Objective 2: To map and correlate the observed rodents distributions with their species-specific environmental landscapes in order to extrapolate their potential "real" range and to anticipate their future distributions in relation to landscape modifications.
Objective 3: Computing epidemiological databases. Crosschecking field data and GIS data. Definition and standardization of a risk-scale. Finalization of maps of risks and distributions. Atlas of Thai Muridae. Reference collection of Thai Muridae. Education and training of students.
Following the listing of the objectives, we expose the first results of our studies and we sketch future projects.

(37) Human macrophage variability of *in vitro* infection by *Leishmania donovani*: a new approach to dissect human susceptibility to visceral leishmaniasis

Frédéric Vezilier[1], Rachel Bras-Goncalves[2], Cristina Riera[3], Salima Fatha[2], Roser Fisa[3], Teresa Serra[4], Maria Udina[5,6], Jaume Carrio[3], Enric Girona[5,6], Teresa Jimenez[5,6], Alejandro Forteza[5,6], Matil de Sedeiro[5,6], Mallorie Hide[1], Anne-Laure Banuls[1], and Bruno Bucheton[1].
1. UMR CNRS/IRD 2724 Genetics and Evolution of Infectious diseases, Montpellier, France; 2. IRD UR008 Pathogénie des Trypanosomatidae, Montpellier, France; 3. Laboratorio de Parasitologia, Facultad de Farmacia, Universtitat de Barcelona, Spain; 4. Servei de Microbiologia, Hospital Universitari San Dureta, Palma, Spain; 5. Fundacio Banc de Sang i Teixit de les Illes Balears, Palma, Spain; 6. Institut Universitari de Investigacio en Ciencies de la Salut (IUNICS), Palma Spain.

In its human host, *Leishmania donovani* is an intracellular parasite of macrophages and parasitism display a wide spectrum of clinical manifestations ranging from asymptomatic infections to fatal visceral leishmaniasis (VL). A bulk of evidence from mice and man now indicate that host genetic factors play an important role in determining susceptibility to VL. Until now studies aimed at unravelling human genetic susceptibility to VL have focussed on the analysis of clinical phenotypes. These clinical phenotypes probably result from the interaction of both host and parasite genetic factors but also environmental factors, making these phenotypes complex for genetic dissection. We propose here a novel alternative approach based on the study of a cellular phenotype established *in vitro.* In this study we have established the *in vitro* macrophage infection status of 20 healthy blood donors and their response to IFN□. We demonstrate the existence of an important inter-individual variability of the macrophage permissive phenotype (parasitic index ranging from 20 to 100 amastigotes/100 macrophages) as well as important differences in the individual response to IFN□□(parasitic index reduced in only half of the subjects upon IFN□ activation). In a second step we attempted to correlate the observed cellular phenotypes with the expression of various macrophage genes implicated in *Leishmania* recognition (CR1, MSF1R), macrophage activation/deactivation (IL1, IL6, IL10, IL12, RANTES, MIP1□, TNF□) and macrophage microbicide activity (NOS2, ARG1, NADPH p40phox). Significant correlations were found between the ratio of NOS2/ARG1 and the p40 phox unit of the NADPH oxidase but none of the measured variables were explicative of the capacity to respond to IFN□. These preliminary results indicate that this approach provide a valuable tool to analyse host-parasite interactions at the host cell level. Indeed studies in mouse derived macrophages or human

monocytic cell line have shown that infection by *Leishmania* has a profound influence on the macrophage transcriptome. However studies are lacking that address specifically the question of the variability of macrophage responses to *Leishmania* infection in human and its relation with resistance/susceptibility to VL.

Symposium "Molecular biology and epidemiology of pathogens and vectors"

(38) Detection of Glutathione S-Transferase e2 (*gste2*) gene in Iranian and Pakistani populations of main malaria vector *Anopheles stephensi*

[1,2]Nooshin Bayat, [1]Saber Gholizadeh, [1]Sedigheh Zakeri,*[1]Navid Dinparast Djadid

1. Malaria Research Group (MRG), Biotechnology Dept., Pasteur Institute of Iran

2. Biology Dept., Science and Research Branch, Islamic Azad University

* Corresponding author: Navid Dinparast Djadid, P.O. Box: 1316943551, Pasteur Avenue, Tehran, Iran, e-mail: ndjadid@yahoo.com; navid@institute.pasteur.ac.ir, Tel: +98 21 66480780; Fax: +98 21 66465132

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One of the most important genes involved with metabolic insecticide resistance (specially DDT resistance) in *Anopheles gambiae* is the epsilon class of the Glutathione S-transferase super family. In current study, PCR analysis of gste2 region have shown nucleotide variations within populations of *Anopheles stephensi,* the most important malaria vector in Iran and middle east. Specimens were collected from three different zones including; Chabahar, Sarbaz, Nikshahr, Iranshahr, Saravan and Khash districts in Sistan and Baluchistan province, Iran, which are under insecticide application for a long time; areas that has not been treated with insecticides for a long time (Kazeron), Fars province, Iran; and *An. stephensi* population from Pakistan. The result revealed that Iranian strains collected from Sistan and Baluchistan province were 100% identical in GSTe2 DNA sequences except Saravan strain which has showed 100% identity with Pakistani strain, and
99% identity with others. Kazeroon strain was 99% identical with both Pakistani and Iranian strains with a C→G transversion and A→C transition in 105th and 174th nucleotides, respectively. Pakistani and Saravan strains showed A→G transition in position 243 and C→T transition in nucleotide number 351. The follow up study on further specimens from those areas has detected two types of nucleotide variation in Sarbaz samples; one type is identical to Saravnian and Pakistani samples and the other type is similar to other Sistan and Baluchisatn samples. However, in amino acid level, all the sequences were 100% identical proving that the nucleotide variation which was observed doesn't involve with the insecticide resistance. We will further discuss the cloning results related to *gste2* in Sarbaz populations of *An. stephensi.*

Vezillier Frédéric, Bras Goncalves Rachel, Riera C., Fatha S., Fisa R., Serra T., Udina M., Carrio J., Girona E., Jimenez T., Forteza A., De Sedeiro M., Hide Mallorie, Banuls Anne-Laure, Bucheton Bruno. (2006).

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