



ENTRE DE RECHERCHE PUBLIC

ACTIVITY REPORT 2010



ACTIVITY REPORT 2010

CONTENT

ADMINISTRATION BOARD	
THE CHAIRMAN'S MESSAGE	6
MEMBERS OF THE ADMINISTRATION BOARD	7
MANAGEMENT BOARD'S MESSAGE	8
RESEARCH DEPARTMENTS	
DEPARTMENT OF CARDIOVASCULAR DISEASES	
LABORATORY OF CARDIOVASCULAR RESEARCH	10
DEPARTMENT OF IMMUNOLOGY	
LABORATORY OF IMMUNOLOGY	12
DEPARTMENT OF ONCOLOGY	
LABORATORY OF EXPERIMENTAL HEMATO-ONCOLOGY	16
NORLUX NEURO-ONCOLOGY LABORATORY	18
DEPARTMENT OF PUBLIC HEALTH	
CENTRE FOR HEALTH STUDIES	20
EUROPEAN MEDICINES AGENCY LUXEMBOURG FOCAL POINT	22
EUROPEAN MONITORING CENTRE FOR DRUGS AND	24
DRUG ADDICTION LUXEMBOURG FOCAL POINT	
LABORATORY OF EMOTIONAL DISORDERS	26
SPORTS MEDICINE RESEARCH LABORATORY	28
DEPARTMENT OF VIROLOGY, ALLERGOLOGY AND IMMUNITY	
LABORATORY OF IMMUNOGENETICS AND ALLERGOLOGY	30
LABORATORY OF PLANT MOLECULAR BIOLOGY	32
LABORATORY OF RETROVIROLOGY	34
COMPETENCE CENTERS	
CLINICAL AND EPIDEMIOLOGICAL INVESTIGATION CENTER (CIEC)	36
LUXEMBOURG BIOMEDICAL RESEARCH RESOURCES (LBR2)	38
ANIMAL FACILITY	38
CONFOCAL MICROSCOPY	39
FLOW CYTOMETRY	40
LABORATORY OF ANALYTICAL HUMAN BIOMONITORING	41
LUXEMBOURG CLINICAL PROTEOMICS CENTER	42
MICROARRAY CENTER	44
METHODOLOGY AND STATISTICS (CCMS)	46
TECHNICAL AND ADMINISTRATIVE DEPARTMENT	
COMMUNICATION	49
ENVIRONMENT, HEALTH & SAFETY (EH&S)	49
FINANCES	49
FINANCIAL CONTROL	49
HUMAN RESOURCES	49
INFORMATION TECHNOLOGIES	50
LEGAL	50
PROJECT MANAGEMENT	50
PURCHASING	50
QUALITY MANAGEMENT	50
TECHNICAL SUPPORT	51
TECHNOLOGY TRANSFER	51
KEY FIGURES	52
CONTACT ADDRESSES	58
LIST OF PARTNERS	61



ADMINISTRATION BOARD

The Chairman's message

Dear reader,

The activity report of 2010 coincides with the completion of the first contract of performance going over the period of three years 2008-2010 signed between CRP-Santé and the Luxembourgish Government. Besides giving a beautiful outline on the activities carried out during the year, the report will give also a faithful image on the achievements of the fixed objectives.

The large achievement of the quality standards worked out jointly with the ministry for research shows in an impressive manner up to what point the restructuring of CRP-Santé during the five last years starts to bear its fruits.

Indeed, the strategic reorganization of the research activities in five different thematic departments was beneficial under several points of view. Initially, the concentration of the scientific knowledge but also the available resources in CRP-Santé contributed to reach a certain critical mass which is essential for any research activity of quality. This reorganization also allowed articulating the research activities of our existing teams around an integrated research program in the field of health. An additional benefit of this was that each researcher is now able to better integrate his research activities in CRP's overall strategy. It is finally crucially important that CRP-Santé is able to show clearly to all its public and private backers, its national and international partners and clients what it stands for: an outstanding research activity in some precise areas of research with promising topics as well in terms of scientific than economic outcomes.

It should be mentioned that even during the last three years with very tough economic conditions, our Government made the right decision not to excessively cut annual budgets for research, knowing that keeping research activities on a high level means investing in the future. That's also why, for a certain time now, the policy of the Luxembourg government stresses on a stronger development of the economic valorization of research projects and activities.

The Board of Administration which is mainly responsible for the design and implementation of CRP's strategy is pleased with the strengthening of this aspect of the national policy. That's why, in terms of valorization, we bet firstly on the creation of international partnerships with outstanding scientists in order to developing our activities in the field of personalized medicine.

Developing of personalized medicine and of some of strongly related domains like proteomics, genomics and bioinformatics in collaboration with external partners in order to contribute to the creation of a new scientific and economic niche for Luxembourg to be filled will for sure be the biggest challenge that CRP-Santé will have to face since its creation nearly 25 years ago.

I am deeply convinced that time is now ripe to move beyond traditional field boundaries and to increase investments in the domain of research for health in general and in the domain of translational predictive medicine in especially. Our research teams have indeed sufficiently been put to the proof during the last three years by the successful achievement of CRP-Santé's first contract of performance and they are now ready for these new missions.



CENTRE DE RECHERCHE PUBLIC

Members of the Administration Board

Mr. Frank GANSEN
President

Dr. François SCHNEIDER
Vice-President

Mr. Serge HOFFMANN
Treasurer

Dr. André KERSCHEN
Secretary

Mr. Pierre DECKER
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Education and Research

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Member

Mr. René ZIMMER
Member

Dr. Jean-Louis ROBERT
Expert

THE MANAGEMENT BOARD'S MESSAGE

CRP-Santé's first performance contract with Government ended in 2010. Therefore, it is now the perfect time to look back and appreciate what has been achieved during the last three years.

Overall, our experience with the performance contract was highly positive, even if we are still aiming for improvement: a recent survey among CRP-Santé employees found that a majority is convinced that the performance contract has been beneficial both for their own and for the institution's performance. For most employees, the performance contract helped to define clearer the mission of CRP-Santé and the scientific strategy to be implemented, allowing collaborators to appreciate better their role in the organizational challenge. This has translated into improvements of our key performance indicators: CRP-Santé has published 210 peer-reviewed publications with an impact factor greater than 1.5, approaching an average impact factor of 5.5 for the 3 years. Thirteen students have successfully finished their PhD training, while 28 new students have been recruited for doctoral training from 2008 to 2010. CRP-Santé plans to improve further these indicators during the second performance contract by focusing on state-of-the-art science and by increasing networking with PhD schools in Luxembourg and abroad.

Reaching high levels of external funding either from contract or competitive research remains challenging for CRP-Santé, even if in 2010 the organization was extremely successful in submitting projects to the Fonds National de la Recherche (FNR), and several other projects have been funded by European Research Programs. Our highly efficient project management team – in collaboration with our national focal point for the 7th framework program – helps researchers to navigate the administrative hurdles of the various submission processes and thereby improves their chances for success.

CRP-Santé has also made significant progress on its way to quality management in view of a certification. A quality management program is now in

place and first internal audits have been performed in several research units. Better performance is also supported by structural reforms: research activities are now grouped in 5 thematic departments with a well-defined purpose and, in addition, researchers benefit from the technical capabilities of 3 specialized competence centers. Our integration efforts will continue, improving collaborations between research groups under the expert leadership of senior heads of departments and competence centers. We have also upgraded, in a pilot phase, our management structure by creating an "extended management board" which meets monthly and allows a deeper discussion of strategic issues with a larger number of senior people. After almost 25 years of existence, CRP-Santé welcomes the initiative of the Minister of Research, who plans to revise and update the law on public research during the next months. We trust that this will result in a more appropriate governance of public research institutions, allowing us to face with confidence the challenging competition in a progressively opening international research environment.

But CRP-Santé is not only inward looking. Much of its strength comes from external collaborations. The activity report clearly shows that all units have built efficient links with outstanding external partners, and CRP-Santé as an institution has developed more strategic collaborations with European and American actors. Our management finds inspiration, e.g. for performance management, economical value creation or technology platform management, from well-known research organizations such as the VIB (Vlaams Interuniversitair Instituut voor Biotechnologie) in Ghent and our scientists enjoy stimulating interactions with key scientists from Europe, the US and more recently China, for instance within the "Luxembourg personalized medicine initiative". Based on a unique set of skills in laboratory, clinical and public health research, CRP-Santé is now a major driver in this personalized medicine initiative in our country. Till personalized medicine is fully implemented however, some challenges lie still ahead of us: we need to involve more clinicians in biomedical research

and one way of doing this is our Clinical and Epidemiological Investigation Center (CIEC) which is now fully operational and provides significant support for research to the medical community. We need also to gain a better understanding of public health issues, and building and following cohorts of healthy individuals over time – together with our colleagues from the Integrated BioBank of Luxembourg (IBBL), is probably an important way to do so. We finally need to create new competences in domains which are still insufficiently developed (e.g. genomics, proteomics, bioinformatics) in our country, but which are indispensable for personalized medicine.

As announced a year ago, we strongly believe that economical value creation must build on excellent science, first. Now that the quality of our research is steadily increasing, time has come to look further into valorization opportunities. Technology transfer at CRP-Santé is well established and managed, and CRP-Santé is doing this in close collaboration with many external actors such as Ministry of Economical Affairs and Foreign Trade, Luxinnovation, Société Nationale de Crédit à l'Industrie (SNCI), Chambre de Commerce and private investors (e.g. Vesalius BioCapital). The inception in 2010 of the spin-off company COMPLIX Luxembourg, active in the field of therapeutics for viral diseases, is a first proof that our collaboration strategy with private and public actors is indeed successful. Leadership from CRP-Santé has also actively participated in many economic missions aboard, explaining to potential new partners the opportunities for biotechnology companies in Luxembourg.

CRP-Santé has laid in 2010 the bases for further growth and development. Expectations for the future are revealed in the second performance contract with Government, which has been developed with the strong involvement of many individuals in our institution. This contract also defines our new mission & vision statements, which will guide our actions till at least 2013. To end this introduction section, we would like to highlight them again:

"CRP-Santé's mission is to deliver scientific, economic and societal value for Luxembourg by performing research, studies and developments in the fields of clinically-oriented biomedical research and public health. CRP-Santé's activities lead to the generation of new knowledge in disease mechanisms, epidemiology, diagnostics and treatments of human diseases, and they improve the understanding of health determinants and of the financial structures of health care.

At the forefront of biomedical research, CRP-Santé aims at translating knowledge into clinical applications impacting on healthcare while shaping personalized medicine.

