of key cellular pathways associated with HCV particle formation. Subsequently, the interaction between HCV and some of the host gene products from these pathways will be elucidated. The potential in vivo implications of these virus-host interactions on the progression of chronic hepatitis C will be examined by exploring the expression of host factors in infected patients. The study seeks also to validate new host factors as potential drug targets for HCV treatment.

Fillatreau Simon

partner countries:

Germany

Israel

France

Anti-Bacterial Immune Regulation (Abir)

Project coordinator: Fillatreau Simon, Deutsches Rheuma-ForschungsZentrum, a Leibniz Institute, Berlin, Germany

Partner countries: Israel, Germany, France

Project description:

The Anti-bacterial Immune Regulation (Abir) project aims at identifying novel resistance mechanisms and developing new therapies (including vaccines) against infections by intracellular bacteria, such as Salmonella and Listeria, which can provoke severe food-borne diseases. Salmonella causes about 600,000 deaths each year, and Listeria infection is among the leading causes of stillbirth. To meet its goals, Abir unifies world-leading experts in immunology including Dr Steffen Jung (Weizmann Institute of Sciences, Israel), Prof. Dr. Stefan H.E. Kaufmann (Max Planck Institute of Infection Biology, Germany), Prof. Bernard Malissen (INSERM Centre d'Immunologie de Marseille-Luminy, France), and is coordinated by Dr. Simon Fillatreau (Deutsches Rheuma-ForschungsZentrum, a Leibniz Institute, Berlin, Germany).

Nassal Michael

partner countries:

Germany France

Poland Belgium

Host factors in hepatitis B virus cccDNA formation as novel antiviral targets and biomarkers - identification, preclinical evaluation and impact for liver disease (HepBccc)

Project coordinator: Nassal Michael, University Hospital Freiburg, Germany

Partner countries: Germany, France, Poland, Belgium

Project description:

Chronic hepatitis B virus (HBV) infection is a leading cause of severe liver disease. Current treatments do not provide a cure because they fail to target the "covalently closed circular" (ccc) DNA which ensures viral persistence. The generation of cccDNA from the "relaxed circular" (RC) DNA in infectious virions is poorly understood. Supported by Vironexx as professional partner, HepBccc combines the virology and technology expertise of the teams of Michael Nassal, Thomas Baumert, Laurent Brino, Krzysztof Bielawski and Johan Neyts/Kai Dallmeier to: a) identify the cccDNA-relevant host repair factors as new anti-viral targets; b) correlate patient-specific factor variations with the disease as new biomarkers; and c) identify cccDNA inhibitors, towards the eventual discovery of a cure for chronic hepatitis B.

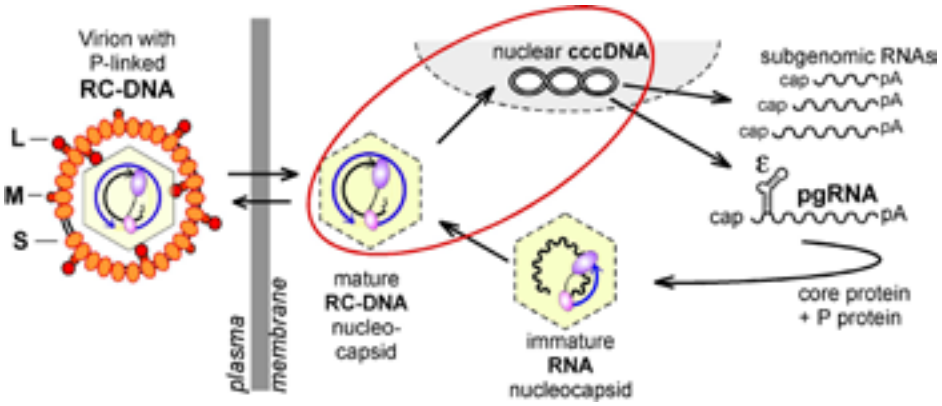


Figure Legend:

Crucial importance of cccDNA to HBV persistence.

HBV brings its genome into the host cell as viral polymerase-linked RC-DNA. Through mechanisms still not understood, RC-DNA is converted into cccDNA from which viral RNAs, including the pregenomic (pg) RNA precursor of new viral DNA, and proteins are generated to create new viruses. Understanding, and eventually targeting cccDNA formation is required to break HBV persistence. NTCP, recently identified HBV receptor; NAs, nucleoside analog therapeutics.

