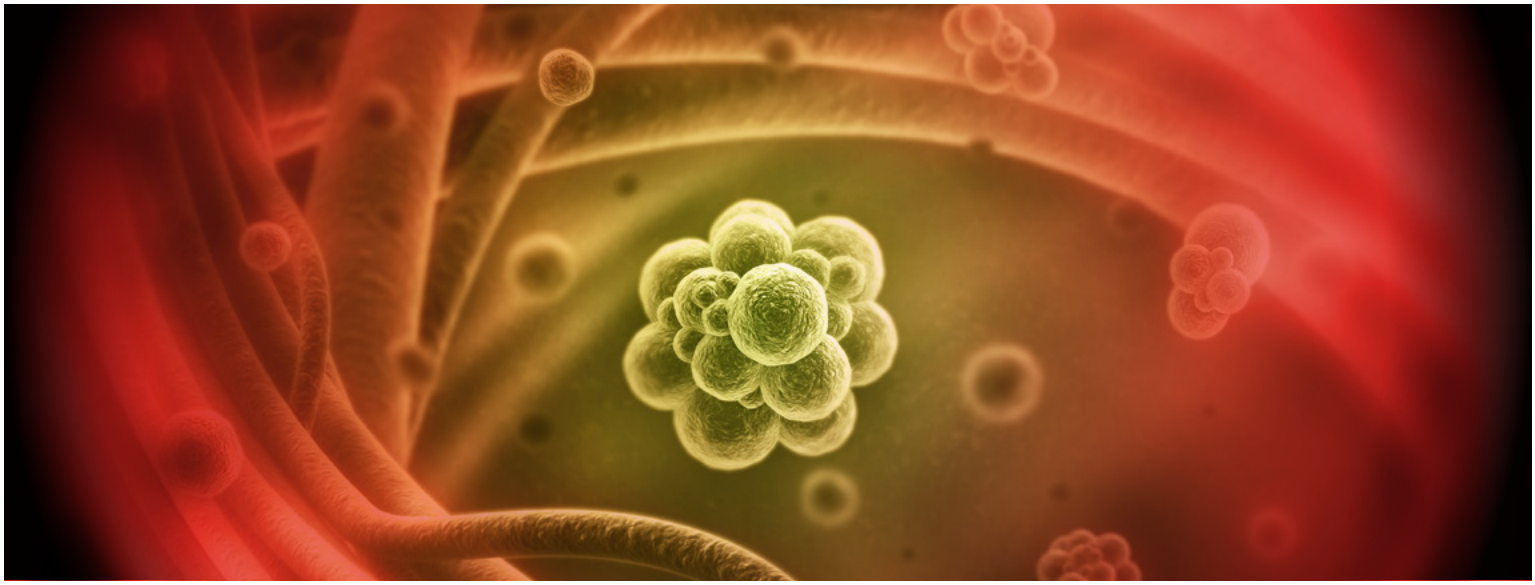


Infect-ERA
February 2016

NEWSLETTER7

The Infect-ERA fourth transnational joint call on human infectious diseases is open, submission deadline: March 17, 2016.

The call encompasses two equally relevant main research topics:

1. The host-pathogen interactions, with regard to clinically relevant microbial clones, focused on host susceptibility (e.g., innate immune response, populations at risk, etc.).

2. Development of innovative strategies for the diagnostic and treatment of high clinically relevant microbial infections; optimisation of antimicrobial therapy in an individual patient and development of biomarkers to allow individual response prediction.

HIV/AIDS, malaria and tuberculosis are excluded from the call.
More details available: http://www.infect-era.eu/4th-call-2016

Produced by CSO-MOH, IL

Summary of the 2015 Joint Transnational Call

- Infect-ERA 2015 joint transnational call was launched in January 2015.
- **500** research groups involved in **110** submitted pre-proposals requested a total of **90 Million €**.
- **35 consortia** were invited to submit a full proposal involving **162 research groups** who requested a total budget of **30 Million €.**
- **9 projects** were selected for funding with a total budget of **12 Million €.**