To reach this vision, CRP-Santé has set the following goals for 2013:

1. to be recognized by the international scientific community for the excellence of biomedical and translational research, while at the same time creating value for the local society,

2. to be the national leader in biomedical and clinical research, implementing personalized medicine in our country in close collaboration with hospitals, health care providers and other national and international actors,

3. to be the first supplier of public health information in Luxembourg, enabling public authorities to make decisions based on scientific data and to communicate validated data to international institutions, and

4. to be a reliable and active partner for training and higher education in close collaboration with national and international universities."

THE MANAGEMENT BOARD

Daniel Cardao
Marie-Lise Lair
Jean-Claude Schmit



Centre de Recherche Public de la Santé

Research Departments

Department of Cardiovascular Diseases

LABORATORY OF CARDIOVASCULAR RESEARCH



HEAD OF LABORATORY
Dr. Daniel WAGNER MD, PhD

ASSOCIATE HEAD OF LABORATORY
Dr. Yvan DEVAUX, PhD





MISSION

The laboratory focuses on therapeutic and prognostic aspects of the development of heart failure following myocardial infarction. Projects running in the laboratory of cardiovascular research can be separated in two main research axis: the study of the effects of adenosine on left ventricular remodeling and the development of heart failure (therapeutic approach of the disease), and the identification of new biomarkers of clinical outcome after myocardial infarction (prognostic approach).

KEY RESULTS IN 2010

- Discovery of new diagnostic biomarkers of myocardial infarction among the microRNA family.
- Identification of new prognostic biomarkers of heart failure and independent validation in foreign patient cohorts.
- Development of a computational biology competence for systemic analysis of large data scales.
- New insights into the angiogenic properties of the cardioprotective molecule adenosine.
- Set up of an international network of collaborators to study microRNAs in heart disease.
- Implementation and characterization by state of the art imaging techniques of a model of myocardial infarction in rats.

PUBLICATIONS IN 2010

- Adenosine up-regulates vascular endothelial growth factor in human macrophages. I. Ernens, F. Léonard, M. Vausort, M. Rolland-Turner, Y. Devaux, and D.R. Wagner. *Biochemical and Biophysical Research Communications* 2010;392:351–56.
- An optimized protocol for microarray validation by quantitative PCR using amplified amino allyl labeled RNA. C. Jeanty, D. Longrois, P.M. Mertes, D.R. Wagner and Y. Devaux. *BMC Genomics* 2010;11:542.
- Circulating microRNA-208b and microRNA-499 reflect myocardial damage in cardiovascular disease. M.F. Corsten, R. Dennert, S. Jochems, T. Kuznetsova, Y. Devaux, L. Hofstra, D.R. Wagner, J.A. Staessen, S. Heymans and B. Schroen. *Circ Cardiovasc Genet* 2010;3(6):499-506.
- Computational discrete models of tissue growth and regeneration. F. Azuaje. *Briefings in bioinformatics*; 1-14.
- Coordinated modular functionality and prognostic potential of a heart failure biomarker-driven interaction network. F. Azuaje, Y. Devaux and D.R. Wagner. *BMC Systems Biology* 2010;4:60.
- Identification of potential targets in biological signalling systems through network perturbation analysis. F. Azuaje, Y. Devaux and D.R. Wagner. *BioSystems* 2010;100:55–64.
- Integrated protein network and microarray analysis to identify potential biomarkers after myocardial infarction. Y. Devaux, F. Azuaje, M. Vausort, C. Yvorra and D.R. Wagner. *Funct Integr Genomics* 2010;10:329–37.
- Integrative pathway-centric modeling

of ventricular dysfunction after myocardial infarction. F. Azuaje, Y. Devaux and D.R. Wagner. *PLoS ONE* 2010;5(3):e9661.

- Ontology- and graph-based similarity assessment in biological networks. H. Wang, H. Zheng and F. Azuaje. *Bioinformatics* 2010;26(20):2643-4. Epub 2010 Aug 27.
- Prognostic transcriptional association networks: a new supervised approach based on regression trees. I. Nepomuceno, F. Azuaje, Y. Devaux, P.V. Nazarov, A. Muller, J.S. Aguilar-Ruiz and D.R. Wagner. *Bioinformatics* 2010. [Epub ahead of print].
- Relationship between pulse transit time and blood pressure is impaired in patients with chronic heart failure. D.R. Wagner, N. Roesch, P. Harpes, H. Körtke, P. Plumer, A. Saberlin, V. Chakoutio, D. Oundjede, C. Delagardelle, J. Beissel, G. Gilson, I. Kindermann and M. Böhm. *Clin Res Cardiol* 2010;99(10):657-64.
- Right coronary artery originating in the left ventricle. A. Ciarka, V. Lens, J. Beissel and D.R. Wagner. *J Am Coll Cardiol* 2010;56(16):1351.
- Supported high-risk percutaneous coronary intervention with the impella 2.5 device. K.D. Sjaauw, T. Konorza, R. Erbel, P.L. Danna, M. Viecca, H.H. Minden, C. Butter, T. Engström, C. Hassager, F.P. Machado, G. Pedrazzini, D.R. Wagner, R. Schamberger, S. Kerber, D.G. Mathey, J. Schofer, A.E. Engström, and J.P.S. Henriques. *Journal of the American College of Cardiology* 2009;54(25).
- Transcriptional networks characterize ventricular dysfunction after myocardial infarction: a proof-of-concept investigation. F. Azuaje, Y. Devaux, M. Vausort, C. Yvorra and D.R. Wagner. *J Biomed Inform* 2010;43(5):812-9.

KEY PARTNERS IN 2010

- Lariboisière Hospital and INSERM U942 of Paris, France
- University of Homburg, Germany
- University Hospital of Nancy and Nancyclotep, Nancy, France
- University of Leicester, UK
- Heart Failure Research Center of Maastricht, The Netherlands

Department of Immunology

LABORATORY OF IMMUNOLOGY



HEAD OF LABORATORY
Prof. Claude P. MULLER, MD, M.S.



Immunology Influenza team 2010

MISSION

Areas of interest range from basic research to applied and clinical research:

- To understand public health issues related to new variants of human and veterinary viruses (influenza, measles, rubella, hepatitis, parvo-, viruses, tickborne pathogens; avian viruses, avian influenza virus),
 - To understand the effect of stress response mediators on the immune system, and the interaction between the immune system and the neuroendocrine system at a molecular level of nuclear receptors,
 - To understand epigenetic mechanisms of perinatal programming of the immune system,
 - To develop immune-preventive strategies against carcinogens, based on novel conjugate vaccines
- The laboratory has been invited to join the Forschungsinstitut für Psychobiologie of the University of Trier, Germany in relation to the Lehrauftrag of Prof. Müller.
 - The Minister of Health of Lao PDR visited the department, which has been invited to serve as expert for infectious diseases for the Laotian Government.
 - Expert of the laboratory invited by the Worldbank to evaluate the antipandemic preparedness programme of Turkmenistan; by WHO to evaluate the measles eradication strategy (Washington DC and Geneva) and polio in Tadjikistan (Alushta, Ukraine), by the Flanders Wetenschappelijke Organisatie - FWO and I'EU to scientific evaluation committees.

KEY RESULTS IN 2010

- Eleven publications plus seventeen publications in press, including four invited book chapters in leading medical textbooks; deposit of a patent. Publications include studies on the molecular epidemiology of measles virus, rubella virus, parvovirus and tick-borne pathogens in Luxembourg, Europe and West-Africa. Two other publications describe the transcriptional control of the glucocorticoid receptor and the role of promoter methylation in health and depression. Another publication describes protective effects of antibodies against a major tobacco carcinogen. In a more fundamental paper we described the phosphorylation of the measles virus nucleoprotein using advanced mass spectrometry.
- Two doctoral theses were submitted at the Universität des Saarlandes, Germany.
- Dr. C.M. Olinger and Prof. C.P. Müller have been awarded the Eduard-Martin Prize 2010 for the best doctoral thesis, Universität des Saarlandes, Germany.





PUBLICATIONS IN 2010

- Measles virus. Invited book chapter for molecular detection of human viral pathogens. J.R. Kremer and C.P. Muller. Edited by Dongyou Liu, Taylor and Francis. Invited Book Chapter 2010;505-20. Extensive phosphorylation flanking the C-terminal functional domains of the measles virus nucleoprotein. E.J. Prodhomme, F. Fack, D. Revets, P. Pirrotte, J.R. Kremer and C.P. Muller. *J Prot Res* 2010;9:5598-609.
- Measles virus strain diversity, Nigeria and the Democratic Republic of the Congo. J.R. Kremer, E. Nkwembe, A.O. Oyefolu, S.B. Smit, E. Pukuta, S.A. Omilabu, F.D. Adu, J.J. Muyembe Tamfum and C.P. Muller. *Emerging infectious diseases* 2010;16:1724-30.
- Transcriptional control of the glucocorticoid receptor: CpG islands, epigenetics and more. J.D. Turner, S.R. Alt, L. Cao, S. Vernocchi, S. Trifonova, N. Battello and C.P. Muller. *Biochem Pharmacol* 2010;80:1860-68.
- Phylogenetic genetic analysis of rubella viruses involved in congenital rubella infections in France between 1995 and 2009. C. Vauloup-Fellous, J.M. Hübschen, E.S. Abernathy, J. Icenogle, N. Gaidot, P. Dubreuil, I. Parent-du-Châtelet, L. Grangeot-Keros and C.P. Muller. *J Clin Microbiol* 2010;48:2530-5.
- Prevalence and seasonality of tick-borne pathogens in questing ixodes ricinus ticks from Luxembourg. A.L. Reye, J.M. Hübschen, A. Sausy and C.P. Muller. *Appl Environ Microb* 2010;76: 2923-31.
- Effects of antibodies induced by a conjugate vaccine, on 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone absorptive transport, metabolism and proliferation of human lung cells. S.S. De Buck, M.T. Schellenberger, C. Ensich and C.P. Muller. *Int J Cancer* 2010;127:513-20.
- Molecular epidemiology of parvovirus infection in Belarus. M.A. Ermolovich, G.V. Semeiko, E.O. Samoilovich, J.M. Hübschen and C.P. Muller. *Voprosy Virusologii* 2010;55:26-31.
- Differential expression of glucocorticoid receptor transcripts in major depressive disorder is not epigenetically programmed. S.R. Alt, J.D. Turner, M.D. Klok, O.C. Meijer, E.A. Lakke, R.H. de Rijk and C.P. Muller. *Psychoneuroendocrinology* 2010;35:544-56.
- Measles – rubeola. Conn's current therapy. J.R. Kremer and C.P. Muller. Invited Book Chapter. Rakel and Bope, Saunders Elsevier 2010;140-41.

