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Anne-France DEKAIRELLE, PhD

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- BADIR Jamal, Technological Logistician CUSL
- BEARZATTO Bertrand, Postdoctoral Fellow IREC
- BENTAHIR Mostafa, Postdoctoral Fellow MOD
- BOUYER Michèle, Technician MOD
- CARLIER Elodie, Technician MOD
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- DECCACHE Yann, Research Assistant MOD
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- DELHEZ Huguette, Technician CUSL
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- DILLEMBOURG Marc, Technical Manager IREC
- DUBOIS Nicolas, Research Assistant IREC
- DUMONT Catherine, Research Assistant MOD
- DURANT Jean-François, Research Assistant IREC
- ELMJOUZI Maimouna, Account Manager IREC
- GALA Jean-Luc, MD, Director CTMA MOD/CUSL
- HANON France, Technician CUSL
- HEUSTERSPREUTE Michel, Postdoctoral Fellow CUSL
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- ISSAOUI Bouchra, Technician CUSL
- MAJOR Karine, Technician IREC
- MARCEL Jean-Paul, Technological Platform Manager CUSL
- MARTIN Christian, Logistics Assistant CUSL
- MINEEVA Olga, Research Assistant IREC
- NIENHAUS Louise, Technician IREC
- PIETTE Anne-Sophie, Postdoctoral Fellow MOD
- SINON Audrey, Postdoctoral Fellow IREC
- SMIT Benjamin, Technician IREC
- TOUFIK Nora, Technician CUSL
- VAN CAUWENBERGHE Stéphane, Technician MOD
- VAN EYCKEN Anne, Clinical Administrative Assistant CUSL
- VERBERCKMOES Steven, Manager Defence Bio-Lab MOD
- VYBORNOVA Olga, Postdoctoral Fellow IREC
- VAN OOSTERHOUT Maria Elka, Research Assistant IREC

CENTRE FOR APPLIED MOLECULAR TECHNOLOGIES (CTMA)

"The Centre de Technologies Moléculaires Appliquées (CTMA - Centre for Applied Molecular Technologies)" is a mixed academic-clinical-military biotechnological platform mutualizing the resources of three partners:

1. UCL/IREC (Université catholique de Louvain/Institut de recherche expérimentale et clinique). CTMA is the IREC-reference biotechnological platform (genetics and molecular genetics); it therefore directly supports IREC-related research activities and teams while also developing proprietary research in the field of technology and security.
2. CTMA carries out clinical routine analysis and clinical research in the field of genetics and molecular genetics to support the medical activity of the academic hospital "Cliniques universitaires St Luc" (CUSL).
3. MOD (Ministry of Belgian Defence). CTMA hosts several research projects and activities for the MOD to better control the biological risks related to the CBRN (Chimical, Bacteriological, Radiological & Nuclear threats) spectrum. As such, CTMA is the "Biothreat control unit of Defence Laboratory Department (DLD)" and is therefore specifically named DLD-Bio; from there its full acronym CTMA/DLD-Bio.

CUSL : Cliniques universitaires Saint-Luc,
MoD : Belgian Ministry of Defense

1. STRUCTURE

Figure 1 shows the working architecture of the integrated CTMA/DLD-Bio platform with NATO-, EU-, ESA-agencies or organizations, BE governmental authorities, academic-, industrial- and military-partners.

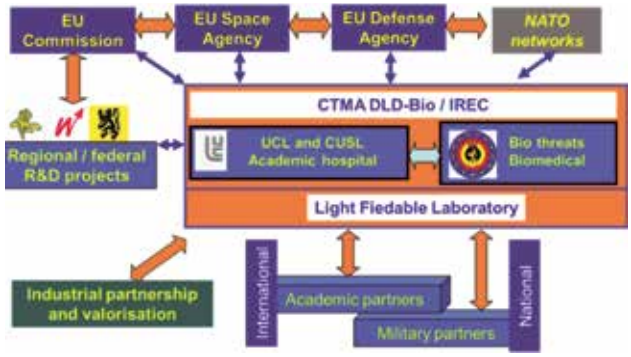

Figure 1 **CTMA/DLD-Bio Organization Architecture**

According to its integrated working structure, CTMA/DLD-Bio hosts at the same location researchers from the Belgian Defense and UCL/IREC/CTMA as well as the clinical staff working for the academic hospital (Cliniques universitaires St Luc - CUSL). Accordingly, this biological platform benefits from a genetics-dedicated infrastructure, emerging technologies, and a panel of equipment specifically acquired to fulfill its academic, military and clinical missions. Taking advantage of this mixed academic-clinical-military platform and associated multidisciplinary activities, CTMA/DLD-Bio has progressively developed a strong and extensive clinical, academic and military national and international networking leading to several fruitful multinational partnerships and projects as well as elective bilateral partnerships throughout Europe and Africa. ■

2. MISSIONS

CTMA/DLD-Bio main missions are (See Figure 2):

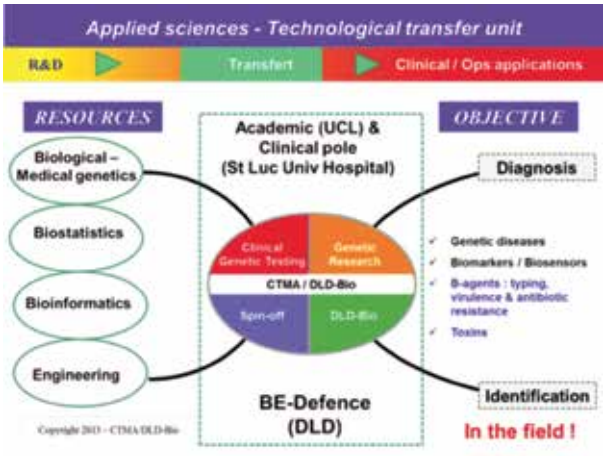

Figure 2 **Missions - multidisciplinary support to the biological spectrum of activities**

• Service activities: CTMA/DLD-Bio offers expertise and technological support to IREC-researchers and beyond; CTMA has also actively developed a service activity for industry (e.g., fungal biomass production for the preparation of vaccines) in CTMA-MYCO premises, Louvain-La-Neuve).

• Dual military-civilian R&D activities: development and/or use of new emerging technologies enabling better detection and protection against known and unknown threatening infectious agents; Low/high density gene expression profiling (biomarkers in malignant and inflammatory diseases); Genome characterization by re-sequencing (including Next Generation Sequencing - High Throughput Sequencing); signal processing, machine learning and biostatistical analysis.

• Expertise in EU Security: study of Belgian and European preparedness and responses to B-threats of the CBRN (Chemical, Biological, Radiological and Nuclear Threats) spectrum; scientific, technical and operational support to Belgian Defense Laboratories (CBRN);

• Clinical activities for CUSL: development of diagnostic assays (e.g., infectious and genetic diseases, pharmacogenomics & new biomarkers...)