Jorge Pedrosa

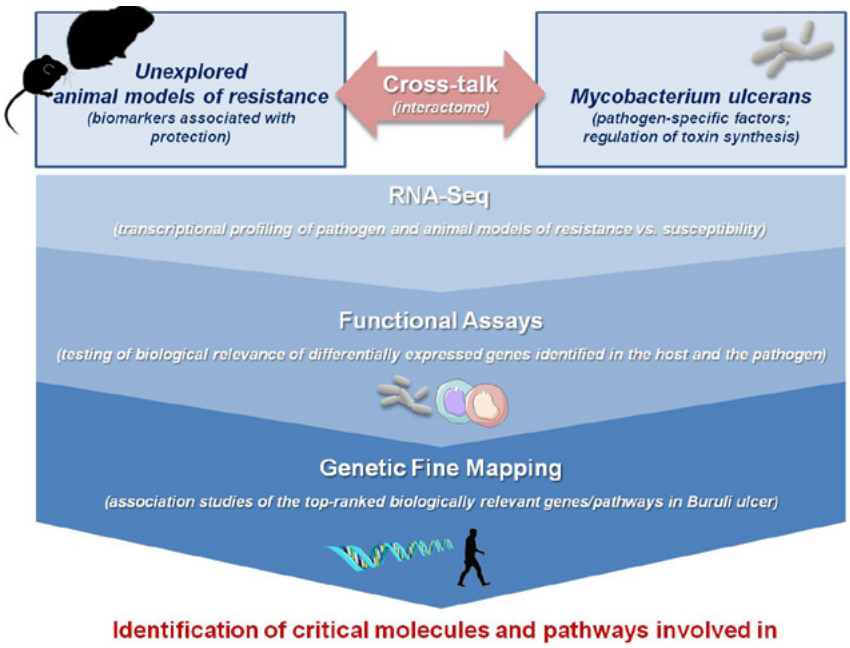
Transcriptome Analysis of Animal Models of Spontaneous Healing of *Buruli Ulcer*

Acronym: BU_SPONT_HEAL

Coordinator: Jorge Pedrosa, Life and Health Sciences Research Institute, University of Minho, Portugal; jpedrosa@ecsaude.uminho.pt

Partners: Laurent Marsollier - France, Ivo Gut - Spain

Buruli ulcer (BU) is a neglected emerging infectious disease of the skin caused by *Mycobacterium ulcerans*. Early stages are treated with long term antibiotics, but advanced lesions require extensive surgery. In spite of treatment, 25% of patients, children in particular, become permanently disabled and mutilated. In some cases, spontaneous healing occurs. The goal of this project is to study the protective mechanism in which healing occurs with new unique animal models. This project will identify critical biomarkers and related pathways involved in the control of BU that will contribute to the future development of new prophylactic and therapeutic strategies.



Uwe Himmelreich

Unraveling host-pathogen interactions in the pathogenesis of cryptococcosis using optical and in vivo imaging methods.

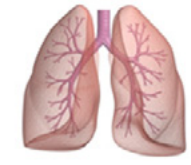
Acronym: CryptoVIEW

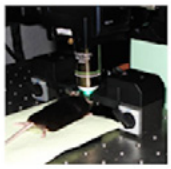
Coordinator: Uwe Himmelreich, University of Leuven, Belgium;
uwe.himmelreich@med.kuleuven.be

Partners: Werner Stenzel - Germany, Marc Vendrell - UK, Jim Swoger - Spain, Alexandre Alanio - France, Rodolfo Lavilla - Spain

The fungi *Cryptococcus neoformans* and *Cryptococcus gattii* are encapsulated yeasts that can cause infections in both immunosuppressed and immunocompetent patients. They mainly cause lung infections that can also spread to the brain. These potentially life-threatening infections are not completely understood. This project will study the interaction between the pathogenic yeast and the immune system by both non-invasive and invasive methods. Clinical and transgenic Cryptococci and novel agents that have the potential to act as contrast agents will be used as experimental models. By this, new insights on the pathogenesis of cryptococcosis will be gained and novel targets for therapy can be identified.