KEY PARTNERS IN 2010

- International Research Training Group on “Psychobiology of Stress” including the Graduate School of Psychobiology, University of Trier, Germany and the Leiden/Amsterdam Center for Drug Research (LACDR), The Netherlands
- Ongoing studies on viral pathogens with numerous institutions in West and Central Africa, Central Asia and South-East Asia
- COST B28 Consortium “Array Technologies for BSL 3 and 4 Pathogens” including institutions from 24 European countries
- WHO Regional Reference Center for Measles and Rubella, responsible for 22 European countries
- VIRIM Network in the Greater Region (Saar-Lor-Lux, Rheinland-Pfalz, Wallonia)
- WHO, CDC Atlanta, Many institutes in Africa, Asia and the New Independent States



Department of Oncology



HEAD OF DEPARTMENT
Prof. Rolf BJERKVIG, PhD

LABORATORY OF EXPERIMENTAL HEMATO-ONCOLOGY



HEAD OF LABORATORY
Dr. Guy BERCHER, MD

ASSOCIATE HEAD OF LABORATORY
Dr. Eric VAN DYCK, PhD



MISSION

The Laboratory of Experimental Hemato-Oncology carries out investigations at the interface of basic and clinical cancer research. Its research focuses on the molecular mechanisms of hematological malignancies and their implications for treatment, and the identification of cancer biomarkers as well as molecular signatures of the tumor cell response to anti-cancer therapeutics. In addition, the laboratory carries out fundamental research on important mechanisms involved in cell death and survival (e.g., autophagy), DNA repair and gene expression.

KEY RESULTS IN 2010

- Identification of plasma microRNAs as sensitive and promising diagnostic biomarkers for chronic lymphocytic leukemia (CLL).
- Identification of molecular signatures (genes, microRNAs) involved in the acquisition of CLL cells resistance to Fludarabine
- Determination of the molecular basis behind the response of CLL cells to a histone deacetylase inhibitor, currently in clinical trial for the treatment of solid tumors and hematological malignancies.
- Identification of a molecular gene signature that distinguishes smokers with and without non-small cell lung cancer (collaborative effort with Dr M. Schlessner, CHL).

PUBLICATIONS 2010

- A population based economic analysis of cross-border payments for fertility services in Luxembourg. C.A. Jones, L.G. Keith, V. Bocquet, J. Arendt, J. Smit J, G. Berchem and M.L. Lair. *J Exp Clin Assist Reprod* 2010;7:pii:3.
- Challenges with advanced therapy medicinal products and how to meet them. Committee for Advanced Therapies (CAT). CAT Scientific Secretariat, C.K. Schneder, P. Salmikangas, B. Jilma, B. Flamion, L.R. Todorova, A. Paphitou, I. Haunerova, T. Maimets, J.H. Trouvin, E. Flory, A. Tsiftoglou, B. Sarkadi, K. Gudmundsson, M. O'Donovan, G. Migliaccio, J. Ancans, R. Maciulaitis, J.L. Robert, Samuel A, Ovelgönne JH, Hystad M, Fal AM, Lima BS, Moraru AS,

Turcáni P, Zorec R, Ruiz S, L. Akerblom, G. Narayanan, A. Kent, F. Bignami, J.G. Dickson, D. Niederwieser, M.A. Figuerola-Santos, I.G. Reischl, C. Beuneu, R. Georgiev, M. Vassiliou, A. Pychova, M. Clausen, T. Methuen, S. Lucas, M. Schüssler-Lenz, V. Kokkas, Z. Buzás, N. MacAleenan, M.C. Galli, A. Lin J. Gulbinovic, G. Berchem, M. Fraczek, M. Menezes-Ferreira, N. Vilceanu, M. Hrubisko, P. Marinko, M. Timón, W. Cheng, G.A. Crosbie, N. Meade, M.L. di Paola, T. VandenDriessche, P. Ljungman, L. D'Apote, O. Oliver-Diaz, I. Büttel and P. Celis. *Nat Rev Drug Discov* 2010;9(3):195-201.

- Determination of genes and microRNAs involved in the resistance to fludarabine in vivo in chronic lymphocytic leukemia. E. Moussay, V. Palissot, L. Vallar, H.A. Poirel, T. Wenner, V. El Khoury, N. Aouali, K. Van Moer, B. Leners, F. Bernardin, A. Muller, P. Cornillet-Lefebvre, A. Delmer, C. Duhem, F. Ries, E. van Dyck and Guy Berchem. *Molecular Cancer* 2010;9:115.
- Immune surveillance of human cancer: if the cytotoxic T-lymphocytes play the music, does the tumoral system call the tune? A. Hamai, H. Benlalam, F. Meslin, M. Hasmmim, T. Carré, I. Akalay, B. Janji, G. Berchem, M.Z. Noman and S. Chouaib. *Tissue Antigens* 2010;75(1):1-8.
- The histone deacetylase inhibitor MGCD0103 induces apoptosis in B-cell chronic lymphocytic leukemia cells through a mitochondria-mediated caspase activation cascade. V. El-Khoury, E. Moussay, B. Janji, V. Palissot, N. Aouali, N.H. Brons, K. Van Moer, S. Pierson, E. van Dyck, G. Berchem. *Mol Cancer Ther* 2010;9(5):1349-60.

KEY IN PARTNERS 2010

- Centre Hospitalier de Luxembourg (CHL), Service de Pneumologie
- Institut de Cancérologie Gustave Roussy, Villejuif, France
- Institute for Systems Biology, Seattle, USA
- Laboratoire de Biologie Cellulaire et Moléculaire de l'Institut Jules Bordet (ULB), Bruxelles, Belgium
- Laboratoire de Recherche en Cancérologie Pulmonaire, Institut Jules Bordet, Bruxelles, Belgium
- Laboratoire de Biochimie et de Biologie Moléculaire, Facultés Universitaires Notre-Dame de la Paix, Namur, Belgique



Department of Oncology

NORLUX NEURO-ONCOLOGY LABORATORY



HEAD OF LABORATORY
Dr. Simone P. NICLOU, PhD

ASSOCIATE HEAD OF LABORATORY
Prof. Rolf BJERKVIG, PhD



MISSION

The Norlux Neuro-Oncology Laboratory is part of the NorLux Neuro-Oncology network ([/www.norlux.lu](http://www.norlux.lu)) a joint network between CRP-Santé, Luxembourg and the Department of Biomedicine, University of Bergen, Norway. The laboratory aims to understand the biological mechanisms underlying the initiation and progression of malignant

brain tumors, and to identify and characterize novel molecular targets for therapies against high grade gliomas. A special focus is on tumor angiogenesis and metabolism, tumor heterogeneity and cell based therapeutic strategies.

KEY RESULTS IN 2010

- A key study using cell encapsulation for the local delivery of a therapeutic agent in the mouse brain, was accomplished. This FNR financed project was the result of a close collaboration between the Norlux team of S.P. Niclou (CRP-Santé) and the team of T. Pillot at Nancy University.
- In 2010, the laboratory has successfully received competitive funding for a new project on escape mechanisms of glioblastoma after anti-angiogenic therapy within the FNR CORE program. The project ESCAPE is expected to start in January 2011.
- Using innovative non-invasive MRI imaging protocols, novel insight into anti-angiogenic treatment of glioblastoma were obtained and discussed at several major international conferences (EANO 2010, SNO 2010, ISMRM 2010). The work has been accepted for publication in Proc. Natl. Acad. Sci. USA.
- The Norlux team received an FNR Award for 'Outstanding Scientific Publication' for its work on a proteome wide profiling of glioma phenotypes, published in Molecular & Cellular Proteomics in 2009 (Rajcevic et al. MCP 2009).
- The GLIOMET EU FP7 preproposal, a European project proposal on glioma metabolism, encompassing 9 European partners and coordinated by S.P. Niclou, has been successfully reviewed and is currently being processed for stage 2 submission.
- In 2010 the Oncology Department was subjected to an independent scientific evaluation commissioned by the MESR, which resulted in a very positive evaluation of the Norlux laboratory. As a result, Prof. Bjerkvig was appointed head of the Department as of January 2011.

PUBLICATIONS IN 2010

- Glioma proteomics: status and perspectives. S.P. Niclou, F. Fack and U. Rajcevic. *J Proteomics* 2010; 73(10):1823-38.
- Cellular toxicity following application of adeno-associated viral vector-mediated RNA interference in the nervous system. E.M. Ehlert, R. Eggers, S.P. Niclou and J. Verhaagen. *BMC Neurosci* 2010;11:20.
- Ciliary neurotrophic factor cell-based delivery prevents synaptic impairment and improves memory in mouse models of alzheimer's disease. P. Garcia, I. Youssef, J.K. Utvik, S. Florent-Bécharde, V. Barthélémy, C. Malaplate-Armand, B. Kriem, C. Stenger, V. Koziel, J.L. Olivier, M.C. Escanye, M. Hanse, A. Allouche, C. Desbène, F.T. Yen, R. Bjerkvig, T. Oster, S.P. Niclou, T. Pillot. *J Neurosci* 2010;30(22):7516-27.
- aB-Crystallin is elevated in highly infiltrative apoptosis-resistant glioblastoma cells. D. Goplen, S. Bougnaud, U. Rajcevic, S.O. Bøe, K.O. Skaftnesmo, J. Voges, P.Ø. Enger, J. Wang, B.B. Tysnes, O.D. Laerum, S.P. Niclou and R. Bjerkvig. *Am J Pathol* 2010;177(4):1618-28.
- Anti-VEGF treatment reduces blood supply and increases tumor cell invasion in glioblastoma. O. Keunen, M. Johansson, A. Oudin, M. Sanzey, S.A. Abdul Rahim, F. Fack, F. Thorsen, T. Taxt, M. Bartos, R. Jirik, H. Miletic, J. Wang, D. Stieber, L. Stühr, I. Moen, C. Brekke Rygh, R. Bjerkvig and S.P. Niclou. *Proc Natl Acad Sci USA* (in press).
- Critical appraisal of the side population assay in stem cell and cancer stem cell research. A. Golebiewska, N.H.C. Brons, R. Bjerkvig and S.P. Niclou. *Cell Stem Cell* (in press).

