

Awarded projects in alphabetical order
New INDIGO: NPP Call on Biotechnology and Health

AlzBioIndigo

Accelerating the development of New Molecular Bio Markers for Alzheimer's Disease

Project coordinators:

- CNRS Université Mediterranee, France
- Nizam Institute of Medical Sciences, India

Project partners:

- Ruhr-Universität Bochum, Medicine Proteome Centre; Bochum, Germany
- University of Lisbon, Clinical Neuropharmacology; Lisbon, Portugal
- CNRS, SysDiag; Montpellier, France

ALZBIOINDIGO aims to develop an indo-euro network to accelerate the development of new molecular biomarkers for Alzheimer's Disease (AD), in full agreement with the EMEA guidelines (EMEA/CHMP/SAWP/72894/2008 Corr), in coherence with the concept of biomarker 'signatures' as followed by PharmaCog IMI project, EuroADNI initiative, supported by French Eurobiomed and Indian Biogenesis clusters.

Objectives are to advance harmonisation in research on AD, to strengthening bilateral S&T cooperation between Europe and India. Specific aims are to: organize seminars, standardize diagnosis criteria and cognitive evaluation (ADNI battery), implement and standardize biomarkers (CSF tau, Ptau, Abeta), harmonize ethical principles, identify new biomarkers by detecting a large diversity of proteins in plasma and CSF using state of the art proteomics techniques, to disseminate/ exploite.

The consortium comprises:

An Indian memory Center and pharmacology team (Prof Borgohain, NIMS, Hyderabad). A French excellence research team for biomarkers, specific monoclonal antibody selection for diagnosis, theranostic and prognosis, system biology for multi-scale modelling in complex pathologies (CNRS Sysdiag, Dr Laune, Montpellier) and a French pharmacology team in France, coordinator of IMI PharmaCog (CNRS, INCM, UnivMed, Prof Blin, Marseille). A proteomics centre in Germany for biomarker discovery and validation, using neuroproteomics and bioinformatics (Prof Meyer, Bochum). A Portuguese Neuropharmacology department (Prof Sampaio, Lisbon) for regulatory aspects.

Techniques: monoclonal antibody, multiplex immunoassays, ESI-ITMS, MALDI-TOF/ TOF, ESI/MALDI-QTOF, 2D gel electrophoresis, DIGE, multidimensional-nano-HPLC, proteomics workflow, immunohistochemistry, protein chips, bioinformatics/ biostatics, and Biomarker qualification. AlzBioIndigo impact: workshops, standardization, joint publications, patents, network and technology transfer.

Anti-CHIK

Structure-based discovery of antivirals for the treatment of Chikungunya virus infections

Project coordinators:

- Universität zu Lübeck, Institute of Biochemistry; Lübeck, Germany
- Birla Institute of Technology, Dept. of Pharmaceutical Sciences; Ranchi, India

Project partners:

- University of Madras, Dept. of Crystallography and Biophysics; Chennai, India
- Université de la Mediterranee, Aix-Marseille II, Dépt. de Viologie Structurale et Drug Design; Marseille, France

Chikungunya virus (CHIKV) infection results in acute febrile illness associated with severe polyarthralgias and rash. Although the disease is not considered life-threatening, atypical clinical neurological, cardiovascular, ocular and renal manifestations can result in significant mortality. No vaccines or antiviral treatments are available. The recent massive epidemics of CHIKV on the islands of the Indian Ocean and India have elevated this anthropod-borne virus to the status of a major global health problem. In India, there was an explosive outbreak in 2006, which involved 1.4 million cases. Right now, there are tens of thousands of cases in India. CHIKV is transmitted to humans by the *Aedes aegypti* mosquito and recently by *Ae. albopictus* (Tiger mosquito), which is also present in Southern France, Spain and Italy. An outbreak of CHIKV involving 254 cases occurred in 2007 in Italy, where the index case was a traveller returning from India. As *Ae. albopictus* is able to survive temperatures of 10 C and below, large regions of Europe are at risk of