• Academic courses in Molecular Biology, Genetics, in Statistical Genetics & Multivariate Data Analysis and CBRN topics and Training to Defense units. ■

3. RESEARCH ACTIVITIES

To mutualize the benefits and resources, all the research activities of CTMA are integrated into a single and global R&D matrix which interconnects together each project in terms of technologies, expertise and know-how. Financial support is obtained from the Belgian Defense as well as from the Brussels (Innoviris) and Walloon (BioWin, WBHealth, Marshall Plan) regions, and from federal (BELSPO) and international (EC, EDA and ESA) institutions.

Figure 3 shows the strong interrelationship of the whole research activity of CTMA and the link with national and international organizations (for funding and cooperation) ■

Figure 3 : **R&D Matrix Civilian-Military Joint contribution**

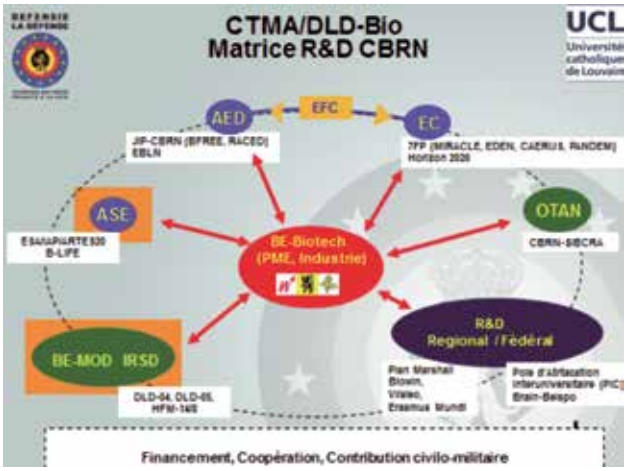

Table 1 presents on-going doctoral thesis works where Prof Jean-Luc GALA is promotor ou co-promotor.

Name	Promotor	Co-Promotor	Thesis
Aydin S. Medical Doctor CUSL	**Gala J-L**	Couyns J-P	TP53 Mutations and Aristolochic Acid-associated Urothelial Cancers
Beteesca V. Pharmacist CUSL	Tombal B.	**Gala J-L**	Prostatic Carcinoma and Pronostic Genetic Markers
Vu Phuong Hoang T. Pediatrician CUD	Vermylen C.	**Gala J-L**	Impact of Pharmacogenetics in Belgian and Vietnamese Childrens with ALL
Rassoe J. Ms. Eng. UCL	Francis L.	**Gala J-L**	Fast electrical detection of microorganisms on porous silicon membranes

Table 1 : On-going doctoral thesis at CTMA

A) Research activities to support IREC-related research activities

As technological platform of the IREC institute, CTMA offers technological support and expertise to IREC-researchers from multiple IREC Research Labs.
CTMA provides to the IREC researchers access and support to use numerous molecular technologies including (see Figure 4): quantitative PCR, Sanger Sequencing, Pyrosequencing and Next-Generation-Sequencing (Illumina-Miseq), microarrays facilities (Affymetrix, Agilent, custom glass slide arrays…).

Figure 4 : **CTMA provides access and support to various technologies**

As illustrated in Figure 5, the multidisciplinary team from CTMA provides a support on different aspect of the research projects from the experimental design until the data analysis and the validation of new devices. ■

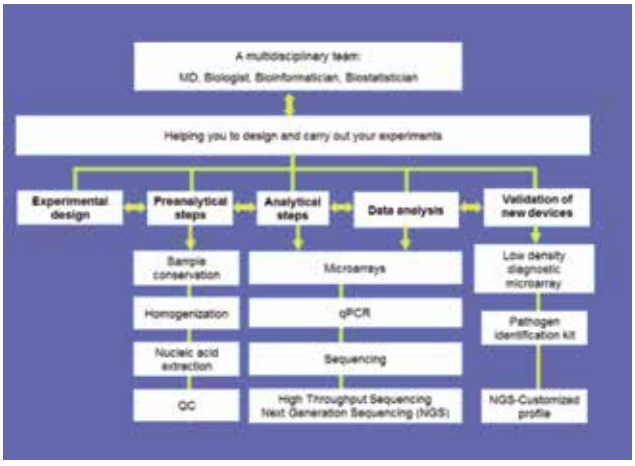

Figure 5 : **CTMA multidisciplinary support to IREC research projects.**

Table 2 presents the main research collaborative projects between the technological platform CTMA and research fellows of other IREC research laboratories.

IREC Research Lab	Contact	Project Description or Publication
LTAP	D. Lison, S. Vandenbrulle	A metagenomic study of theeffects impact of Ag nanoparticles on gut microbiota (to submit in 2015)
GYNE	M. Soarres & M.M. Dolmans	Soares, M ; Sahrari, K; Chiti, MC ; Amorim, C ; Ambroise, J ; Donnez, J ; Dolmans, MM. The best source of isolated stromal cells for the artificial ovary: medulla or cortex, cryopreserved or fresh?. In: Human Reproduction, 2015
	M.M. Dolmans & M. Binda	Dolmans, MM ; Binda, MM ; jacobs, s ; Dehoux, JP ; Squifflet, JL ; Ambroise, J ; Donnez, J ; Amorim, C. Impact of the cryopreservation technique and vascular bed on ovarian tissue transplantation in cynomolgus monkeys. In: Journal of Assisted Reproduction and Genetics, Vol. 32, no.8, p. 1251-1262 2015
	M.M. Dolmans & G. Courtoy	Statistical analysis of PCR array
PEDI	E. Sokal & S. Varma	Histological quantification of apha smooth muscle actin predicts future graft fibrosis in pediatric liver transplant recipients? (Submitted in 2015)
	E. Sokal & S. Varma	Allograft inflammation and fibrosis among maintenance pediatric liver transplant recipients – genetics predisposition and antibodies, connecting the missing links; (Submitted in 2015)
CHEX	B. Tombal & V. Butoescu	Ambroise, J ; Butoescu , V ; Robert , A ; Tombal, B ; Gala, J-L. Multiplex pyrosequencing assay using AdvISER-MH-PYRO algorithm: a case for rapid and cost-effective genotyping analysis of prostate cancer risk-associated SNPs. BMC Medical Genetics, 2015
EPID	A. Robert & K. Savadogo	K. Sawadogo, J. Ambroise, S. Vercauteren, M. Castadot, M. Vanhalewyn, J. Col, A Rober; tInteraction between the Kansas City Cardiomyopathy Questionnaire and the Pocock's clinical score in predicting heart failure outcomes, 2015
RUMA	B. Lauwerys	Lauwerys, B ; Hernández-Lobato, D; Gramme, P ; Ducreux, J ; Dessy, A ; Focant, I ; Ambroise, J; Bearzatto, B ; Nzeusseu T, Adrien ; Van den Eynde, B; Elewaut, D; Gala, JL; Durez, P ; Housiau, F ; Hellepute, T ; Dupont, P. Heterogeneity of synovial molecular patterns in patients with arthritis. In: PLoS One, Vol. 10, no. 4, p. e0122104 [1-18] (2015)
IIP	C. Bouzin	Bouzin, C ; Lamba S, M ; Khaing, K ; Ambroise, J; Marbaix, E; Grégoire, Vi; Bol, V. Digital pathology : elementary, rapid and reliable automated image analysis. In: Histopathology (2015)
PNEU	C. Pilette & M Lecocq	PCR data analysis - best housekeeping gene determination
	C. Pilette et S. Dupasquier	Targeted RNA-sequencing design of probes for the targetting of 203 transcipts of Wnt and Notch pathways (n=96)
CARD	JL Vanoverschelde & C. De-Meester	Gene expression microarray on cardiac hypertrophic patients (n=12). Microarray experiments & biostatistical data analysis
	B. Gerber & AC. Pouleur	NGS : resequencing of 46 genes implicated in hypertrhophic Cardiomyopathy on 16 patients. Validation of 2 library preparation methodologies (Nextera from Roche and TruSight from Illumina). Identification of pathogenic variants.