KEY PARTNERS IN 2010

- University of Bergen, Department of Biomedicine, Norway
- Centre Hospitalier de Luxembourg, (CHL): Neurosurgery Department
- Umeå University, Department of Radiation Sciences, Oncology, Umeå, Sweden
- Translational Genomics Research Institute (TGen), Oncology Division, Arizona
- University Medical Center Groningen, The Netherlands



Department of Public Health

CENTRE FOR HEALTH STUDIES



HEAD OF UNIT
Marie-Lise LAIR

ASSOCIATE HEAD OF UNIT
Dr. Sophie COUFFIGNAL, MD



MISSION

Through its research and surveillance systems, the Centre for Health Studies provides reliable information about the population's state of health, health determinants and risk prediction indicators, which allows public authorities to build their prevention and healthcare finance projects and to evaluate their effectiveness. The centre identifies the health services resource requirements and carries out healthcare economic analyses.

KEY RESULTS IN 2010

- Publication of the final report of the EUROLIGHT project about the social and economic impacts of headache in 10 European countries.
- Publication of the report to the Ministry of Health " National Strategy in favor of Mental Health for Children and Youth in Luxembourg: promotion, prevention, support and integration".
- Publication of the report to the Ministry of Health: "Feasibility study for a national injuries register in Luxembourg".
- First time in Luxembourg, publication of all European perinatal indicators in 2009; Development and implementation of the DIANE-Neonatology software for prematurity survey.
- Publication of the prevalence of the metabolic syndrome in the general population in Luxembourg and determination of cardiovascular risks in children and youth population with obesity.
- In collaboration with the Ministère de l'Education Nationale, carrying out of a new research project on the relation between mental health and school desertion.
- Prevalence of headache in Europe: a review for the Eurolight project. L.J. Stovner and C. Andree. *J Headache Pain* 2010;11(4):289-99.
- Pharmacokinetics and comparative bioavailability of artesunate and mefloquine administered separately or as a fixed combination product to healthy volunteers and patients with uncomplicated plasmodium falciparum malaria. P. Olliaro, S. Ramanathan, M. Vaillant, S.E. Reuter, A.M. Evans, S. Krudsood, S. Looareesuwan, J.R. Kiechel, W.R.J. Taylor and V. Navaratnam. *Journal of Bioequivalence & Bioavailability* 2010;2(3):59-66.
- Myocardial MIBG scintigraphy: a useful clinical tool? : a retrospective study in 50 parkinsonian patients. I. Fröhlich, W. Pilloy, M. Vaillant and N. Diederich. *J Neurol Sci* 2010;31(3):403-6.
- Headache-associated dizziness in a headache population: prevalence and impact. A. Bisdorff, C. Andrée, M. Vaillant and P.S. Sándor. *Cephalalgia* 2010;30(7):815-20.
- First nationwide survey on cardiovascular risk factors in Grand-Duchy of Luxembourg (ORISCAV-LUX). A. Alkerwi, N. Sauvageot, A.F. Donneau, M.L. Lair, S. Couffignal, J. Beissel, C. Delagardelle, Y. Wagener, A. Albert and M. Guillaume. *BMC Public Health* 2010;10:468.
- Comparison of participants and non-participants to the ORISCAV-LUX population-based study on cardiovascular risk factors in Luxembourg. A. Alkerwi, N. Sauvageot, S. Couffignal, A. Albert, M.L. Lair and M. Guillaume. *BMC Med Res Methodol* 2010;10:80.
- Development and validation of the EUROLIGHT questionnaire to evaluate the burden of primary headache disorders in Europe. C. Andrée, M. Vaillant, J. Barre, Z. Katsarava, J.M. Lainez, M.L. Lair, M. Lanteri-Minet, C. Lampl, T.J. Steiner, L.J. Stovner, C. Tassorelli and P.S. Sándor. *Cephalalgia* 2010;30(9):1082-100.
- Characterizing the spatio-temporal dynamics of the neural events occurring prior to and up to overt recognition of famous faces. B. Jemel, A.M. Schuller and V. Goffaux. *J Cogn Neurosci* 2010;22(10):2289-305.
- New fixed-dose artesunate-mefloquine formulation against multidrug-resistant plasmodium falciparum in adults: a comparative phase IIb safety and pharmacokinetic study with standard-dose nonfixed artesunate plus mefloquine. S. Krudsood, S. Looareesuwan, N. Tangpukdee, P. Wilairatana, W. Phumratanapapin, W. Leowattana, K. Chalermrut, S. Ramanathan, V. Navaratnam, P. Olliaro, M. Vaillant, J.R. Kiechel and W.R. Taylor. *Antimicrob Agents Chemother* 2010;54(9):3730-7.
- A population based economic analysis of cross-border payments for fertility services in Luxembourg. C.A. Jones, L.G. Keith, V. Bocquet, J. Arendt, J. Smit, G. Berchem and M.L. Lair. *J Exp Clin Assist Reprod* 2010;7:pii:3.
- Nutrition, environment and cardiovascular health (NESCAV): protocol of an inter-regional cross-sectional study. A. Alkerwi, M. Guillaume, F. Zannad, U. Laufs and M.L. Lair. *BMC Public Health* 2010;10:698.
- Isokinetic versus one-repetition maximum strength assessment in chronic heart failure. P. Feiereisen, M. Vaillant, D. Eischen and C. Delagardelle. *Med Sci Sports Exerc* 2010;42(12):2156-63.
- Alternative visual displays of metaanalysis of malaria treatment trials to facilitate translation of research into policy. P. Olliaro and M. Vaillant. *Diagn Microbiol Infect Dis* 2010;68(4):422-31.

PUBLICATIONS IN 2010

- Take action to prevent diabetes-the IMAGE toolkit for the prevention of type 2 diabetes in Europe. J. Lindstrom et al and A. Alkerwi on behalf Image Study Group for Luxembourg. *Horm Metab Res* 2010;1:37-55.
- Quality indicators for the prevention of type 2 diabetes in Europe-IMAGE. P. Pajunen P et al and A. Alkerwi on behalf Image Study Group for Luxembourg. *Horm Metab Res* 2010;1:56-63.
- A European evidence-based guideline for the prevention of type 2 diabetes. B. Paulweber et al and A. Alkerwi on behalf Image Study Group for Luxembourg. *Horm Metab Res* 2010;42(1):3-36.
- An exciting field of advice in the pharmacy: acute migraine pain. C. Andrée and V. Vogelsgesang. *PharmaJournal* 2010;10:1-2.
- Discriminative power of different non motor signs in early Parkinson's disease. A case-control study. N.J. Diederich, V. Pieri, G. Hipp, O. Rufra, S. Blyth and M. Vaillant. *Mov Disord* 2010;25(7):882-7.

KEY PARTNERS IN 2010

- Ministère de la Santé et Direction de la Santé, Luxembourg
- Ministère de la Sécurité Sociale, Inspection Générale de la Sécurité Sociale, Luxembourg
- Caisse Nationale de Santé, Luxembourg
- Université de Liège, Ecole de Santé Publique, Belgique
- Hôpitaux et médecins cliniciens, Luxembourg

EUROPEAN MEDICINES AGENCY – LUXEMBOURG FOCAL POINT



EXTERNAL EXPERT
Dr. Jean-Louis ROBERT

MISSION

Through its EMEA focal point, CRP-Santé has been providing support to the Luxembourg Government since 1995 and especially to the Pharmaceutical and Drugs Division (DPM) of the Health Ministry which fulfils the role of a Luxembourg Drug Agency, as well as to the Medicines Control Service of the National Health Laboratory. Experts have been delegated to participate in the activities of the European Medicines Agency in London, where they provided scientific opinions on the efficacy, quality and safety of medicines being authorized for marketing in Europe.

KEY RESULTS IN 2010

- Assessment reports on new drugs, by Dr. Jean-Louis Robert, as expert from Luxembourg, for Committee for Medicinal Products for Human Use.
- Participation, as expert from Luxembourg, of Dr. Carine de Beaufort in the Pediatric Committee for assessment of pediatric drugs.
- Participation, as expert from Luxembourg, of Dr. Guy Berchem in the Committee on Advanced Therapies.
- Participation, as expert from Luxembourg, of Dr. Henri Metz in the Committee for Orphan Medicinal Products.

KEY PARTNERS IN 2010

- Organisation Mondiale de la Santé, Geneva, Switzerland
- Ministère de la Santé, Direction de la Santé, Division de la Pharmacie et des Médicaments, Luxembourg Mme. Jacqueline Genoux-Hames
- European Medicines Agency, London, UK
- Agence Française de Sécurité Sanitaire des Produits de Santé, Saint Denis, France



CENTRE DE RECHERCHE P

C R P

Observe
Santé

Department of Public Health

EUROPEAN MONITORING CENTRE FOR DRUGS AND DRUG ADDICTION LUXEMBOURG FOCAL POINT



NATIONAL DRUG COORDINATOR
Alain ORIGER



MISSION

The National EMCDDA Focal Point is the national centre of excellence in the fields of drug use surveillance, tracking emerging or illegal psychoactive substances and new consumer trends. The main objective of the National Focal Point is to collect, produce, analyze and provide valid, reliable and

comparable data on drugs and drug addiction in Luxembourg. This includes epidemiological surveillance, targeted research activities, publication of research results and release of a national annual report on the state of the drugs problem in Luxembourg.

KEY RESULTS IN 2010

- Further improvement of epidemiological surveillance of problem drug use and validation of applied methodologies. The RELIS surveillance system does currently produce EU comparable data on problem drug use and provides indispensable data for targeted research.
- Peer-reviewed publication on hepatitis B (HBV), hepatitis C (HCV) and HIV infections in problem drug users (PDU) and intravenous drug users (IDU) in Luxembourg. Measurement of the validity of self-reported test results versus serological diagnosis.
- Participation in research projects of the EMCDDA and the Council of Europe.

PUBLICATIONS IN 2010

- Annual report on the state of the drugs problem - Grand Duchy of Luxembourg, EMCDDA Focal Point, Luxembourg. A. Origer, EMCDDA Focal Point - CRP-Santé, Luxembourg, 2010.
- Prevalence of hepatitis B and C and HIV infections among problem drug users in Luxembourg: self-report versus serological evidence. A. Origer and J.C. Schmit. J Epidemiol Community Health.
- Treatment system overview. R. Muscat, L. Meulenbergs, A. Origer et al. Council of Europe Publishing, Strasbourg 2010.