Cryptococci





Carles Ubeda

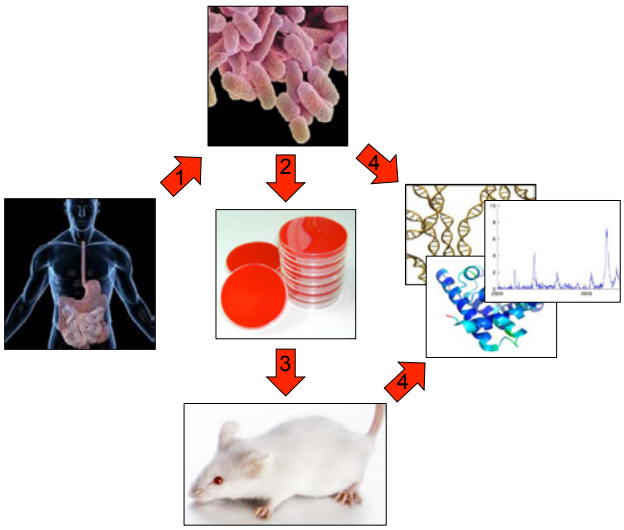
Role of the microbiota in the defense against multidrug-resistant Enterobacteriaceae

Acronym: FloraStopMRE

Coordinator: Carles Ubeda, FISABIO, Valencia, Spain; ubeda_carmor@gva.es

Partners: Karina Xavier - Portugal, Bernhard Kuster - Germany,
Jean Marc Rolain - France, Laurent Debrauwer - France, Miguel Angel Sanz - Spain

Multidrug-resistant Enterobacteriaceae (MRE) pose a major health problem. These infections generally begin by colonization of the gut. In normal conditions, the microbiota suppresses MRE colonization, but the mechanisms of protection are not well understood. This project will use novel "omic" techniques to study the microbiota and identify mechanisms of protection. Commensal bacterial species associated with MRE resistance will be identified in hospitalized patients and germ free mice will be colonized with these species to test their protective role against MRE. The obtained results will help to develop biomarkers, probiotics and drugs to combat infections by these pathogens.



Role of microbiota in the defense against MRE: (1) Using high-throughput sequencing, microbiota from hospitalized patients will be characterized. (2) Commensal bacterial species will be isolated from fecal samples using culturomics. (3) Germ free mice will be colonized with the isolated species to test their protective effect against MRE. (4) Genes, proteins and metabolites derived from protective species will be characterized using omic techniques.

Andreas Herrmann

Structure and function analyses of the Hantavirus envelope glycoproteins and their role in virus assembly, virus entry and immune recognition, as novel targets for antiviral treatment

Acronym: HantaHunt

Coordinator: Andreas Herrmann, Humboldt-Universität, Berlin, Germany; andreas.herrmann@rz.hu-berlin.de

Partners: Detlev H. Krüger - Germany, Yechiel Shai - Israel, Felix Rey - France

Hantaviruses are emerging viruses causing life threatening infections with case fatalities of up to 50%. Hantavirus infections with even mild clinical course lead to very severe outcomes. Treatment of the infection is currently only symptomatic as other antiviral treatment options do not exist. To date, little is known about Hantavirus entry and replication mechanisms. This consortium will address the molecular mechanisms of Hantaviruses exit from and entry into cells in order to identify and validate specific targets for vaccines and virostatics. Hantavirus glycoproteins provide promising targets for development of vaccine and/or virostatics blocking different steps of the virus cycle.