Table 2 : On-going collaborative projects between CTMA and IREC.

B) CTMA/DLD-Bio research studies within the frame of the Belgian Defense Research Program

DLD 04 - Development of a mobile platform for simultaneous identification of main pathogenic biological agents under operational conditions – (bacterial agents of Class A CDC and WHO list of 12 bastards)

(2012-2015) (688 k€)
Cathy DELCORPS, Anne-Sophie PIETTE, Stéphane VAN CAUWENBERGHE

This study develops a portable microarray detection platform of all biological agents during a single test, using patented sequence (CTMA/DLD-Bio WO/2005/090596). Previous studies have developed an operational identification of hazardous biological agents capacity, but often detecting only one agent at a time. In the absence of clinical or epidemiological guidance, the identification of biological agents is done sequentially, which may require the completion of dozens of tests. This leads to very high expenses and waste of time, limitation in sample analysis rate according to the expending number of analyses required and the risk of contamination. This study combines the Rolling Circle Amplification (RCA) with the tridimensional microarray Pamgene ® for the development of tests enabling simultaneous identification of main biological agents on a single platform and a single multiplex assay. ■

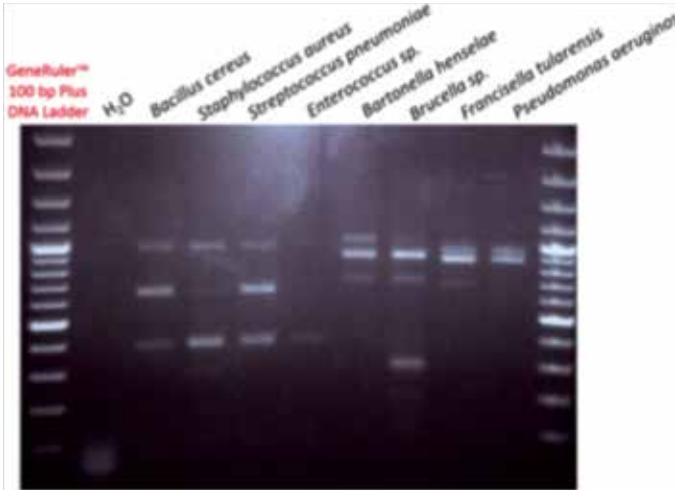

Figure 6 : Result from the multiplex PCR multiplex.

DLD05 - Rapid detection and characterization of micro-organisms responsible for orthopedic infections

(2013-2017) (566 k€)
Catherine DUMONT, Elodie CARLIER

The aim of this project is to validate the diagnostic value of transcriptomic and/or proteomic profiles of synovial material in early inflammatory or infectious disease (arthritis). It is based on preliminary data showing that gene expression profiles in synovial biopsies from patients with arthritis are able to discriminate the samples according to the underlying disorder. The large-scale confirmation of these data after will lead to the development of a prototype of a diagnostic tool to be used in routine rheumatology practice. ■

HFM14/8 - Novel multiplex method for identification of genetically modified or acquired bacterial resistance mechanisms

(2014-2018) (478 k€)
Yann DECACCHE
Cooperation : Department of Epidemiology and Hygiene (Belgium Ministry of Health), Military Medical Academy (Sofia, Bulgaria), Spitalul Clinic de Urgenta (Bucharest, Romenia

The purpose of this new study is to integrate the different tests created and validated during the previous studies (MED-04 and MED-20) in a multiplex test single, simple, rapid and sensitive. This test will be adapted to the clinical samples (hospital use or in an operational setting) and environmental (intentional dispersion or accidental biological agents in infrastructure). It will allow to clarify the priori antibiotics ineffective or inefficient panel in a therapeutic setting.

This project targets 2 goals :

The first one is the identification of bioterrorism bacteria and the bacteria responsible for nosocomial infections (clinical samples). The result of this research will be applicable to the medical sector (e.g. bacteria EBLN) and the operating environment. For clinical samples, the objective will be to establish the respective detection limits of tests on real biological samples and to adapt the test conditions accordingly.
For the fight against bio-terrorism, the aim is to develop a protocol for identifying fast, reliable and operational resistance markers of the bioterrorism-related infectious agents of class III (B. anthracis, Y. Pestis, F. tularensis, B. melitensis et B. Mallei). The objective is to transfer the tests validated clinical strains from class II to class III strains: gene sequences used in valid tests will be compared to the new target strains sequences and tests will be adapted and validated on basis of DNA extracted or inactivated cultures. The second one aims to develop a new methodology called "multiplex pyrosequencing". Several successive parameters will be tested, compared and validated in order to optimize the quality of the signals of pyrosequencing obtained: the ratio of various products of differential gene amplification, order of dispensation of the nucleotide and the quantity of each pyrosequencing primer, the amount of DNA necessary for amplification... These signals will be then handled by a bio-informatics software which has been developed within the CTMA and which allows to break a global signal of pyrosequencing in each of its components, each component corresponding to a particular target sequence. ■

MSP 16-4 Development of procedures of biological agents inactivation allowing their identification in optimal security conditions for the laboratory personnel

(2016-2019) (388 k€)
Cathy DELCORPS, Stéphane VAN CAUWENBERGHE

The aim of this study is to develop new procedures for the inactivation of biological agents, without impeding or decreasing the sensitivity of their detection and identification methods.
Taking into account all of the available data on inactivation of biological agents, the close interaction of this procedure with the identification by molecular biology methods, and the established criteria for the implementation in the deployable mobile laboratory, the methods to be tested in this study will be mainly chemical methods with and without additional exposure to UV.
In order to evaluate the different methods of inactivation, models of biological agents and their method of specific detection by real time PCR will be developed. Different methods will be tested by comparing their effect on the viability of biological agents and on detection by PCR.
Finally, the selected method or methods will be tested on a wide range of matrices and biological agents. ■

Short Expertise Study: Validation of an ultra-fast and innovative method for the detection and identification of spores of Bacillus anthracis on the field

(2015) (6 k€)
Mostafa BENTAHIR

Detection by qPCR is fast and reliable. However, new emerging technologies for ultra-fast amplification of nucleic acids are most appropriate for use in the field in a context of crisis where the speed of gaining results is very important for the decision makers in order to take the appropriate decisions.
These new isothermal technologies allow the targeted nucleic acid amplification at a constant optimal temperature between 37 and 65°C. This amplification is done by means of easy to use instrument: the fluorimeter which could replace the classical thermocyclers used in the qPCR based analysis process.