KEY PARTNERS IN 2010

- Inpatient & outpatient treatment centres (Centre Thérapeutique Manternach, Jugend an Drogenhelf, Centre Emmanuel, Solidarité Jeunes)
- Hospital and detox units in Luxembourg
- Low threshold agencies (Tox-in)
- Services in prison (Programme Tox, Centre Pénitenciaire Luxembourg)
- Drug supply reduction agencies (Police Judiciaire)

Department of Public Health

LABORATORY OF EMOTIONAL DISORDERS



HEAD OF LABORATORY
Prof. Charles PULL, MD, MA



MISSION

The focus of the laboratory is the study of fear and sadness in anxiety disorders, major depressive disorders and obesity. In addition, the laboratory investigates the impairment in functioning and the reduction in quality of life that accompany such disorders as well as their course and outcome following treatment. Emotions are investigated using a battery of specific questionnaires and rating scales, personality tests and physiological measurements. An original aspect of the laboratory is the use of virtual reality.

KEY RESULTS IN 2010

- Exposure to virtual environments elicits significant psychological and physiological manifestations of fear in subjects with fear of flying or fear of driving.
- Severe obesity is associated with significant psychopathology (in particular depression), impairment in functioning and distortion of body image perception.

PUBLICATIONS IN 2010

- Current psychological assessment practices in obesity surgery programs: what to assess and why. C.B. Pull. *Curr Opin Psychiatry* 2010;23(1):30-6.
- Developing the World Health Organization Disability Assessment Schedule 2.0. T.B. Ustün, S. Chatterji, N. Kostanjsek, J. Rehm, C. Kennedy, J. Epping-Jordan, S. Saxena, M. von Korf, C. Pull. *WHO/NIH Joint Project. Bull World Health Organ* 2010;88(11):815-23.

KEY PARTNERS IN 2010

- Clinique des Troubles Emotionnels, Centre Hospitalier de Luxembourg
- Unité polyvalente de l'obésité or UPO of the Centre Hospitalier de Luxembourg
- Université du Québec in Gatineau, Quebec, Canada
- Universitat Jaume I, Castellon, Spain



Department of Public Health

SPORTS MEDICINE RESEARCH LABORATORY



HEAD OF LABORATORY
Prof. Daniel THEISEN, PhD



MISSION

The general aim of the Sports Medicine Research Laboratory is to study the impact of movement, training and sports, as well as inactivity on healthy and injured or ill individuals to provide decisive information for prevention, therapy, rehabilitation and sports. The major objective of the laboratory in 2010 was to create opportunities to generate new research projects and expand the team.

KEY RESULTS IN 2010

- Acceptance of an AFR grant from the National Research Fund for a postdoctoral fellowship (Dr. Joakim Genin). This grant allowed starting a new research project on running-related injuries in novice and experienced long-distance runners.
- Sports injury surveillance at the "Sportlycée" was pursued on behalf of the Ministry of Sport in 2010. All athletes were followed regarding their training characteristics and sports injuries. Pertinent prevention measures can now be taken based on a detailed descriptive report.
- New collaborations were established with LionSystems S.A. (G.D. of Luxembourg) and TNO (The Netherlands), as well as with the University of Maastricht (Prof. Kenneth Meijer).
- Two master students doing their internship in the laboratory in 2010 submitted a grant application at the National Research Fund to start a PhD project within the laboratory.
- Twelve conferences related to sports medicine and sports orthopedics were organized in Luxembourg during the year, in collaboration with the Centre de l'Appareil Locomoteur, de Médecine du Sport et de Prévention of the Centre Hospitalier de Luxembourg. They featured national and international speakers.

PUBLICATIONS IN 2010

- Influence of the anteromedial and posterolateral bundles of the anterior cruciate ligament on external and internal tibiofemoral rotation. O. Lorbach, D. Pape, S. Maas, T. Zerbe, L. Busch, D. Kohn and R. Seil. Am J Sports Med 2010,[Epub ahead of print].

KEY PARTNERS IN 2010

- Département Ministériel des Sports, Luxembourg
- Centre de l'Appareil Locomoteur de Médecine du Sport et de Prévention du Centre Hospitalier de Luxembourg
- Comité Olympique et Sportif Luxembourgeois
- Université de Liège, Belgium
- Universität des Saarlandes, Germany
- Maastricht University, The Netherlands



Department of Virology,
Allergology and Immunity

LABORATORY OF IMMUNOGENETICS AND ALLERGOLOGY



HEAD OF LABORATORY
Dr. François HENTGES, MD



MISSION

Allergic and immune diseases are a major health problem for hundreds of millions of people worldwide. The aim of the Laboratory of Immunogenetics and Allergology is to strengthen its skills in applied research, to develop competitive basic research and to create an optimal environment for improved diagnosis, prevention and treatment

of patients with allergic and immune-mediated diseases. Research is being performed in close collaboration with the national unit of Immunology and Allergology at the Centre Hospitalier de Luxembourg.

KEY RESULTS IN 2010

- Tools were developed for quantification of parvalbumin, the main fish allergen. Parvalbumins from 8 fishes were isolated and extensively purified. We could show that the concentration of this clinically important allergen varies greatly among different fish species which are consumed in Europe.
- Two allergens were isolated from guinea pig. cDNAs were cloned and the proteins were produced as recombinant molecules. A number of guinea pig allergic patients were screened by in vitro IgE testing and the new allergens proved to be valuable in component resolved diagnosis of guinea pig allergy.
- TLR ligands LPS, CpG and Flagellin were introduced as adjuvants in mouse co-immunisations with the allergen cat serum albumin and used in mouse dendritic cell-T cell assays. The data collected will be used to try to shift a Th2 allergy-prone mouse immune response towards a Th1 or Tr1 response.
- A new, very efficient method was developed for the purification of rat natural killer (NK) cells, based on immuno-magnetic depletion of non-NK cells via an antibody cocktail designed in our lab. After depletion, NK cell purity exceeds 95%. The cells can be used immediately for functional studies.
- The laboratory has shown the anti-inflammatory role of neurturin (NTN), a member of the neurotrophin family, in a model of allergic airway inflammation using NTN knockout mice. These mice developed a pronounced worsening of inflammatory features. This phenotype is partially rescued by adding NTN.
- The expression patterns of the nerve growth factor (NGF) receptors TrkA and p75NTR on mouse NK cells were described. TrkA is expressed by 20 % of resting and 100 % of IL-2 activated NK cells. p75NTR is expressed by a minor subset (2 %) of NK cells. NGF does not seem to influence NK cell functions.

PUBLICATIONS IN 2010

- A positive review for PLoS ONE. J. Zimmer. Science 2010;330(6000):34.
- Mouse natural killer (NK) cells express the nerve growth factor receptor TrkA, which is dynamically regulated. N. Ralainirina N, N.H. Brons, W. Ammerlaan, C. Hoffmann, F. Hentges and J. Zimmer. PLoS One 2010;5:e15053.
- The role of haematopoietic growth factors granulocyte colony-stimulating factor and granulocyte-macrophage colony-stimulating factor in the management of drug-induced agranulocytosis. E. Andrès, F. Maloisel and J. Zimmer. Br J Haematol 2010;150(1):3-8.
- Important variations in parvalbumin content in common fish species: a factor possibly contributing to variable allergenicity. A. Kuehn, T. Scheuermann, C. Hilger, F. Hentges. Int Arch Allergy Immunol. 2010;153(4):359-66.
- Novel method for isolating untouched rat natural killer cells with higher purity compared with positive selection and fluorescence-activated cell sorting. A. Poli, N.H. Brons, W. Ammerlaan, T. Michel, F. Hentges, M. Chekenya and J. Zimmer. Immunology 2010.[Epub ahead of print].
- Monosensitivity to pangasius and tilapia caused by allergens other than parvalbumin. D.G. Ebo, A. Kuehn, C.H. Bridts, C. Hilger, F. Hentges, and W.J. Stevens. J Invest Allergol Clin Immunol 2010;20(1):84-8.
- Fisch ist nicht gleich Fisch. A. Kuehn, T. Scheuermann, C. Hilger and F. Hentges. Allergo-Journal 2010;19(3):164
- Anaphylactic reactions to bites of the pigeon tick argas reflexus. S. Weckesser, C. Hilger, D. Lentz, and T. Jakob. Eur J Dermatol 2010;2:244-5.
- Natural killer cells in atopic and autoimmune diseases of the skin. D. von Bubnoff, E. Andrès, F. Hentges, T. Bieber, T. Michel and J. Zimmer. J Allergy Clin Immunol. 2010;125(1):60-8.
- Fish allergy: a comprehensive review of recent developments in fish allergy diagnosis and fish allergen detection, in food

allergies: symptoms, diagnosis, and treatment. A. Kuehn, C. Hilger and F. Hentges. Novapublishers NY 2010.

- Natural killer cells: at the forefront of modern immunology. J. Zimmer. Springer-Verlag Berlin Heidelberg 2010.

KEY PARTNERS IN 2010

- Département de Pneumologie, Hôpitaux Universitaires de Strasbourg, France
- Center for Clinical and Experimental Allergy, Rome, Italy
- Centre d'Ingénierie des Protéines, Université de Liège, Belgium
- Department of Biomedicine, University of Bergen, Norway
- Southampton General Hospital, University of Southampton, UK

Department of Virology,
Allergology and Immunity

LABORATORY OF PLANT MOLECULAR BIOLOGY



HEAD OF LABORATORY
Dr. André STEINMETZ, PhD



MISSION

The Plant Molecular Biology Laboratory combines basic research in molecular and cell biology to study fundamental biological processes in plant and animal cells and to elucidate the mechanisms of action of novel bioactive components from Chinese medicinal plants.

KEY RESULTS IN 2010

- The laboratory has shown that LIM family members function as highly specialized actin filament crosslinkers involved in the formation and the stabilization of high-order cytoskeletal structures and respond differently to cellular factors, such as pH and calcium.
- Human cysteine-rich proteins (CRPs), a muscle-enriched family of LIM proteins structurally related to plant LIMs, also act as direct actin-binding proteins that stabilize the actin cytoskeleton.
- A plant actin depolymerizing factor (ADF) with an unusually high and constitutive actin-bundling activity has been characterized. This ADF will be used as a model to study the molecular mechanisms underlying ADF/cofilin-mediated actin rod formation in diseases.
- From a screen of about 30 local (medicinal) plants the lab has identified several extracts exhibiting cytotoxicity in a variety of cancer cell lines.
- In a more detailed study one of the above extracts was shown to induce apoptosis in several cancer cell lines at very low concentrations, while other cancer cell lines were only moderately sensitive or not sensitive at all to this extract.