experiencing CHIKV outbreaks. Over the past few years, CHIKV has adapted to the new vector by introducing mutations into its E1 and E2 surface proteins. The project aims at determining crystal structures for the four non-structural proteins (nsPs) of CHIKV that are involved in replication. The 3D structures will be used for the design of anti-CHIKV compounds. UzL is specialized in proteases of RNA viruses and will focus on nsP2, the CHIKV protease. UnivMed will determine the crystal structures of nsP1 and nsP4. This group has recently elucidated the structure of nsP3. BIT will use the structures for structure-based design of antivirals and synthesize the molecules found. UoM will participate in the crystal structure determination of nsP2 and in using fragment screening to create inhibitors. UoM will provide extracts from Indian medicinal plants for testing for antiviral activity. Candidate antivirals will be tested by UnivMed.

CML Standardization

Standardization of response assessment in chronic myeloid leukemia (CML)

Project coordinators:

- Universitätsklinikum Jena, Klinik für Innere Medizin II; Jena, Germany
- All India Institute of Medical Sciences, Institute Rotary Cancer Hospital; New Delhi, India

Project partners:

- Université Victor Segalen Bordeaux 2, Laboratoire Hematopoïèse Leucémique et Cible Thérapeutique ; Bordeaux, France
- Nizams Institute of Medical Sciences, Dept. of Medical Oncology; Hyderabad, India
- Tata Memorial Centre, Dept. of Medical Oncology; Mumbai, India

The high efficacy of the standard treatment of chronic myeloid leukemia (CML) with imatinib has prompted the need for accurate methods to monitor response at levels below the landmark of complete cytogenetic remission. Quantification of BCR-ABL transcripts has proven to be the most sensitive method available, and has shown prognostic impact with regard to progression-free survival. Until recently, variations in methods and calculations used to quantify BCR-ABL mRNA transcripts made it difficult to compare results between laboratories. Laboratories in 28 countries in Europe have been harmonized the reporting of results according to an international scale (IS). In this projects, we plan to spread this experience to laboratories in India, to allow treatment optimization for a large number of CML patients in India as well. We aim to establish recommendations for the propagation of the international scale for BCR-ABL quantification in India. In parallel, the exact quantification of imatinib drug levels will be established in India to provide an opportunity to adjust treatment in case of suboptimal response or unexpected side effects. Imatinib blood level are considered a prognostic indicator. An imatinib trough plasma threshold for optimal response of 1,000ng/ml has been proposed but needs further validation in different ethnical groups. There is insufficient evidence to define any relationship between plasma levels and adverse events and, although it is not yet possible to define and validate a comprehensive algorithm for the application of blood level testing clinical practice, a working model has been developed in Europe. A collaboration with labs in India, data pooling and initiation of a comparative epidemiological study would be important steps in addressing current questions regarding management and treatment optimization of CML patients. Scientific workshops and exchange of scientists will be organized between Germany, France and India to foster cooperation.

GASB

Identification of Genetic Alterations in the Stromal Cells Associated with Breast Cancer.

Project coordinators:

- Champalimaud Cancer Centre; Lisbon, Portugal
- MNJ Institute for Oncology & Regional Cancer Centre; Hyderabad, India

Project partners:

- German Cancer Research Centre; Heidelberg, Germany

Increasing evidence suggests that tumor initiation and progression involves the interplay between the cancer cells and the stromal cells in the tumors. Tumors are unorganized organs that contain an ensemble of stromal cells such as fibroblasts and endothelial cells that are all embedded in fibrotic extracellular matrix. Most of the studies involving the tumor microenvironment are focused on how the stromal cells may influence the cancer cells via paracrine actions and vice versa. While the notion that tumor progression is driven by mutations that accumulate in the cancer cells is well accepted, the contribution of genetic defects in the stromal cells to cancer progression is unknown. The project is designed to procure tissue samples from 500 breast cancer patients via approved