First step of the study: Validation of the sensitivity and the specificity of the detection of Bacillus Anthracis genetic markers ADK, B5345, LEF and CapA by the RPA technology (Recombinase Polymerase Amplification).
Second step: Field validation of the reliability and robustness of the RPA technology in the Light Fieldable Bio laboratory deployed for exercises within B-LiFE and EC projects framework. ■

C) Research within the frame of the European Space Agency (ESA)

B-LiFE- Biological Light Fieldable Laboratory for Emergencies
– Phase II /Demonstration Phase/ESA IAP/ARTES2

(2014-2017) (Total consortium: 1.501 k€ / CTMA : 769 k€)
Nicolas DUBOIS, Jean-Luc GALA, Jean-Paul MARCEL, Leonid IRENGE, Olga VYBORNOVA
Consortium: CTMA (Coordinator), Aurea Imaging (Belgium), nazka mapps (Belgium), SES TechCom (Bezdorf – Grand Duchy of Luxemburg)
Phase II / Demonstration Phase aims at delivering a demonstrator at the highest Technology Readiness Level (TRL 9).

The successful management of sanitary crises such as CBRN threats, life threatening emerging diseases, outbreaks in remote areas, relies on the ability to perform rapid detection and identification of pathogens. National and international agencies dealing with the response to bio-security crises will need mobile laboratory capacities rapidly deployed close to the crisis area, autonomous and transmission and geo-location capabilities.

The B-LiFE project motivation is to bring the diagnostic capacity as close as possible to the crisis area, thus providing an essential element of the fast response. The B-LiFE project is adding to the bio-laboratory a set of space technologies and functions improving considerably the quality of the offered services (See Figure 6): satellite telecommunications to communicate with the distant reach back home base laboratory, stakeholders and end users, GNSS (Global Navigation Satellite System) for geo-location and Earth Observation for site selection and monitoring.

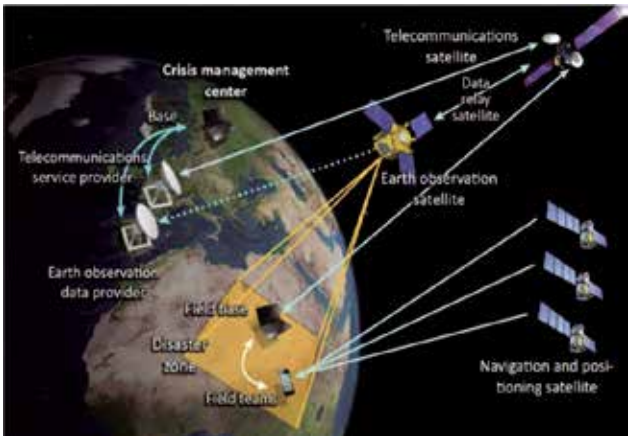

Figure 7 : **B-LiFE – Integration of Space Assets to a Biological Lab**

The proposed B-LiFE system will deliver its services to the end-user based on geographical distant units (see Figure 7): the light mobile field laboratory B-LiFE on one side and various local and distant command and control centers on the other, representing the backend of the applications and services connecting on the one hand to additional medical / biological expertise and on the other hand to local/regional/national emergency response authorities.

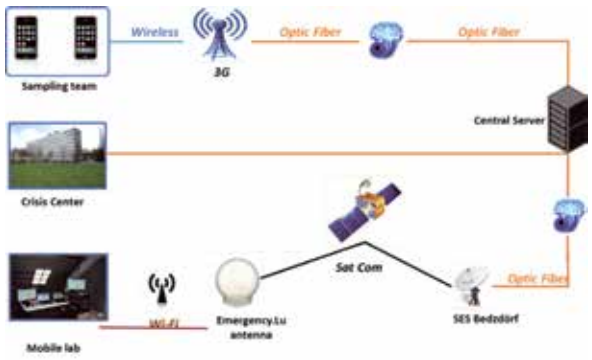

Figure 8 : **B-LiFE - Transmission flow between the Sampling Team, the CTMA Crisis Center and the Mobile Laboratory**

The demonstration phase methodology aims to develop and/or integrate stepwise each sub-system of the B-LiFE system in order to reach at the end of the process a full validated demonstrator at a maturity level TRL (technology readiness Level) 9. Step-wise validation against the specified B-LiFE performance requirements will be applied during the Pre-operational Pilots on the field in Democratic Republic of Congo. The Pre-operational Pilots will allow to demonstrate that integration of three categories of space assets (satellite communication, satellite navigation and EO/GIS) to a laboratory platform will result in a highly performant field capacity for rapid assessment of bio-threats anywhere in the world.

The main tasks of Phase II will focus on development/integration of satellite communication and navigation tools, integration of laboratory and mission management software into communication systems for interoperability purposes, operational site selection and monitoring, optional UAVs, development of inactivation system for biological samples, possible transfer and integration of technologies developed for space applications for power supply, portable glovebox and reduction of cold chain dependency. ■

B-LiFE- Biological Light Fieldable Laboratory for Emergencies

– Ebola Mission at N'Zerekore (Guinea Conakry) Phase II – CCN#1 /Demonstration Phase/ESA IAP/ ARTES20

((Dec 2014- March2015) (Total consortium : 335 k€ / CTMA : 215 k€)

Jean-Luc GALA, Mostafa BENTAHIr, Elodie CARLIER, Yann DECCACHE, Catherine DUMONT, Jean-François DURANT, Leonid IRENGE, Jean-Paul MARCEL, Anne-Sophie PIETTE, Nora TOUFIK, Stéphane VAN CAUWENBERGHE

The B-LiFE consortium [CTMA (Coordinator), Aurea Imaging (Belgium), nazka mapps (Belgium), SES TechCom (Bezdorf – Grand Duchy of Luxemburg)] is operating in cooperation with B-FAST and emergency.lu in order to support the French NGO ALIMA

Following international request assistance and approval of the Belgian government authorities, the B-LiFE laboratory is deployed since 20 December 2014 in Guinea (NZERE KORE) as part of the humanitarian assistance protocol B-FAST (Belgian First Aid and Support Team).

This Ebola mission is a new task (first addendum to the B-LiFE Phase II contract (CCN#1)), performed in parallel with the planned activities in the B-LiFE Demonstration Project. The CCN#1 provides the opportunity of a precursor deployment in the frame of which user needs and requirements will be gathered and consolidated in a realistic scenarios. ■

B-LiFE / B-Fast
Guinea - Nzere Kore

Figure 9 : **B-LiFE / B-FAST Team departing to Conakry at MELSBROECK (Belgium) Military Airbase**

The B-LiFE laboratory is deployed in the Ebola Treatment Center NEZERE KORE led by the French non-governmental organization ALIMA (The Alliance for International Medical Action). There are actively contributing to the fight against the spread of the Ebola virus in Guinea. B-LiFE mission is focused to quickly identify the virus in biological samples and confirm infection in suspected patients. The mobile laboratory is also actively involved in the evaluation of the effectiveness of a new clinical trial testing the antiviral drug Favipiravir (French INSERM Study «JIGI» meaning «hope» in the local dialect). The aim is to reduce mortality among people infected with Ebola virus. Started on 26th of December 2014 the antiviral - developed by the laboratory Toyama Chemical, a subsidiary of Fujifilm - has fully held its promises (cf INSERM press release, 5th and 15th Feb 2015). There is a 15% reduction in the number of deaths in adults and adolescents with low viral load. The lab is also piloting the evaluation of the Biofire technology, a new extremely rapid diagnostic strategy promoted by Biomerieux.