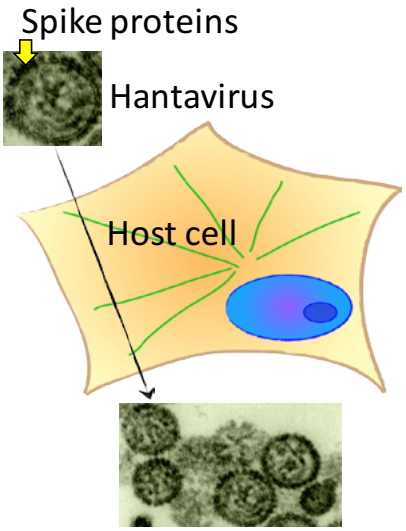


Figure: Role of the viral spike proteins in entry and genesis of Hantaviruses

Françoise Bachelerie

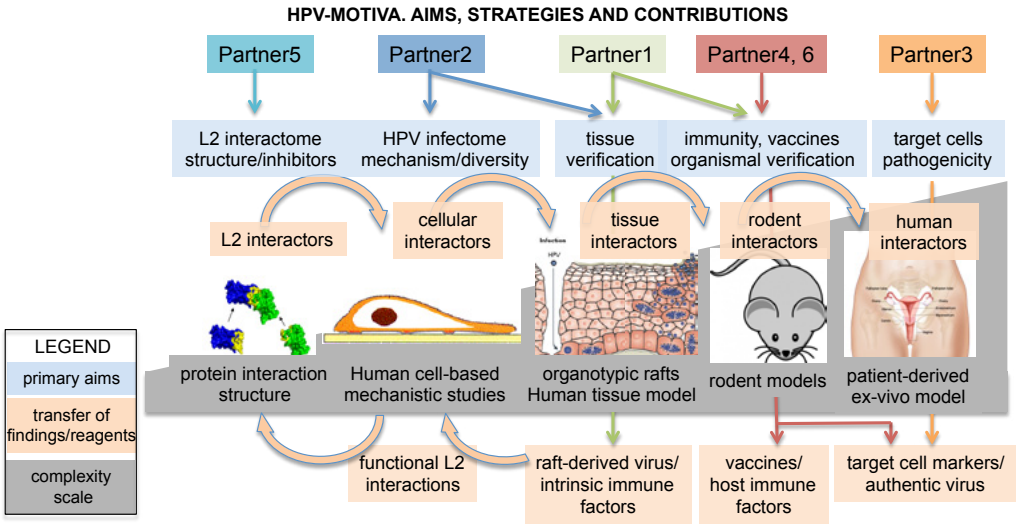
Human papilloma virus infection: from molecules to tissue prevention

Acronym: HPV-motiva

Coordinator: Françoise Bachelerie, INSERM, Clamart, France; francoise.bachelerie@u-psud.fr

Partners: Mario Schelhaas - Germany, Philippe Delvenne - Belgium, Reinhard Kirnbauer - Austria, Gilles Trave - France, Frank, Rösl - Germany

The outcome of viral infections is determined by the interaction between the viral and host proteins, influenced by the cellular microenvironment. This project addresses the human papillomavirus (HPV)-host interactions in the context of different cellular microenvironments that may be translated into anti-viral and anti-cancer strategies. The goal is to characterize the influence of host immune and epithelial cell subsets on HPV infection and the virus-host protein interactions with a focus on the L2 viral protein-interactome. This may lead to the development of biomarkers as well as next generation anti-HPV vaccines and medications.



Ohad Gal-mor

Understanding the Human-Restricted Host Tropism of Typhoidal Salmonella

Acronym: Sal host trop

Coordinator: Ohad Gal-mor, Sheba Medical center, Ramat-Gan, Israel;
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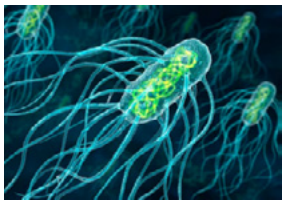
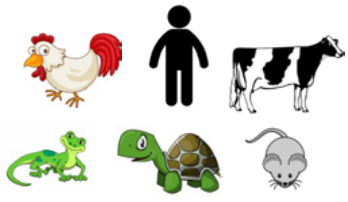
Partners: Isabelle Virlogeux-Payant - France, Josep Casadesus - Spain,
Thomas Schiex - France, Michael Hensel - Germany, Guntram Grassl - Germany

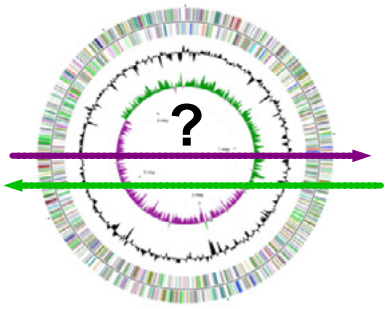
Salmonella enterica is one of the most prevalent human and animal pathogens. S. Typhi and S. Paratyphi A and B are human-adapted (infect only humans) serovars that cause enteric (typhoid) fever. This is an invasive disease with a global annual estimate of over 25 million cases, resulting in more than 200,000 deaths. The molecular basis underlying the human host-specificity of typhoidal Salmonella is still not well understood. The goal of this project is to identify, characterize and understand the mechanisms underlying the human restricted tropism of typhoidal Salmonella. Such data may lead to identification of new targets to combat infections by these pathogens.