Hilby Hubert

partner countries:

Germany

France

Austria

Israel

Eukaryotic genes in vacuolar pathogens and symbionts - Implications for virulence, metabolism and ecology (EUGENPATH)

Project coordinator: Hilby Hubert, Ludwig-Maximilians University Munich, Germany

Partner countries: Germany, France, Austria, Israel

Project description:

To evolutionarily adjust to their intracellular niches, pathogenic bacteria acquire and adapt a plethora of genes termed EUGENs from their unicellular eukaryotic hosts. In EUGENPATH the role of distinct EUGENs for Legionella and Coxiella pathogenesis, Protochlamydia symbiosis, and bacterial metabolism will be analyzed on a molecular and cellular level. This consortium brings together distinct yet complementary biological and technological expertise on Legionella, Coxiella; and Protochlamydia, as well as know-how in the fields of proteomics and metabolomics. The analysis of common classes of EUGENs and their products will provide mechanistic insights into parasitic and symbiotic processes, elucidate the relationship between parasitism and symbiosis and establish a link between bacterial virulence or symbiosis and intracellular metabolism. We seek to reveal novel targets for anti-bacterial compounds and identify effector proteins useful for vaccine and molecular probe development.

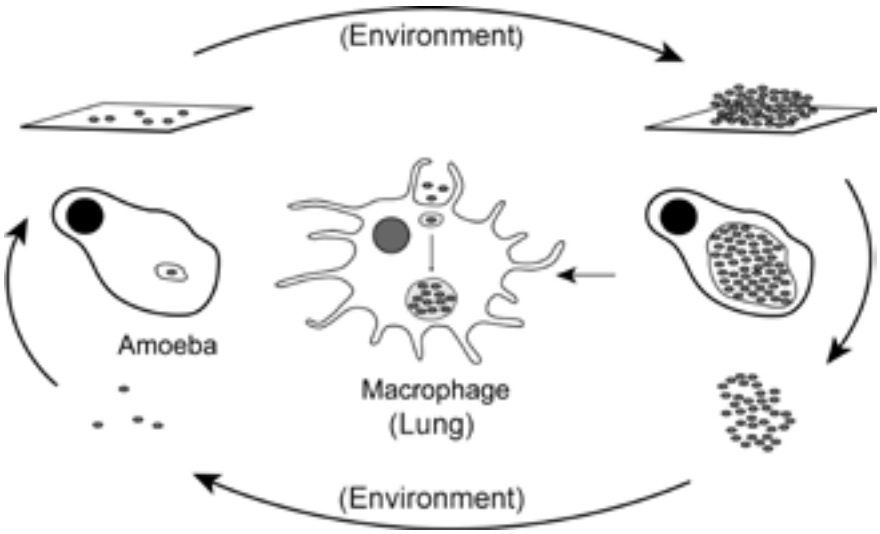


Figure Legend:

Role of EUGEN products for bacterial virulence or symbiosis. In the environment, bacteria persist and grow as planktonic cells, form biofilms or infect amoebae. Upon inhalation, amoebae-resistant bacterial pathogens also replicate within macrophages in the human lung. EUGEN (eukaryotic-like gene) products are injected into host cells by the bacteria and define their distinct intracellular life styles.

Meyer F. Thomas

partner countries:

Germany Sweden

Austria UK

Co-infection as a cause of ovarian cancer (CINOCA)

Project coordinator: Meyer F. Thomas, Max Planck Institute for Infection Biology, Department Molecular Biology, Berlin, Germany

Partner countries: Germany, Sweden, Austria, UK

Project description:

CINOCA will investigate the contribution of chronic co-infections with human herpes viruses (HHVs) and the intracellular bacterium Chlamydia trachomatis (Ctr) to the onset of ovarian cancer. An important paradigm shift in recent years now firmly assigns the origin of ovarian cancer to the epithelial lining of the Fallopian tube (FT), a prime meeting site for chronic, often asymptomatic infections. Mounting evidence of a correlation between infection and ovarian cancer warrants a careful analysis of the molecular events by which these pathogens synergize to establish an infectious niche and promote malignant transformation. CINOCA aims at understanding the impact of FT-associated pathogens on the integrity of the host cell genome, including the deregulation of the DNA damage response, and how this becomes a key driver of cell transformation and cancer. The study will generate clinical information on the relative significance of FT infections to ovarian cancer and may substantiate the clinical indication for salpingectomy as a means of cancer prevention for women at risk.

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