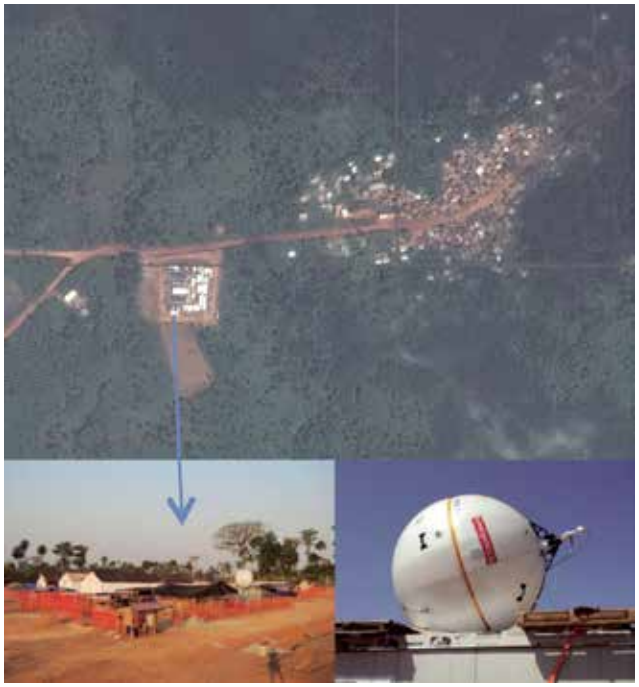

Figure 10 : **Copernicus Image of B-LiFE deployed within the CTE ALIMA and close-up on the GART inflatable SatCom Antennae.**

In addition to its rapid diagnostic capacity of Ebola virus, it also featured premium satellite communication capabilities provided by the Grand Duchy of Luxemburg Government emergency.lu that enabled secure communications at very high speed to Belgian and international operational centers. It also has an epidemiological mapping capability of the disease through its collaboration with the European Space Agency, the European Commission (DG ECHO and ERCC) and COPERNICUS. ■

Figure 11 : **B-LiFE Bio Lab with its Staff at work.**

Figure 12 : **Cured children after Favipiravir treatment with B-LiFE bio-monitoring.**

D) EU Seventh Framework Programme (7FP) Funded Research on Security

MIRACLE
- Mobile Laboratory for the Rapid Assessment of CBRN Threats Located within and outside the EU

(2013-2015) (Total consortium: 1.131 k€ / CTMA: 403 k€)
Pierre-Alain FONTEYNE, Mostafa BENTAHIR, Olga VYBORNOVA
Consortium: Astrium-SAS–AST (France), Bundes-ministerium der Verteidung–IMB (Germany), Forsvarets forskningsinstitutt (FFI) (Norway), Totalförsvarets forskningsinstitut (FOI) (Sweden), Netherlands Forensic Institute (NFI) (The Netherlands), Public Health Agency Canada (PHAC) (Canada), Police Service of Northern Ireland (PSNI) (Ireland), Institute for Public Health and the Environment (RIVM) (The Netherlands)

Development of mobile laboratories, structures and functions to support rapid assessment of CBRN events with a cross-border or international impact.

CTMA is the coordinator of the project aiming at the harmonization of the definition of a CBRN mobile laboratory and identification of the needs and solutions for deployment in and outside the EU.

The overall objective of this feasibility study is to provide a global deliverable "CBRN mobile laboratory architecture(s)" that relies (a) on a better understanding and definition of the need and optimal solutions for mobile lab, and (b) on a clear and straightforward interface with existing EU capabilities / structures. ■

EDEN
– End-user driven DEmo for CBRNE

(2013-2014) (Total consortium : 24.767 k€ / CTMA : 285 k€)
FONTEYNE Pierre-Alain, VYBORNOVA Olga
Consortium: BAE Systems (United Kingdom), Astrium-SAS-AST (France), FFI (Norway), Technoalimenti (Italy), Selex (Italy), University Paris XII - SAMU (France), Skola Glowna Slubzby Pozarniczej SGSP (Poland), Centre for Science, society and citizenship (CSSC) (Italy), Astri Polska Spolka Z Ograniczona Odpowiedzialnoscia APL (Poland), Instituto Affari Internazionali IAI (Italy), CBRNE Ltd (United Kingdom), CTMA, LDI Innovation OU LDI2 (Estonia), Fraunhofer-Gesellschaft zur Foerderung der Angewandten Forschung E.V (Germany), Teknologian Tutkimuskeskus VTT (Finland), Fondation sur la recherche stratégique (FRS) (France), Indra Sistemas (Spain), Institut national de l'envirronnement et des risques (INERIS) (France), SICPA Product Security (Switzerland), Magen David ADOM in Israel (MDA) (Israel), Premyslowy Instytut Automatyki I Pomiarow (PIAP) (Poland), Hotzone Solutions BENELUX (HZS) (The Netherlands), Agenzia Nazionale per le Nuove Technologie, L'ENERGIA - ENEA (Italy), Société Nuclétudes (NUC) (France), Omnidata (OMNI) (Romania), Universidao del Pais Vasco UPV/EHU (Spain), University of Reading (UREAD) (United Kingdom), Bruker Daltonics (BRU) (United Kingdom), Ldiamon (Estonia), Microfluidic Chipshop (Germany), Robert Koch Institut (RKI) (Germany), European Virtual Institute for Integrated Risk Management (EU-VRi) (Germany), Centrum Badan Kosmicznych Polskeij Akadamii Nauk (Poland), Asociacion de Investigacion de la Industria Agroalimentaria (AINIA) (Spain), Universita Cattolica del Sacro Cuore (UCSC) (Italy), Umea University (UMU) (Sweden)

EDEN aims at demonstrating the added value of a Light Fieldable Biology Laboratory (LBFL) for the response to specific B threat scenarios. The LFBL integrates a set of bricks either operational or at least characterized by high TRL. Short cycle R&D in collaboration with EDEN partners is required to allow full integration of innovative system (e.g. rapid low cost bio inactivation assessment).