institutional protocols and use these samples to isolate fibroblasts and endothelial cells via cell culture and FACS analysis. These samples will be compared to cells isolated from normal breast tissue obtained after cosmetic or non-cancer related reduction mammoplasty. These samples are processed to perform gene expression analysis, CGH analysis, epigenetic analysis and microRNA analysis. The studies related to the patient sample procurement and initial genetic analysis will be performed in Hyderabad, the genetic analysis of fibroblasts will be performed in Libson and the genetic analysis of endothelial cells will be performed in Heidelberg. A comparison will be drawn between non-invasive ductal carcinoma in situ (DCIS) and invasive ductal carcinoma with respect to the genetic alteration in the stromal cells. Identification of possible genetic alterations will serve as a cancer cell autonomous biomarker to predict DCIS and invasive breast cancer. Collectively, our proposal will address novel questions and probe tumor microenvironment associated stromal cells for possible genetic alterations that can serve as predictive biomarkers for cancer progression.

HeartSEN

Surface Engineered Coatings on Mechanical Heart Valves: Diagnostics of Thrombosis

Project coordinators:

- Leibniz-Institut für Neue Materialien, Biosurfaces Department; Saarbrücken, Germany
- Indian Institute of Technology Madras, Semiconductor Laboratory; Madras, India

Project partners:

- Saarland University Faculty of Medicine, Paediatric Cardiology Department; Homburg/Saar, Germany
- Kocaeli University, Laser Technologies Research and Application Centre; Kocaeli, Turkey

The project aims at bringing a new concept for the detection of early prosthetic valve thrombosis (PVT) and minimizing this effect by developing new engineered surfaces alternative to conventional coatings used for prosthetic heart valve (PHV) leaflets. PHV leaflets coated with bi-layer of magnetic and hemocompatible films (diamond like carbon) will be prepared. These coated leaflets will be tested with in an ex vivo shunt. Within the shunt system, the magnetic thin film over the valve will be under an external applied field of few kHz, and the magnetization signal will be acquired. The movement of the leaflets, at a cardiac simulated rhythm, will induce a modulation in the amplitude of the signal and this modulated signal can be analyzed with a system consisting of an amplifier. In addition, a digital camera can record the movements of the magnetic layer coated leaflet which may enable us to characterize the signal changes when the valve begins to fail due to thrombosis.

MTBSS

Mycobacterium Tuberculosis: bioinformatic and structural strategies towards treatment

Project coordinators:

- Instituto de Tecnologia Quimica e Biologica, Depot. Of Biological Chemistry; Oeiras, Portugal
- Centre for DNA Fingerprinting and Diagnostics, Dept. for Structural Biology; Hyderabad, India

Project partners:

- Centro de Investigacion Principe Felipe, Dept. Of Structural Biology; Valencia, Spain
- Instituto Gulbenkian de Ciencia, Dept. Of Bioinformatics ; Oeiras, Portugal

Tuberculosis is a debilitating infectious disease that is a serious health threat, particularly in its multi-drug-resistant forms. We aim to combine bioinformatics tools and resources with NMR structural biology to identify and screen new drug targets against TB.

Chemical screening generates a large number of positive 'hits' that require time-consuming and expensive verification in cell and animal models before clinical trials can take place. Many 'hits' fail the toxicology screens. Using bioinformatics, we will use in-silico methodologies to identify the key proteins involved in the biochemical pathways of pathogen survival and evaluate their influence on human toxicity. We will develop chains of in-silico screening steps to apply to our positive, TB 'hits' against the identified tox-blocks. The molecular modelling methods will be verified by experimental NMR methods. Our second aim is to develop a rapid, inexpensive and computer-based filter within a self contained and narrow targeted pilot study that can be widely applied to the early stages of other drug screening projects.