PUBLICATIONS IN 2010

- Arabidopsis LIM proteins: a family of actin bundlers with distinct expression patterns and modes of regulation. J. Papuga, C. Hoffmann, M. Dieterle, D. Moes, F. Moreau, S. Tholl, A. Steinmetz and C. Thomas. *The Plant Cell* 2010;22:3034-52.
- Organ-specific alternatively spliced transcript isoforms of the sunflower SF21C gene. E. Lazarescu, W. Friedt and A. Steinmetz. *Plant Cell Rep* 2010;29:673-83.
- Comparison of ginsenosides Rg1 and Rb1 for their effects on improving scopolamine-induced learning and memory impairment in mice. Q. Wang, L.H. Sun, W. Jia, X.M. Liu, H.X. Dang, W.L. Mai, N. Wang, A. Steinmetz, Y.Q. Wang and C.J. Xu. *Phytother Res.* 2010;24:1748-54.
- Anti-cancer effects of 20(S)-protopanaxadiol on human acute lymphoblastic leukemia cell

- lines Reh and RS4;11. L. Sun, Q. Wang, X. Liu, N.H. Brons, N. Wang, A. Steinmetz, Y. Lv, Y. Liao, H. Zheng. *Med Oncol* 2010.[Epub ahead of print].
- EST analysis reveals putative genes involved in glycyrrhizin biosynthesis. Y. Li, H.M. Luo, C. Sun, J.Y. Song, Y.Z. Sun, Q. Wu, N. Wang, H. Yao, A. Steinmetz and S.L. Chen. *BMC Genomics* 2010;11:268.
- Comparison of 454-ESTs from *huperzia serrata* and *phlegmariurus carinatus* reveals putative genes involved in lycopodium alkaloid biosynthesis and developmental regulation. H. Luo, Y. Li, C. Sun, Q. Wu, J. Song, Y. Sun, A. Steinmetz and S. Chen. *BMC Plant Biol* 2010;10:209.
- An unprecedented sesquiterpenoid spirolactone with a 6/6/5 ring system from *Abies delavayi*. X.W. Yang, S.M. Li, Y.L. Li, J.H. Xia, L. Wu, J.M. Tian, N. Wang, Y.H. Liu and W.D. Zhang. *Abiesatrines A Eur J Org Chem* 2010;11:6531-34.
- Anti-inflammatory and anti-tumor triterpenoids from *Abies georgei* Orr. X.W. Yang, S.M. Li, L. Wu, Y.L. Li, L. Feng, Y.H. Shen, J.M. Tian, J. Tang, N. Wang, Y.H. Liu and W.D. Zhang. *Abiesatrines A-J, Organic & Biomolecular Chemistry* 2010;8:2609-16.
- Isolation, structure, and bioactivities of abiesadines A-Y, twenty-five new diterpenes from *Abies georgei* Orr. X.W. Yang, L. Feng, S.M. Li, X.H. Liu, Y.L. Li, L. Wu, Y.H. Shen, J.M. Tian, X. Zhang, X.R. Liu, N. Wang, Y.H. Liu and W.D. Zhang. *Bioorganic & Medicinal Chemistry* 2010;18:744-54.

KEY PARTNERS IN 2010

- University of Bergen, Department of Biomedicine, Norway
- Institute of Medicinal Plant Development, Research Center for Pharmacology and Toxicology, Beijing, China
- Institute of Medicinal Plant Development, Resource and Conservation Research Center, Beijing, China
- Modern Research Center for Traditional Chinese Medicine, Shanghai, China
- Institut de Biologie Moléculaire des Plantes, Molecular Mechanisms of Phenotypic Plasticity, Strasbourg, France

Department of Virology,
Allergology and Immunity

LABORATORY OF RETROVIROLOGY



HEAD OF LABORATORY
Dr. Jean-Claude SCHMIT, MD, PhD

ASSOCIATE HEAD OF LABORATORY
Dr. Carole DEVAUX, PhD



MISSION

Chronic viral infections caused by HIV and HCV are an ever-growing public health problem in Luxembourg as in the rest of the world. More than 700 patients infected with HIV and 1700 patients infected with HCV have been followed in the Centre Hospitalier de Luxembourg during the past decade. The laboratory of Retrovirology performs fundamental and applied research in the field of chronic viral infections (HIV, HCV). The activities of the laboratory focus on two research domains, which interact closely: immuno-virology and clinical virology.

KEY RESULTS IN 2010

- Creation of Complix Luxembourg S.A., a biopharmaceutical company focused on the discovery and development of novel protein therapeutics against HIV.
- Identification of a gp120 neutralizing HCDR3 peptide from the repertoire of a Long Term Non Progressor (LTNP) and three cross-reactive mimotopes from plasmatic IgA of 5 LTNP.
- Description of HIV-2 Integrase polymorphisms from 47 patients and identification of two novel mutations selected under Raltegravir selective pressure in vitro.
- Development of a software for automated HIV sequence analysis within the ART-A (Affordable Resistance Testing for Africa) international consortium and a new subtyping tool for HIV, COMET (available on <http://comet.retrovirology.lu>), also suited for pyrosequencing analyses.
- Identification of novel single nucleotide polymorphisms and allele combinations in the CYP2B6 gene of HIV-infected patients from Rwanda.
- Comparison of the Roche COBAS® AmpliPrep/COBAS® TaqMan® HIV-1, v2.0 and the Abbott m2000 RealTime HIV-1 assays for quantification of viral load using 546 plasma samples of HIV-1 B and non-B subtypes from Luxembourg and Rwanda.
- E.J. Schouten and K. Kamoto. *Lancet Infect Dis* 2010;10(1):60-5.
- Only slight impact of predicted replicative capacity for therapy response prediction. H. Weisser, A. Altmann, S. Sierra, F. Incardona, D. Struck, A. Sönnernborg, R. Kaiser, M. Zazzi, M. Tschochner, H. Walter and T. Lengauer. *PLoS One* 2010;5(2):e9044.
- Polymorphisms of HIV-2 integrase and selection of resistance to raltegravir. D.P. Bercoff, P. Triqueneaux, C. Lambert, A.A. Oumar, A.M. Ternes, S. Dao, P. Goubau, J.C. Schmit and J. Ruelle. *Retrovirology* 2010;7(1):98.
- Prevalence of hepatitis B and C and HIV infections among problem drug users in Luxembourg: self-report versus serological evidence. A. Origer and J.C. Schmit. *J Epidemiol Community Health* 2010.[Epub ahead of print].
- Prosperi MC, Rosen-Zvi M, Altmann A, Zazzi M, Di Giambenedetto S, Kaiser R, Schülter E, Struck D, Sloat P, van de Vijver DA, Vandamme AM, Sönnernborg A; EuResist study group; Virolab study group. Antiretroviral therapy optimisation without genotype resistance testing: a perspective on treatment history based models. *PLoS One* 2010;5:e13753.

PUBLICATIONS 2010

- Cellular HIV-1 DNA levels in drug sensitive strains are equivalent to those in drug resistant strains in newly-diagnosed patients in Europe. V.L. Demetriou, D.A.M.C. van de Vijver, I. Kousiappa, C. Balotta, B. Clotet, Z. Grossman, L.B. Jørgensen, S.Z. Lepej, I. Levy, C. Nielsen, D. Paraskevis, M. Poljak, F. Roman, L. Ruiz, J.C. Schmit, A.M. Vandamme, K. Van Laethem, J. Vercauteren, L.G. Kostrikis. *PLoS ONE* 2010;5(4):e10976.
- Diagnosis and management of antiretroviral-therapy failure in resource-limited settings in sub-Saharan Africa: challenges and perspectives. A.D. Harries, R. Zachariah, J.J. van Oosterhout, S.D. Reid, M.C. Hosseinipour, V. Arendt, Z. Chirwa, A. Jahn,

KEY PARTNERS 2010

- EuroSIDA, EuroHIV, Euresist, EuropeHIVResistance, European Society for Antiviral Resistance (ESAR), ART-A and MONOD networks
- PMEs: Complix, Ghent, Belgium, ABL, Luxembourg, Institut für Immunologie und Genetik, Kaiserslautern, Germany
- Service National des Maladies Infectieuses, Centre Hospitalier de Luxembourg
- AIDS Reference Laboratories of Belgium
- University Medical Center Utrecht, The Netherlands
- National Reference Laboratory and Treatment and Research on AIDS Center, Rwanda, Kigali



CLINICAL AND EPIDEMIOLOGICAL INVESTIGATION CENTER (CIEC)



HEAD OF CIEC
Dr. Anna CHIOTI, MD



MISSION

The mission of the CIEC is:

- To promote clinical research according to Good Clinical Practice (ICH-GCP),
- To develop national clinical research network,
- To consolidate fundamental and experimental findings by the conduct of clinical research, and
- To provide access to new and innovative therapeutic approaches through means of a clinical study.

KEY RESULTS IN 2010

- 167 patients included in 2010 in 18 clinical trials: 7 investigator-driven clinical trials and 11 industry-driven in diverse therapeutic areas (oncology, diabetes, cardiovascular, neurology, nutrition, hematology).
- 413 inclusion and follow-up visits took place in 2010. 196 additional visits were performed at the CIEC for the MEMOVIE and VERTIGO studies. A total of 609 visits were coordinated by CIEC.
- Monitoring of 1100 patient data related to nosocomial infections in 7 hospitals (Ministry of Health - Nosix).
- Set-up of one compassionate use program giving early therapeutic access to lung cancer patients with no alternative treatment option.
- Consolidation of existing collaborations with major hospitals, institutions and pharmaceutical industry partners. Initiation of new collaborations with professional societies and pharmaceutical industry.
- Organization of the 2nd Clinical Research Day (27 Octobre 2010): presentation of clinical research activities in Luxembourg, 89 participants (25% international participants).

KEY PARTNERS IN 2010

- Luxembourg Hospitals
- CRP-Tudor, IBBL
- Spanish Lung Cancer Group, UCL-Cliniques Universitaires, St. Luc, ULB-Oncology Centre
- Pharma companies: Amgen, AstraZeneca, Bayer, Celgene, Johnson & Johnson, Novartis, Roche, Sanofi Aventis, Pfizer



LUXEMBOURG BIOMEDICAL RESEARCH RESOURCES (LBR2)



HEAD OF LBR2
Prof. Bruno DOMON, PhD

The creation of the proteomics center (LCP) is imbedded in long term strategy of CRP-Santé to focus on Translational Research, and promote technologies. All platforms were then integrated in the new LBR2 department.

ANIMAL FACILITY



Dr. Simone NICLOU, PhD

The CRP-Santé animal facility is a high quality infrastructure allowing animal experimentation under strictly controlled conditions (e.g. specific pathogen free facility). Hygienic standards and internal regulations follow the guidelines and recommendations of the Federation for Laboratory Animal Science Associations (FELASA).