Understanding the Human-Restricted Host Tropism of Typhoidal Salmonella

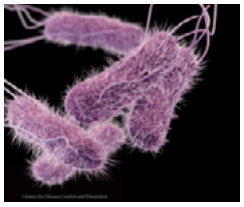


Non-typhoidal Salmonella

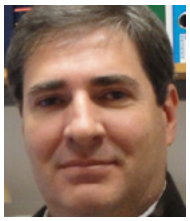




Salmonella



Non-typhoidal Salmonella



Alexandre Carmo

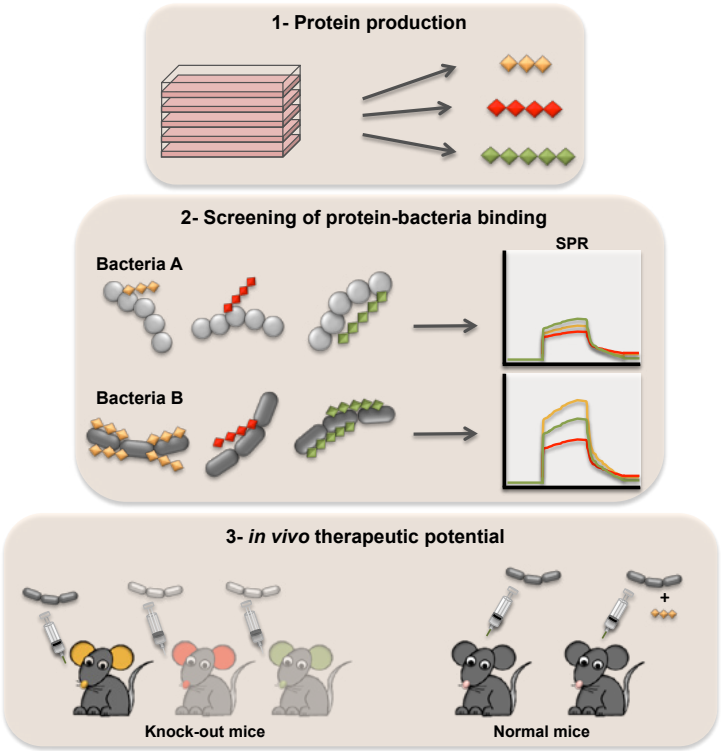
SRCR proteins as microorganism pattern recognition receptors: a wide search for interactions with pathogenic bacteria

Acronym: Srecognite

Coordinator: Alexandre Carmo, IBMC - Instituto de Biologia Molecular e Celular, Porto, Portugal; acarmo@ibmc.up.pt

Partners: Bernard Malissen - France, Francisco Lozano - Spain, Sebastian Krause - Germany Claire Poyart - France

In this project the natural medicinal potential of the scavenger receptor cysteine-rich (SRCR) superfamily will be studied. Members of this family are able to bind to conserved molecular patterns in bacteria, fungi or viruses. The best SRCR proteins that target and neutralize specific pathogenic bacteria will be searched, after which animal models will validate the level of protection that these SRCR confer against the pathogens. Concomitantly, recombinant human SRCR proteins will also be produced in collaboration with industrial partners to develop SRCRs as therapeutic agents.



Daniel Lopez

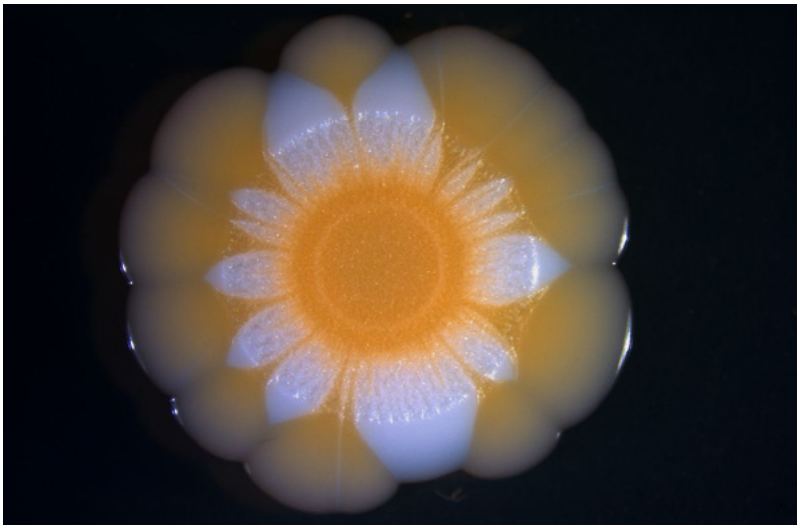
Intracellular *Staphylococcus aureus*: deciphering bacterial and cellular factors involved in host cell invasion by clinically relevant strains to define new therapeutic approaches