Our consortium consists of bioinformatics and structural biology groups in India (CDFD), Portugal (ITQB, IGC) and Spain (CIPF). The bioinformatics studies will be carried out at IGC, CIPF and

CDFD. NMR screening will be supported by established teams at ITQB and CIPF. Structural biology at CDFD and CIPF will be supported by ITQB. Molecular modelling will be performed at CIPF with support from IGC and CDFD. We plan two management meetings, in India and Iberia (Portugal/ Spain) for the team leaders. Symposia, workshops and training sessions will be associated with the main exchanges: external experts will be invited and future collaboration discussed. Existing training programs will offer innovative opportunities for younger researchers in the scope of NEW Indigo. The working methodologies will be evaluated and results published in established peer-reviewed scientific journals.

NANOLINEN

Nanotoxicology link between India and European Nations

Project coordinators:

- Gazi University, Faculty of Pharmacy, Dept. of Toxicology; Ankara, Turkey
- Indian Institute of Toxicology research, Nanomaterial Toxicology Group; Lucknow, India

Project partners:

- Medical University of Innsbruck, Division of Biological Chemistry, Biocenter; Innsbruck, Austria
- University of A Coruña, Dept. of Psychology (Toxicology Unit); A Coruña, Spain
- Instituto Nacional de Saude Dr. Ricardo Jorge, Environmental Health Department; Porto, Portugal
- University of Amsterdam, Netherlands Centre for Occupational Diseases; Amsterdam, the Netherlands
- Federal Environment Agency, Section of Toxicology and Health-related Environmental Monitoring; Dessau-Rosslau, Germany
- French Atomic Energy Commission, Nanometric Structure Group; Paris, France

Nanotechnology is a rapidly growing converging technology bringing a growing amount of nanotech-based products on the market. This is associated with potential environmental and occupational health risks. The manufacturing, trade and use of nanoproducts may lead to worker exposure and environmental emissions of nanoparticles while the extent and the potential effects are still uncertain. Due to limited knowledge on the toxic effects of nanoparticles, there is a need to undertake studies in this new area.

This project aims at establishing strong scientific links between EU and India in the emerging area of nanotoxicology. As envisaged, the mobility of scientists among the eight participating countries will identify niches for perusing collaborative research. To create awareness and understanding of this new area, six workshops will be organized with participants from academia, industry, regulatory agencies and civil society. Collaborative projects focused on effects of nanomaterials on human health will be developed. Risk research, the development of good practices and tools for the safe handling of nanomaterials in practice, as well as establishment and validation of tests and biomarkers in R&D and production is envisaged. This is considered to provide contribution to the preparation of international guidelines for safe handling of NM. The complementary expertise of the partners will lead to R&D projects with a focus on sustainability. This contributes to the filling of knowledge gaps on safety aspects of nanoparticles on human and environmental health. Our ultimate goal is to develop robust risk assessment methodologies which will be useful and comprehensible for the community manufacturing and using nano-products, while bringing a precautionary approach into practice. We believe that the key to this goal lies under setting up a strong link over EU and India.

Nitroxdiab

Post-translational modifications induced by nitroxidative stress as biomarkers of vascular damage in diabetes

Project coordinators:

- Consejo Superior de Investigaciones Cientificas, Instituto de Biologia Molecular; Madrid, Spain
- CSIR Central Drug Research Institute/Pharmacology Division; Lucknow, India

Project partner:

- Johan Wolfgang Goethe Universität Frankfurt, Institute of Biochemistry; Frankfurt, Germany