CONFOCAL MICROSCOPY



Dr. Céline HOFFMANN, PhD

MISSION

The microscopy platform provides support to scientists for high quality cell imaging. The facility offers technical support for confocal microscope handling and operation, sample preparation and experimental design, data processing and image analysis. Confocal microscopy allows imaging of cells or tissues in three dimensions and over time, in one to four colors. The platform offers training sessions or collaborative work for sample processing and data analysis. The platform is also open to academic or industrial users from Luxembourg and surrounding areas.

KEY RESULTS IN 2010

- A confocal picture showing the actin cytoskeleton in Arabidopsis roots has been selected for the cover of Plant Cell (September issue, Papuga et al.). Plant Cell is a peer-reviewed journal with the highest impact factor of primary research journals in plant biology.
- We implemented a multi-position time-lapse experiment system. We were able to simultaneously image several cells (up to 10 cells) at different positions on the microscope slide. We followed cytosolic pH modification (with a ratiometric dye SNARF5F) and observed actin binding protein behavior.
- Using the FRAP technique (Fluorescence Recovery after Photobleaching) we showed the effect of L-plastin phosphorylation on actin dynamics (Al Tanoury et al.).
- We imaged the nerve growth factor receptor TrkA in activated and non-activated NK cells and showed that the mouse NK cells express the NGF receptor TrkA and that this expression is dynamically regulated (Ralainirina et al.).

KEY PARTNERS IN 2010

- Cytoskeleton & Cell Plasticity Laboratory, Prof. Evelyne Friederich, University of Luxembourg
- Plateforme de Microscopie et d'Imagerie, Dr. Jérôme Mutterer, IBMP, Strasbourg, France
- Plateforme de Cytométrie et de Microscopie, Dr. Sébastien Plançon, University of Luxembourg

FLOW CYTOMETRY



Mr. René BRONS

MISSION

The Core Facility Cytometry is the centralized flowcytometry service of CRP-Santé. It assists researchers with flowcytometry experimental design, data acquisition, cell sorting and data analysis. Currently the facility is equipped with a FACSria cell sorter and a FACSCanto analyser. It is an open facility accessible for personnel from CRP-Santé as well as external researchers.

KEY RESULTS IN 2010

- Implementation 13 color flowcytometry for a NK-cell project.
- Implementation of multi-color phenotyping on the Side Population.
- Organisation of an international cytometry congress for 150 participants November 2010 (Joint Belgian Luxembourgish Cytometry Meeting).

PUBLICATIONS IN 2010

- The histone deacetylase inhibitor MGCD0103 induces apoptosis in B-cell chronic lymphocytic leukemia cells through a mitochondria-mediated caspase activation cascade. V. El Khoury, E. Moussay, B. Janji, V. Palissot, N. Aouali, N. Brons, K. Van Moer, S. Pierson, E. van Dyck and G. Berchem. *Mol Cancer Ther* 2010;9:1349.
- Anti-cancer effects of 20(S)-protopanaxadiol on human acutelymphoblastic leukemia cell lines. L. Sun, Q. Wang, X. Liu, N.H.C. Brons, N. Wang, A. Steinmetz, Y. Lv, Y. Liao, H. Zheng. *Med Oncol*;DOI 10.1007/s12032-010-9508-1.
- Novel method for isolating untouched rat natural killer cells with higher purity compared with positive selection and fluorescence-activated cell sorting. A. Poli, N.H.C. Brons, W. Ammerlaan, M. Tatiana, F. Hentges, M. Chekenya and J. Zimmer, *Immunology* 2010;131(3):386-94.
- Mouse Natural Killer (NK) cells express the nerve growth factor receptor TrkA, which is dynamically regulated. N. Ralainirina, N.H.C. Brons, W. Ammerlaan, C. Hoffmann, F. Hentges, and J. Zimmer. *Plos One* 2010;5(12):e15053.

KEY PARTNERS 2010

- Integrated Biobank of Luxembourg (IBBL)
- University of Luxembourg
- Luxembourg Cytometry Association (LCA)
- Translational Genomics Institute (TGen), Phoenix, USA
- BectonDickinson
- DutchFlowgroup
- Belgian Society for Analytical Cytology (BVAC/ABCA)



LABORATORY OF ANALYTICAL HUMAN BIOMONITORING



Dr. Brice APPENZELLER, PhD



MISSION

Fields of competences of Laboratory of Analytical Human Biomonitoring cover analytical toxicology and development of biomarkers for the assessment of occupational and environmental exposure to organic pollutants and for therapeutic drug monitoring. Analytical techniques available at LAHB are based on chromatography coupled with tandem mass spectrometry.

KEY RESULTS IN 2010

- Setting up of a method for the analysis multi-residue pesticides in hair
- Evaluation of the exposure of Luxembourg population to polycyclic aromatic hydrocarbons by hair analysis.

PUBLICATIONS IN 2010

- Gas/particle partitioning of currently used pesticides in the atmosphere of Strasbourg (France). C. Schummer, E. Mothiron, B.M.R. Appenzeller, R. Wennig and M. Millet. *Air Qual Atmos Health*; DOI 10.1007/s11869-010-0065-8.
- Internet suicide guidelines: report of a life-threatening poisoning using tobacco extract. S. Schneder, N. Diederich, B. Appenzeller, A. Schartz, C. Lorang and R. Wennig. *J Emerg Med* 2010;38(5):610-3.
- Temporal variations of concentrations of currently used pesticides in the atmosphere of Strasbourg, France. C. Schummer, E. Mothiron, B.M. Appenzeller, A.L. Rizet, R. Wennig and M. Millet. *Environ Pollut* 2010;158(2):576-84.

KEY PARTNERS IN 2010

- Centre de Géochimie de la Surface de Strasbourg, UMR 7517 CNRS – Université Louis Pasteur, France
- Agence Française de la Sécurité Sanitaire de l'Environnement et du Travail, Maison-Alfort, France
- Laboratoire de Toxicologie - Laboratoire National de Santé, Luxembourg

LUXEMBOURG CLINICAL PROTEOMICS CENTER



HEAD OF LABORATORY
Prof. Bruno Domon, PhD

ASSOCIATE HEAD OF LABORATORY
Dr. Yeoun Jin KIM, PhD



MISSION

The mission of the Luxembourg Clinical proteomics Center is:

- To build robust proteomic platforms with state-of-the-art mass spectrometry technology,
- To implement proteomic platforms focused on clinical applications,
- To discover biomarkers for diagnosis, prognosis of diseases and monitor drug response, and
- To build a research unit to perform translational research.

KEY RESULTS IN 2010

- A new unit, the LCP was created in 2010 – thanks to a PEARL grant from Fonds National de la Recherche (FNR). The head of the center has been able to hire a team throughout the year, while new laboratory space (approx 250 m²) was created in the building rue Thomas Edison. The inauguration of the new Center took place on September 10. A group of twelve persons, including experts in analytical chemistry, mass spectrometry, bioinformatics, constitutes an interdisciplinary team capable of addressing the challenging questions associated to the application of proteomics to personalized medicine. The laboratory is equipped with cutting-edge mass spectrometry technologies enabling development of novel proteomics applications, which will accelerate their implementation in a clinical environment.
- A partnership with ThermoFisher Scientific, one of the world leaders in life science technologies, ensured LCP an early access to novel technologies and new reagents, and thus increases its visibility in the international clinical proteomics arena.
- LCP has been able to attract significant external and competitive funding, including in-kind contributions through the partnership with Thermo-Fisher, the award of a CORE grant (to develop new proteomics based assays), and one AFR for a PhD student grant.
- During the year, five (first/last author) publications have been submitted and accepted in peer-reviewed journals.

PUBLICATIONS IN 2010

- Options and considerations when selecting a quantitative proteomics strategy. B. Domon and R. Aebersold. *Nat Biotechnol* 2010;28:710-21.
- Increased selectivity, analytical precision, and throughput in targeted proteomics. R. Kiyonami, A. Schoen, A. Prakash, S. Peterman, V. Zabrouskov, P. Picotti, R. Aebersold, A. Huhmer and B. Domon. *Mol. Cell. Proteomics* 2011; 10:M110.002931
- Selected reaction monitoring applied to proteomics. S. Gallien, E. Duriez and B. Domon. *J. Mass Spectrom* 2011(in press).
- Systematic quantification of peptides / proteins in urine using selected reaction monitoring. N. Selevsek, M. Matondo, M. Sanchez Carbayo, R. Aebersold and B. Domon. *Proteomics* 2011 (in press).
- Towards a standardized urine proteome analysis methodology. M. Court, N. Selevsek, M. Matondo and B. Domon. *Proteomics* 2011 (in press).

KEY PARTNERS IN 2010

- ThermoFisher Scientific, San José, USA and Bremen, Germany
- Commissariat à l'Énergie Atomique – CEA, Grenoble, France
- Translational Genomics Institute (TGen), Phoenix, USA
- IBBL
- Department Life Sciences and LCSB - University Luxembourg



MICROARRAY CENTER



HEAD OF LABORATORY
Dr. Laurent VALLAR, PhD



MISSION

The Microarray Center aims to provide academic and private sector scientists alike with comprehensive and flexible microarray services for genomic studies. State-of-the-art procedures and integrated quality controls are combined with industry-leading technology platforms to ensure projects are delivered to the highest standards with in-depth data mining. Microarray team is multi-disciplinary and provides a full range of expert support services in sample preparation, microarray analysis, biostatistics and bioinformatics.

KEY RESULTS IN 2010

- Microarray Center participated in 29 research projects funded either by Fonds National de la Recherche (FNR) (2), CRP-Santé (7), University of Luxembourg (7), private foundations (3) or foreign institutions (10). It is also the coordinator of a FNR CORE project focused on the study of alternative splicing in lung cancer.
- In collaboration with IBBL and Norlux laboratory, Microarray Center implemented an innovative technique called Clonal Sorting which has great potential for application in the field of oncology. Team members were trained at TGen, Phoenix, Arizona, where this cutting-edge procedure was initially developed.
- Two other microarray applications with high interest for genomic and epigenetic studies were implemented at MC: array comparative genomic hybridization (aCGH) and methylation array (MeDIP).
- Activities of Microarray Center were positively evaluated by external experts through a peer-review mandated by the Ministry of Research, as well as by MC users through a satisfaction survey.
- Joana Corte-Real, a graduate student from University of Luxembourg, successfully completed her Master's degree in Systems Biology after having conducted her research projects for six months in the laboratory.