CTMA is in charge of testing and validating the LFL in the integrated demonstration of CBRN resilience along the whole food chain, from suppliers to potential casualties and integrates the LFL tool in the EDEN toolbox. ■

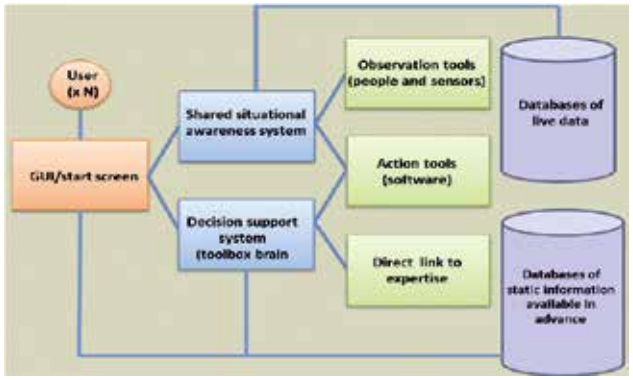

Figure 13 : **The Toolbox provides a common gate-way for CBRNE service providers and users to easily access data and added value products used and developed during the project (Communication, Track & Trace, Situation Awareness, Modeling, Procedures, Protocols, Guidelines…**

PANDEM - Pandemic Risk and Emergency Management

Accepted in December 2014 to start in 2015 (2015-2016) (Total consortium: 1.410 k€ / CTMA and CRED: 188 k€)
Anne-Sophie PIETTE
Consortium: Coordinator - National University of Ireland Galway (NUIG), Intelligence & Science Applications (ISA), IGS Consulting, London School of Hygiene and Tropical Medicine (LSHTM), Public Health Agency of Sweden (FOHM), Swedish Defence Research Agency (FOI), UCL/CTMA, World Health Organization/ EURO (WHO/EURO)

The European Union (EU) faces a growing health security threat posed by pandemics due to the convergence of risk factors driving disease emergence, amplification and dissemination of pathogens with pandemic potential. Protecting the health and security of citizens in the EU in the face of these pandemic threats requires a coherent response by all stakeholders driven by effective pandemic risk management. PANDEM aim is to contribute to the reduction in the health, socio-economic and security consequences of future pandemics so that society will be better prepared at regional, national, EU and global level. PANDEM will assess current pandemic preparedness and response tools, systems and practice at national, EU and global level in priority areas including risk assessment and surveillance, communication and public information, governance and legal frameworks. PANDEM aims to identify gaps and improvement needs leading to the development of viable innovative concepts and analysis of the feasibility of a future demonstration project to strengthen capacity-building for pandemic risk management in the EU.

PANDEM specifically addresses the needs and priorities detailed in the Horizon 2020 Work Programme crisis management topic DRS-4. PANDEM will focus on the needs and requirements of users and first responders across the spectrum of pandemic risk management. PANDEM will bring together highly skilled and multi-disciplinary senior experts from the health, security, defence, microbiology, communications, information technology and emergency management fields. Given the cross-border and multi-sectoral context of the health and security challenge for building pandemic risk management capacity, a systems-based methodology will be applied and the final outcome will be developed for use in a pan-European setting. ■

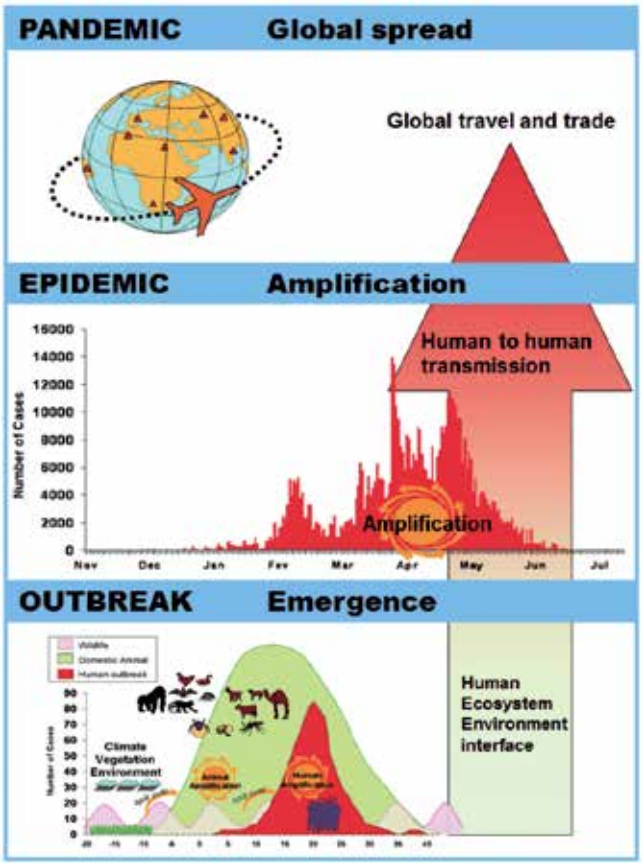

Figure 14 : **Pandemic Generation Process**

REACHING OUT
– DRS-03-2015 demonstRation of EU effective lArge sCale tHreat and crIsis maNaGement OUTside the EU

Accepted to start in 2016
(2016-2019) (Total consortium:18.812 k€ / CTMA: 821 k€)
Anne-Sophie PIETTE, Olga VYBORNOVA
Consortium:
Industry : Airbus Defence and Space SAS (AIRBUS) (France) (Coordinator), Astri Polska Spolka z Ograniczona Odpowiedzialnoscia (APL) (Poland), BAE Systems (Operations) Ltd (BAES) (United Kingdom), Selex ES Spa (SES) (Italy)
SME's : Atrisc (ATRISC) (France), LDI Innovation OU (LDI2) (Estonia), Rinicom Limited (RINI) (United Kingdom), Eureka Comunicazione Telematica srl (EUREKA) (Italy)
Institutes : Istituto Affari Internazionali (IAI) (Italy), Austria Institut fur Europa und Sicherheitspolitik (AIES) (Austria)
Universities : Universitet I Agder (UIA) (Norway), Université de Nice Sophia Antipolis (UNS) (France), Universita degli studi di Napoli Federicao II (UNINA) (Italy), Stockholms Universitet (SU) (Sweden),
End Users : Universita Cattolica del Sacro Cuore (UCSC) (Italy), UCL/CTMA, Arbeiter-Samariter-Bund Deutschland e.V. (ASB) (Germany), Magen David Adom In Israel (MDA) (Israel), Service Départemental d'Incendie et de Secours de la Haute-Corse (SDIS 2B) (France), Public Health England - Department of Health (PHE) (United Kingdom), Institut de Radioprotection et de Sûreté Nucléaire (IRSN) (France), Ministère de l'Intérieur (SDPTS) (France), Fédération Internationale des sociétés de la Croix-Rouge et du Croissant Rouge – Shelter Research Unit (RCSRU) (Luxemburg), Ecole Normale Supérieure de Lyon (ENSL) (France), Ayuntamento de Madrid – civil protection (DGEPC) (Spain)
EU agency : European Union Satellite Centre (SATCEN) (Spain)
NATO/STO : Teknologian tutkimuskeskus VTT Oy (VTT) (Finland)

Effective EU support to a large external crisis requires new approaches. In response to this challenge and to identified user and market needs from previous projects, Reaching Out proposes an innovative multi-disciplinary approach that will optimize the efforts, address a wide spectrum of users and maximize market innovation success.
This approach results in six main objectives: to
1. Develop a Collaborative Framework, with distributed platforms of functional services,

2. Implement a flexible and open "collaborative innovation" process involving users and SMEs, suppliers, operators and research organisations,

3. Develop, upgrade and integrate 78 new connectable and interoperable tools,

4. Conduct 5 large scale demonstrations on the field:
• Health disaster in Africa (Epidemics in Guinea, with strong social and cultural issues),
• Natural disaster in a politically complex region and a desert environment (Earthquake in the Jordan Valley, led jointly by Jordan, Israel and Palestine),
• Three global change disasters in Asia targeted at large evacuation and humanitarian support in Bangladesh (long lasting floods, huge storms and associated epidemics,), EU citizen support and repatriation in Shanghai (floods & storm surge), radiological and industrial disasters impacting EU assets in Taiwan (flash floods, landslides, storm surge and chemical and radiological disasters), supported and co-funded by local authorities,

5. Provide recommendations and evaluations for future legal and policy innovations. The project will be conducted under the supervision of senior end-users. It will be performed with flexible and proven procedures by a balanced consortium of users, industry, innovative SMEs, RTO and academia in the EU and the demonstration regions. The main expected impact is to improve external disaster and crisis management efficiency and cost-benefit and increase the EU visibility whilst enhancing EU industry competitiveness and enlarging the market. ■

E) European Defense Agency (EDA) Research

BFREE (Biological Free mixed CBRN samples for safe handling and analysis)

– European Defense Agency (EDA) 1st Joint Investment Programme on CBRN Issues (JIP-CBRN1).