Nitric oxide (NO) is an ubiquitous diatomic free radical with essential functions. Signalling by NO may occur through the activation of soluble guanylate cyclase and generation of cGMP or by interaction of NO with metal centers, heme groups or other free radicals. Crosstalk between reactive oxygen and nitrogen species ((ROS/RNS) provides the biochemical basis for nitroxidative stress (NS). This term connotes an altered production of ROS/RNS and/or impairment of cellular antioxidant defenses, leading to a disruption of redox signaling and molecular damage. NS promotes the induction of post-translational modifications (PTMs) in proteins. The best characterized are tyrosine nitration, S-nitrosylation and S-glutathionylation. Their occurrence has been related to changes in protein function in health and disease. Diabetes is a highly prevalent illness where a dysfunctional vascular wall and a pro-inflammatory environment co-exist and where there is a fundamental need to identify biomarkers for damage. Nitroxidative stress is an important pathogenetic mechanism in diabetic vascular injury. PTMs have been poorly characterized in this context. We will focus on PTMs which could represent useful biomarkers in animal models of diabetes and in diabetic patients combining the expertise in NS of the three laboratories involved in this proposal. We will use neutrophils (Indian partner), macrophages (German partner) and endothelial cells (Spanish partner) and identify NS-related PTMs with latest generation proteomic approaches. Initially we will study the interaction between macrophages, neutrophils and endothelial cells in co-culture systems, employing diabetic mice to characterize PTMs. In a second stage these PTMs will be characterized in neutrophils and macrophages from diabetic patients co-incubated or not with human endothelial cells. We will deliver a set of PTMs in each cell type representing biomarkers for NS-related vascular and inflammatory damage present in diabetes.

Planty

Valorisation of plant-derived by-products as functional ingredients in animal and human health

Project coordinators:

- Veterinaermedizinische Universitaet Wien, Institute for Applied Botany and Pharmacognosy; Vienna, Austria
- National Chemical Laboratory, Dept. of Biochemical Engineering; Pune, India

Project partners:

- Institut de Recerca i Tecnologia Agroalimentaries, Food Technology; Barcelona, Spain
- Wageningen University and Research Centre, Institute for Animal Science and Health; Wageningen, the Netherlands
- Anadolu University, Faculty of Pharmacy; Eskisehir, Turkey
- Universität Hohenheim, Institute of Food Science and Biotechnology; Stuttgart, Germany

The vegetal processing industry produces tons of organic wastes annually. This might be valuable starting materials for food chain with significant health benefits. PLANTY-project will bring together experts from academia and decision-makers to exchange know-how and to discuss, to identify promising research fields in health via food chain from such plant-derived by-products. The objective is to bridge the gap between European and Indian research teams to find actual research tendencies for the future. The 24-months project activities include promoting and facilitating the dissemination, exploitation and transfer of the European and Indian research project results and will further integrate researchers and experts from both continents. The PLANTY-project has the overall objective to disseminate state-of-the-art of research results in feed quality topics through a series of expert work shops including disseminating research results of recently funded EC-projects (REPRO, SAFEWASTES, PIG for HEALTH, REPLACE, FLAVO) focusing on feed/food safety, the consortium will develop new research proposals for future calls. Detailed plans and actions to foster livestock and human health research in Europe are part of the work plan and objectives. PLANTY will address the issue by taking a comprehensive approach looking for sustainable processes to turn food processing by-products into new feeds/foods: an inter-disciplinary approach. The proposal sets the basis of exchange of researchers between Indian partners with complementary skills and subject to Indian DBT and PLANTY EU performers.

Collaborative project PLANTY combines six partners from universities and research institutions of five different European NEW Indigo funding member countries and India with diverse expertise. PLANTY-project is a research project in coordination with an Indian research consortium that submits a proposal to DBT (Department of Biotechnology India). This proposal is a follow-up of the finalised EU-FP6-project SAFEWASTES.

Plasfalsyn

Structure/Function studies of Plasmodium falciparum GMP synthetase

Project coordinators:

- CNRS, Laboratory of BioCrystallography; Lyon, France
- Jawaharlal Nehru Center for Advanced Scientific Research, Molecular Biology and genetics Unit; Bangalore, India

Project partners:

- University of Groningen, Laboratory of Biophysical Chemistry; Groningen, the Netherlands
- CNRS Lyon, IBCP/BICI; Lyon, France