Acronym: StaphIN

Coordinator: Daniel Lopez, National Centre of Biotechnology (CNB-CSIC), Madrid, Spain; dlopez@cnb.csic.es

Partners: Ana Eulalio - Germany, Miguel Mano - Portugal, Francois Vandenesch - France, Tristan Ferry - France

Staphylococcus aureus (*S. aureus*) infections represent a major health problem in both hospital and community settings. *S. aureus* ability to fight antimicrobial therapies is associated with its capacity to form biofilms and to acquire resistance to conventional antibiotics. This consortium will perform a systematic analysis of a large collection of *S. aureus* clinical isolates to assess the ability of the different strains to invade, replicate and persist within host cells. In addition, bacterial and host factors relevant for *S. aureus* intracellular lifestyle will be characterized. The ultimate goal is to exploit the acquired knowledge to develop therapeutic strategies, with impact on the prevention and/or treatment of persistent nosocomial infections.



Hartmut Hengel

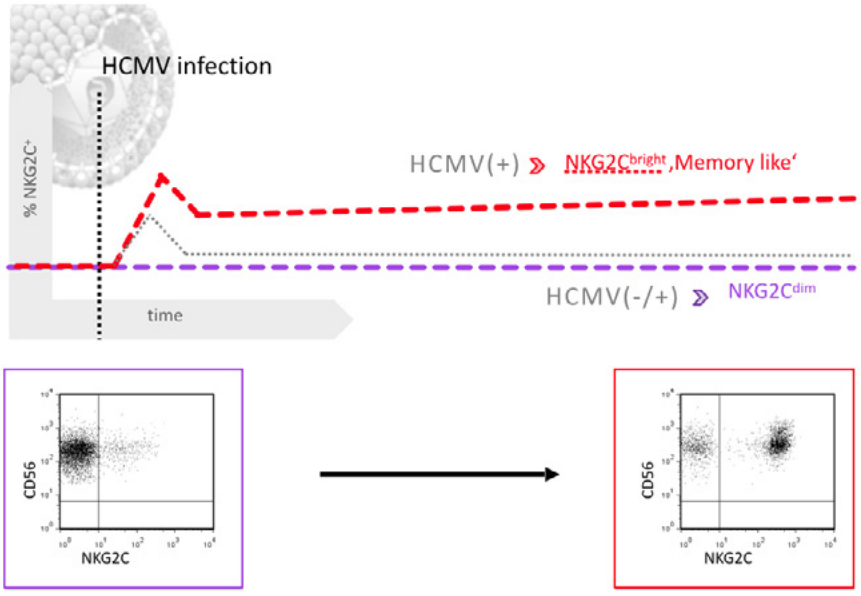
Targeting natural killer cells against cytomegalovirus

Acronym: TANKACY

Coordinator: Hartmut Hengel, University Medical Center, Freiburg, Germany; hartmut.hengel@uniklinik-freiburg.de

Partners: Carlos Vilches - Spain, Miguel López-Botet - Spain, James Di Santo - France, Noam Stern-Ginossar - Israel

Human cytomegalovirus (HCMV) is a herpes virus infecting humans worldwide at a high frequency. HCMV is characterized by a long state of latency intermitted by periodic reactivation, problematic especially in the immunocompromised. Natural Killer (NK) cells are important to the control of viruses by their ability to destruct infected cells. HCMV is able to expand a subset of mature "memory-like" NK cells. This project will study the protective capacity of NK cells in novel mouse models using transplanted human cells. Altogether, the results will lay the grounds for novel immunotherapies against HCMV disease.



Human Cytomegalovirus-mediated reconfiguration of the NK cell compartment

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