(2012-2014) (Total consortium: 1.200 k€ / CTMA: 200 k€)
Mostafa BENTAHIR
International cooperation: FFI (Norway) (Coordination), Swedish Defence Research Agency (FOI) (Sweden), CTMA, Bundeswehr Research Institute for Protective Technologie NBC Protection – WIS (Germany), TNO (The Netherlands), Ministère de la Défense - DGA - CBRN Defence – CEB (France), Austrian Federal Ministry of Defence and Sport – BMLVS (Austria)

The project aims at obtaining an efficient sample processing and risk mitigation method for both ensuring safe handling and the following analysis of CBRN mixed samples. It will focus on developing a set of validated procedures agreed among a network of European nations to separate a potential mixture of CBRN agents into distinct C, B, RN aliquots that are further prepared and analysed simultaneously, in parallel and/or successively, independent of sample matrix and reducing the turn-around-time for analysis.
The scientific and technological innovation is highlighted and edged on the development of methods/protocols for removal of B agents, and which do not have a negative impact on the CRN agents, to ensure safety of personnel when performing the analysis of C and R agents. Various methodologies will be tested among several European nations to recommend the most optimal methods for rapid, reliable, sensitive, specific, efficient and cost effective analysis of CBRN mixed samples. BFREE will consider previous studies and results from NATO, EDA and EU projects while focusing on improving one of the first crucial steps in preparing the mixed CBRN samples for analysis ■

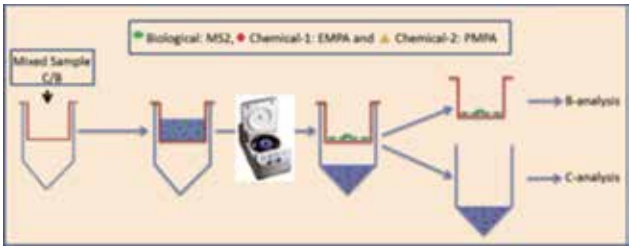

Figure 15 : **Filtration model developed by CTMA for separation and safe analysis of CBRN mixed samples.**

The outcome of BFREE will provide European harmonized approaches for civilian and military laboratories and standardized operating procedures for handling such samples.

Risk Assessment for CB Exposure after Decontamination (RACED)

– European Defense Agency (EDA) 2d Joint Investment Programme on CBRN Issues (JIP-CBRN2)
– European Defense Agency (EDA) 1st Joint Investment Programme on CBRN Issues (JIP-CBRN1).

CBRN Issues (JIP-CBRN2).
(2013-2015) (Total consortium : 865 k€ / CTMA : 169 k€)
Mostafa BENTAHIR
International cooperation: TNO (The Netherlands) (Coordination), FFI (Norway), CTMA, Instituto de Tecnologia Química e Biológica (ITQB - UNL) research centre of Universidade Nova de Lisboa (Portugal), Centro de Investigação da Academia Militar (CINAMIL) Laboratório de Bromatologia e Defesa Biológica (Portugal), Integrated Microsystems Austria GmbH (IMA) (Austria)

In military protection against chemical and biological (CB) warfare agents, decontamination is a crucial step. In case of exposed surfaces, this process aims at removing chemical and biological hazards from equipment, vehicles, buildings and outdoor areas. Essential for successful response to an attack involving CB agents is to recover contaminated surfaces into assets sufficiently clean to return for use. Ideally, decontamination is quick, extremely thorough and environmentally inert.

However, removal of the last molecule or last viable cell is utopic. This does not need to be a danger, as long as the remaining number of

agent molecules or viable cells is below a critical level and does not pose a health hazard. The challenge is to obtain insight into the status decontaminated objects with regard to the remaining hazard. This exactly formulates the problem the RACED project intents to tackle. In an operational military setting it is not possible to assess the remaining hazard. Moreover, even in state-of-art laboratories it is very difficult to measure the residual contamination after a standard decontamination procedure. And even if residual contamination is known, it is not possible to relate that to the remaining health hazard, let alone how to handle the forthcoming risk. The overall challenge can subsequently be formulated as: the need to find out how much of what is left, how that can reach and affect humans and how can that risk be managed.

To counteract this cascade of challenges, RACED takes the following staged approach: 1. Decontaminate a representative number of CB agents / surfaces by standard means and procedures. 2. To apply state-of-the art analytical and micro/molecular biological assays to identify and quantify residual agent. 3. Simulate and understand transport from decontaminated surface to exposure of human airways and skin. 4. Relate exposure to toxicity and infectiousness, respectively. 5. Design a risk profile and identify measures to mitigate or at least manage those risks.

The end-result is a risk management tool that allows the operational decision maker to rationally and confidently declare an asset clean, or to re-launch a decontamination step or to abandon an asset as too dangerously contaminated to maintain. In achieving this, RACED will deliver a crucial contribution towards answering the how-clean-is-clean paradigm. ■

EBLN – European Biodefense Laboratory Network

(On going activity since 2008)
Leonid IRENGE, Anne-Sophie PIETTE, Mostafa BENTAHIR, Elodie CARLIER.
International cooperation: Armament and Defence Technology Agency - NBC & Environmental Protection Technology Division (Austria), CTMA, Centre for Military Medicine - CB Defence and Environmental Health Centre (Finland), DGA Maîtrise NRBC Le Bouchet (France) ; Institut für Mikrobiologie der Bundeswehr (Germany) ; Army Medical and Veterinary Research Center (Italy); FFI (Norway); Ministry of National Defence, Science and Military Education Department (Poland)

The objective of this project is to contribute to the establishment of a laboratory network and common genetic database. The project will improve the EU capability to verify the use of biological agents (B – agents) in the military and civil context such as international regulations, e.g. BTWC (Biological and Toxin Weapon Convention). In the case of a suspected use of B-agents, unambiguous identification of the agent has to be performed. The forensic proof of use of these agents must be such that it cannot be refuted. Microbial forensics has been implemented in the US to ascertain whether an event was natural or intentional and to verify the intentional use of B-agents. Currently, Europe has capability gaps caused by a lack of coordination, standardization, and evaluation of methods to detect, identify type B-agents. Coordinated efforts will contribute to discourage B-terrorism and improve European bio defense capabilities.