Malaria caused by *Plasmodium falciparum* is responsible for more than 1-2 million deaths worldwide annually. Lack of a vaccine along with widespread occurrence of drug resistance necessitates developing new drugs. Metabolic pathways indispensable for parasite survival are obvious targets for the development of new antimalarials. One potential target is the purine salvage pathway as it provides the sole source of purine nucleotides to the rapidly multiplying parasite. Importance of the pathway as a drug target, is further highlighted by recent research efforts to biochemically and structurally characterize the constituent enzymes. During the parasite's intraerythrocytic stages when the disease is manifested, synthesis of the purine nucleotide GMP proceeds through two steps: conversion of IMP to XMP catalyzed by IMP dehydrogenase followed by GMP synthetase (GMPS) converting XMP to GMP. This project aims to structurally and biochemically characterize PfGMPS, dock and identify potential inhibitor molecules and test inhibitors for effect on enzyme activity and parasite growth in *in vitro* cultures. GMPS catalyses the amination of XMP to GMP with the reaction occurring in two domains, the GAT (glutamine amidotransferase) and ATPase (ATP pyrophosphatase). Activity coordination across the two domains, through channelling of ammonia from GAT to the effector domain, is the hallmark of amidotransferases. Unique features of PfGMPS both in sequence and biochemical characteristics along with essentiality of the pathway for parasite survival justify PfGMPS as a potential drug target. Preliminary work from the Indian project coordinator provides a platform for further investigations. This partnership encompassing expertise in biochemistry, crystallography, simulation, *in silico* drug screening and parasitology ensures high rate of success and a framework for strong future international ties.

PotBIO

Generating Biomarkers for breeding healthy potatoes

Project coordinators:

- Wageningen University and Research Centre, Lab. Of Plant Breeding, Dept. of Plant Sciences; Wageningen, the Netherlands
- Central Potato research Institute, Division of Plant Protection; Shimla, India

Project partners:

- Friedrich-Alexander-University, Institute of Biology; Biochemistry; Erlangen, Germany
- Consejo Superior de Investigaciones Cientificas, Dept. Of Plant Molecular Genetics ; Madrid, Spain
- Scottish Crop Research Institute, Genetics Programme; Dundee, UK (not funded)

Potato is a member of the Solanaceae: a plant family that includes several other economically important species, such as tomato, eggplant, petunia, tobacco and pepper. Potato is an important global food source. After wheat and rice, potato is the third most important food crop with a worldwide production of 325 thousand tons in 2007 (FAO). Tuber crops will play an important role in feeding the developing world in the coming decades. The growth rates in production are particularly strong for potato with an annual average increase of 4.5 million tons per year, exceeding those estimated for rice and wheat. Recent increases in India have been particularly striking. By 2020, more than two billion people in Asia, Africa and Latin America will depend on these crops for food, feed, or income. Current decisions on research investments for root and tuber crops and the strategy chosen for this research will have profound global implications for decades to come. For developing countries, breeding efforts should be focused on high yielding and highly nutritious crops in adverse abiotic conditions. Potato has the potential to fulfil a large part of the human nutritional demands for both calories and several vitamins such as Vitamin C, B and D. With the recent completion of the potato genome sequence (undertaken together with the CPRI in Shimla, India), the way is now open to systematically generate molecular markers from sequence analysis of cultivars. In this project we aim to establish a collaborative framework between India

(CPRI, Shimla), Germany (University of Ehrlangen), Spain (CSIC, Madrid) and the Netherlands (Wageningen-UR, Wagenigen). The basic approach will be to identify cultivars and wild accession with desirable phenotypes for health giving compounds and screen for SNPs in candidate genes that are known to be involved in the biosynthesis of the corresponding metabolites.

SAP

Elucidating the pathogenesis of staphylococcal diseases by studying virulence factors of Indian Community Associated Methicillin Resistant Staphylococcus aureus.