Identifying agents and sources in a forensic context relies on a spectrum of features, including epidemiological data and high-resolution analysis. A secure database on B-agents will be established (e.g. sample handling and processing, detection and diagnostic methods, genome sequence and other typing data) to further strengthen the European bio defense capability. In addition, implementation of technical developments in terms of more rapid analysis and higher resolution will be pursued. Sharing experiences on standardization and quality controls are also essential elements of the project. Creation of a strategic European bio defense network around the database based on agent specific expertise will be the end results of the project. ■

F) Walloon Region (RW), Regional R&D Programme (WALLEO3, Biowin, Other)

University's development cooperation (UDC) - Targeted Interuniversity Pole

PIC– Support to improve the capacity for detecting and identifying infectious agents in the province of South Kivu in the Democratic Republic of Congo

(2012 - 2016) (Total consortium : 330 k€ / CTMA : 200 k€)
Leonid IRENGE
International Cooperation: CTMA, ULB Ecole de santé Publicque (Bruxelles), Université catholique de Bukavu Laboratoire biologie Clinique (Bukavu, RDC), Institut National de Recherche Biomédicale (Kinsasha, RDC)

Africa is the cradle of some of the most deadly infections. Management of infectious diseases in the province of South Kivu (DR Congo) is a challenge according to the serious impact of infectious disease on related morbidity and mortality and the risk of extension of outbreaks from remote areas to crowded cities and from RDC to European countries. The goal of the project is to improve the capabilities of identifying infectious agents in each health district hospital in the province of South Kivu.

ALLERT– Handheld Allergens Detector

Accepted in 2013 to start in 2014 (2014 – 2016) (Total consortium : 1.538 k€ / CTMA : 350 k€)
Jamal BADIR, Bertrand BEARZATTO, Jérôme AMBROISE
National Consortium: ZENTECH SA , LAMBDA-X, CER GROUPE, CTMA

The scope of ALLERT project is to provide a practical, portable, rapid and effective diagnostic system to detect allergens in foods. This project does not focus on the IgE detection against specific allergens. The first level is our answer to the need of testing quickly several allergens in the same time.
The second level includes innovation in photonic allowing a better collection of image data to enhance quality of detection adapted to a mobile testing
The third innovative level will be the preparation of samples. By using a standard preparation device and a standard sample collection and filtration technique we will avoid the extreme variation in sample preparation quality.The fourth innovative level will be in the data analysis using specific algorithms to clean images, analyze multiplexed spots and delivering a result with traceability, communication features.

BIOBACTIL WB – Health Optofluidic biosensor immunoassay for detecting and identifying bacteria in human samples matrixes.

(2014 – 2016) (Total consortium : 1.000 k€ / CTMA : 180 k€)
Mostafa BENTAHIR, Olga MINEEVA
Consortium: UCL TELE, CTMA, MULTITEL, SIRRIS, L. FUNDP, ULG Microsys Lab

The aim of the project is to develop a lab-on-chip demonstrator for detecting and identifying the presence of Neisseria meningitidis in cerebrospinal fluid samples. The untreated sample is deposited on the chip, than a "all or nothing" diagnostic answer is provided within 15 minutes. During the development, the effectiveness of the system will be compared to a standard enzyme-linked immunosorbent assay.

G) Industry

Stallergènes

(2013 – 2016)
Marc DILLEMBOURG, Amandine DUPRAZ-FRAIZIER, Karine MAJOR, Audrey SINON

The project aims at producing freeze dried, gamma inactivated, fungal raw material for use in allergy research & treatment, starting from pure cultures & inert substrates. A service type contract has recently been signed with a biopharmaceutical industry leader specialized in the treatment of severe respiratory allergies. Consequently, selected strains have been deposited at Mycothèque de l'Université catholique de Louvain (BCCM/MUCL). The production of biomasses can be adjusted to the specificities of any customer (scientific community or industrial sector) in order to guarantee the quality of allergen extracts made using our products. UCL-CTMA/MYCO meets strict quality & safety standards, in compliance with European regulatory requirements (origin, processing, identification & purity). It has the equipment & expertise allowing detection, identification & monitoring of microbial contaminants of indoor & outdoor air. Detection & monitoring is based on surface & air sampling methods. Identification of airborne particles is achieved by standard light microscopy, culture, SDS-PAGE profiling & DNA signature sequences.
Another goal of the project is to perform research on the quantification and analysis of proteins for test and control purposes and in the context of allergy test. ■

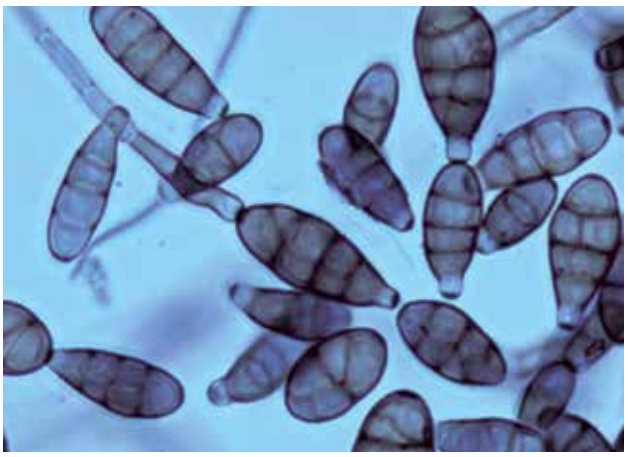

Figure 16 : **Conidia of Alternaria alternata (standard light microscopy, x 400)**

EQUIPMENT

Infrastructure :

- **Distant pre- and post-PCR rooms;**
- **Specific rooms for DNA extraction;**
- **PCR amplification and post-amplification activities;**
- **Several Biosafety level 2 (BSL2) rooms and one biosafety glove box;**
- **Access to academic and the federal Laboratoire fédéral d'orientation (FOL) BSL3 facility at Peutie Defense barrack.**

Major equipment :

- **Standard molecular genetic laboratory equipment: conventional DNA sequencer, pyrosequencer, several PCR and quantitative real-time PCR cyclers, spectrophotometer and synchronous fluorimeter, nucleic acid and protein extraction robots and quantification apparatus, etc…;**
- **Automated Luminex bead plate multiplex reader;**
- **Automated Enzyme-linked immunospot (ELISpot) reader;**
- **HPLC Prominence Liquid chromatograph (Shimadzu)**
- **FreeZone 2.5 Liter Benchtop Freeze Dry System (LabCongo)**
- **Emerging technologies : two dimensional low and high density microarray scanner, colorimetric array scanner, tridimensional-microarray scanner, automatic spotters for large scale and micro-piezoelectric spotting, hybridization station, probe station.**
- **New Generation Sequencer (NGS) Illumina MiSeq II**

Patents

• Method for normalization of quantitative PCR and microarrays.
Filed under No. 61/556.655 (U.S. provisional filed 07/11/2011).

• Method for analysing a pyro-sequencing signal.
(AdvISER-PYRO: Amplicon Identification using SparsE Representation of PYROsequencing signal). Patent application number 13 07 913.2, 2 May 2013 (internal file reference number: UCL-057)

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Figure 17 : **Ecole de santé Publique CTMA at level +1**

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Figure 18 : CTMA mobile laboratory B-LiFE