Project coordinators:

- Sir Dorabji Tata Centre for Research in Tropical Disease, Dept. of Microbiology; Bangalore, India
- Faculté de Médecine Lyon Est, Equipe Pathogénie des Staphylococques ; Lyon, France

Project partners :

- Erasmus Medical Center, Clinical Microbiology ; Rotterdam, the Netherlands
- Karolinska Institutet, Centre for Infectious Medicine; Stockholm, Sweden (not funded)

Staphylococcus aureus is a versatile human pathogen causing diseases ranging from mild infections to life threatening sepsis. Infections due to methicillin-resistant strains were mainly considered nosocomial, but recent years have witnessed the rise of skin and soft tissue infections, necrotizing pneumonia, and fasciitis, caused by CA-MRSA. Several reports have indicated that CA-MRSA are replacing hospital associated MRSA in hospitals. Studies on Indian CA-MRSA are just beginning. We have genotyped Indian HA-MRSA and are now characterizing CA-MRSA isolates to understand the differences in factors responsible for pathogenicity between the two. Our studies till now indicate large diversity in the sequence types present in Indian CA-MRSA unlike other countries where one or two sequence types dominate. We are looking at the staphylococcal toxin profiles including the presence of Panton Valentine leucocidin (PVL) gene in the Indian isolates. Our data show that a high percentage of Indian MRSA and methicillin sensitive *S. aureus* isolates are PVL positive. These strains have a wide variety of staphylococcal exo and entero toxins, hemolysins and pathogenicity islands. All these elements are considered important virulence factors but their roles are not entirely clear. Several epidemiological studies point to the importance of PVL in skin and soft tissue infections although data from animal models are equivocal. We would like to study first the impact of PVL in the Indian isolates on staphylococcal disease burden and second, the effect of over use of antibiotics on the levels of various toxins especially PVL.

The research targets of the three groups are complementary and this grant will give us an opportunity to study patterns of nasal colonization of humans living in a tropical country. Simultaneously, we will resolve the role of staphylococcal virulence factors during antibiotic usage and the role that these factors play in initiation and progression of infectious diseases.

TRICONT

Target specific small molecules to control infections due to Trypanosomatids

Project coordinators:

- National Institute of Pharmaceutical Education and Research, Institute of Biotechnology; SAS Nagar, India
- Instituto de Biologia Molecular e Celular; Porto, Portugal

Project partners:

- National Institute of Pharmaceutical Education and research, Computer Center; SAS Nagar, India
- Universidade de Porto, Instituto de Biologia Molecular e Celular; Porto, Portugal
- Universita de Modena e Reggio Emilia, Dipartimento di Scienze Farmaceutiche ; Modena, Italy (not funded)
- Instituto de Salud Carlos III, Dept. of Parasitology; Madrid, Spain

Infectious disease burden imposed by the parasites of Trypanosomatidae family continues to represent a huge problem on people's lives and human suffering in developing countries. Problems associated with currently available drugs are inefficient delivery, insufficient efficacy, excessive toxicity and steady loss of effectiveness due to increasing resistance. New drugs are urgently needed now and in the foreseeable future. Availability of the genome sequence of pathogens of this family offers a unique avenue for identification of novel drug targets and opportunities for the target based discoveries of new lead compounds.

By using a comparative genomic approach we have identified two common and potential targets against Trypanosomatidae family members with no human homologue to avoid potential toxicity issues. These targets (ribose isomerase and asparagine synthetase from *L. infantum*, *L. major*, *T. brucei* and *T. cruzi*) were cloned and recombinant proteins expressed in bacteria systems. The enzymatic assays to screen new inhibitors are ongoing.

The objectives in this project will be to identify new ligands (India), synthesize focused-ligand libraries (Italy), test and validate them in vitro biochemical and cell based assays as well as their effect on the immune system (Portugal and Spain). To further improve the biopharmaceutical properties of the new synthesized small molecules; drug delivery systems, based on liposomal and nano-particles formulations, specific to Trypanosomatidae will be developed (Portugal). If successful, this consortium expects to identify, synthesize, characterized new anti-parasitic molecules towards Trypanosomatidae and to develop a protozoa specific targeted-drug delivery system.