PUBLICATIONS IN 2010

- Signatures of MicroRNAs and selected MicroRNA target genes in human melanoma. D. Philippidou, M. Schmitt, D. Moser, C. Margue, P.V. Nazarov, A. Muller, L. Vallar, D. Nashan, I. Behrmann and S. Kreis.
Cancer Res 2010;70(10):4163-73.
- Determination of genes and microRNAs involved in the resistance to fludarabine in vivo in chronic lymphocytic leukemia. Etienne Moussay, Valerie Palissot, Laurent Vallar, Helene A Poirel, Thomas Wenner, V. El Khoury, N. Aouali, K. Van Moer, B. Leners, F. Bernardin, A. Muller, P. Cornillet-Lefebvre, A. Delmer, C. Duhem, F. Ries, E. van Dyck and G. Berchem.
Molecular Cancer 2010;9:115.
- miR-661 expression in SNAI1-induced epithelial to mesenchymal transition contributes to breast cancer cell invasion by targeting Nectin-1 and StarD10 messengers. G. Vetter, A. Saumet, M. Moes, L. Vallar, A. Le Béche, C. Laurini, M. Sabbah, K. Arar, C. Theillet, C.H. Lecellier and E. Friederich.
Oncogene 2010;29:4436-48.
- A mathematical model of actin filament turnover for fitting FRAP data. A.A. Halavatyi, P.V. Nazarov, Z. Al Tanoury, V.V. Apanasovich, M. Yatskou and E. Friederich.
Eur Biophys J 2010;39(4):669-77.
- Viruses: incredible nanomachines. New advances with filamentous phages. M.A. Hemminga, W.L. Vos, P.V. Nazarov, R.B. Koehorst, C.J. Wolfs, R.B. Spruijt and D. Stopar.
Eur Biophys J 2010;39(4):541-50.

KEY PARTNERS IN 2010

- Institut de génétique moléculaire, CNRS UMR5535-IFR122, Montpellier, France
- Translational Genomics Institute (TGen), Phoenix, USA
- Unité INSERM/UMRS 961, Faculté de Médecine, Nancy, France
- Integrated Biobank of Luxembourg (IBBL)
- Department of Life Sciences, University of Luxembourg

METHODOLOGY AND STATISTICS (CCMS)

HEAD OF CCMS
To be appointed



MISSION

The Centre of Excellence for Methodology and Statistics was established in March 2010 in order to meet the methodological and statistical needs of the public health department and of other CRP-Santé laboratories. It also aims to develop contractual public health management and data handling activities for other national and international bodies. It provides its expertise during the preparation of studies in order to determine the design best suited to the research questions. It defines the data management methods which guarantee the highest quality of the results.

KEY RESULT IN 2010

- First contracts have been signed with WHO-Tropical Diseases Research (TDR) to analyze data from TDR studies.

KEY PARTNERS 2010

- World Health Organization - Tropical Diseases Research
- Université Victor Segalen, Bordeaux 2, ISPED, France



Centre de Recherche Public de la Santé

Technical and Administrative Department



HEAD OF DEPARTMENT
Daniel CARDAO, MBA



Communication

The communication group is headed by Aurélia Derischebourg.

MISSION

The communication group develops both the internal and external communication strategy. It takes actively part in improving the institution's image to the scientific community and to the public. The group is also in charge of event management (e.g. conferences, workshops)

KEY RESULTS IN 2010

- June: Creation of a new website. The first CRP-Santé Newsletter is launched.
- September: Inauguration of the Luxembourg Clinical proteomics Center and proteomics workshop.
- October: Inauguration of CRP-Santé's intranet.
- December: Publication of a comprehensive document on CRP-Santé and its research departments.

Environment, health and security (EH&S)

The EH&S group is headed by Elodie Fontaine.

MISSION

The group is in charge of the risk assessment of health, safety and environment at work and provision of safe working conditions in respect to legal regulations. It provides also safety equipment and devices and EH&S training and assuring the monitoring of technical safety equipment. Finally, the group is in charge of health surveillance, and is taking care of the waste and hygiene management.

KEY RESULTS IN 2010

- Improvement of individual health surveillance and risk assessment by inventory of risk at work for 35 people.
- Treatment of EH&S issues for the setup of the new CRP-Santé building.

Implementation of EH&S procedures at IBBL according to their quality system.

- Cost improvement of infectious and chemical waste management.

Finances

The finances group is headed by Jérémy Klein.

MISSION

The group manages the day-to-day financial aspects of research projects following the accounting rules and collaboration agreements with partners. It prepares the annual CRP-Santé budget together with the head of units and prepares also individual budgets per research projects in collaboration with the principal investigators. Finally, it establishes financial statements for partners, management and the board of administration.

KEY RESULTS IN 2010

- Establishment of a new amortization method for fixed assets in order to reevaluate the total assets of CRP-Santé.
- Development of an online travel fees statement tool.
- Preparation of the budget for the new performance contract 2011-2023.
- Assistance in the set-up of the spin-off company Complix Luxembourg.
- Performing the accounting for IBBL.

Financial control

The controlling is exercised by Joseph Gautot.

MISSION

Provide reasonable assurance regarding the achievement of objectives in the following fields of i) reliability of financial reporting, ii) compliance with laws, regulations and internal procedures and iii) effectiveness and efficiency of operations.

KEY RESULTS IN 2010

- Design and implementation of a monthly based dashboard covering the activities and providing

performance indicators for the administrative and technical services (Health & Safety, Human Resources, Project Management, Technical Services, IT, Communication, Purchasing, Legal & Finance).

- Determination of unit costs for the various platforms in the Luxembourg Biomedical Research Resources (LBR2) in order to establish a pricing policy for internal users (transfer price) as well as external (public or private) users.

Human Resources

The human resources group is led by Natacha Beicht-Claude.

MISSION

Human resources are in charge of the management and follow-up of labor contracts, scientist exchange agreements and payroll. They are responsible for employee policies and compliance with legal regulations. The recruitment is done based on the rules of the "European Charter for Researchers and the Code of Conduct for the Recruitment of Researchers (C&C)" and the new hires benefit from a detailed induction process, which can be assimilated to a welcome day for newcomers. Human resources provide also assistance for people coming from abroad. The group is in charge of employee development and organizes training in soft skills. All activities are reported in a monthly dashboard for the board of management.

KEY RESULTS IN 2010

- HR strategy: CRP-Santé received the HR Excellence in Research recognition from the European Commission for our engagement in C&C.
- CRP-Santé has recruited 26 new collaborators in 2010.
- Payroll process: HR set up a new HR database, a new data payroll and have simulated the salaries internally during 2010 in order to setup an internal payroll system in 2011.
- Participation at the recruitment Career fair in Paris and meeting with the HR strategy group for C&C in Maribor.

Information Technologies (IT)

In 2010 the IT group was headed by Patrick Schild.

MISSION

The group guarantees the quality of IT services, the high availability of IT infrastructures, and provides professional support. It is in charge of the successful realization of IT projects and implements technology evolution to fulfill business requirements. Therefore, it must keep the technical skills in the team up to date through involvement in challenging projects and by external training.

KEY RESULTS IN 2010

- Server consolidation and virtualization based on Blade Server technology running VMware.
- Review of IT security, two level firewall strategy and high availability.
- Development and implementation of the new intranet.
- Starting migration of Lotus Notes servers and clients to version 8.5.

Legal

Legal advice is given by Guillaume Byk.

MISSION

The mission of the lawyer consists in drafting and following contractual agreements related to CRP-Santé's collaboration with scientific partners. He implements also data protection regulations within CRP-Santé and guarantees proper insurance coverage for CRP-Santé research projects. Finally, he assists researchers in the legal protection of their intellectual property.

KEY RESULTS IN 2010

- In collaboration with the Technology Transfer Officer, setup of standardized processes for the management of intellectual property.
- Ongoing consolidation of legal requirements for research projects.

Project Management

The project management group is headed by Jo Schroeder.

MISSION

The group is in charge of the transversal management of all research projects at CRP-Santé. It supports the principal investigators in the application process for competitive projects on national and European levels. It constantly looks out for new competitive funding opportunities on national and European levels and informs the research groups.

KEY RESULTS IN 2010

- In 2010, the overall number of projects realized at CRP-Santé grew by 46% and reached 150 units by the end of the year.
- 13 applications for EU funding programs have been submitted. 4 applications were accepted, 2 are still pending.
- Implementation of standard operating procedures according to the Project Management Institute methodology. Set-up automated work-flows for key processes.

Purchasing

Purchasing is under the responsibility of Marc Weisen.

MISSION

The purchasing group is in charge of centralizing purchases in order to create synergies and negotiate prizes with providers within the institution. Together with management and other technical services it is also involved in the planning for new facilities.

KEY RESULTS IN 2010

- Implementation of the Luxembourg Clinical Proteomics center laboratory (facilities).
- Synergies in purchasing of different laboratory equipments and consumables.
- Assistance in the advanced planning phases for the new CRP-Santé building.

Quality Management

Blandine Valet is responsible for quality management.

MISSION

Quality management oversees and monitors the development and implementation of the Quality Management System at CRP-Santé. It creates and sustains a climate of acceptance for continuous improvement and works to satisfy efficiently and effectively the needs and desires of CRP-Santé's partners.

KEY RESULTS IN 2010

- Organization and realization of internal quality audits.
- Review of the documentation to introduce changes and improvements.
- Definition of the major processes of CRP-Santé.

Technical Service

The technical service group was headed in 2010 by Dr. Laura Martins.

MISSION

The group is responsible for the multiple technical issues in the CRP-Santé buildings. It has the responsibility for the day-to-day operations, including maintenance and waste collection.

KEY RESULTS IN 2010

- Contribute to the advanced planning phases for the new CRP-Santé building.
- Implementation of new software (GMAO) for the tracking of equipment in buildings.
- Maintain and improve the performance of building systems (e.g. lights and heating).
- Carry out of a preventive maintenance program for improving performance and extension of life of buildings, equipment, furniture and interior finishes.
- Set up a maintenance program for our partner institution IBBL and providing support for setting up new equipment.

Technology Transfer

Technology transfer is managed by Dr. Philippe De Backer.

MISSION

Technology transfer is in charge of pro-active protection and tracing of inventions with commercial potential, with the aim to secure the necessary intellectual property rights for CRP-Santé research. It further aims at marketing the technology through negotiating and executing agreements with companies and the foundation of start-ups. By its activities, it facilitates the valorization and commercialization of CRP-Santé research results.

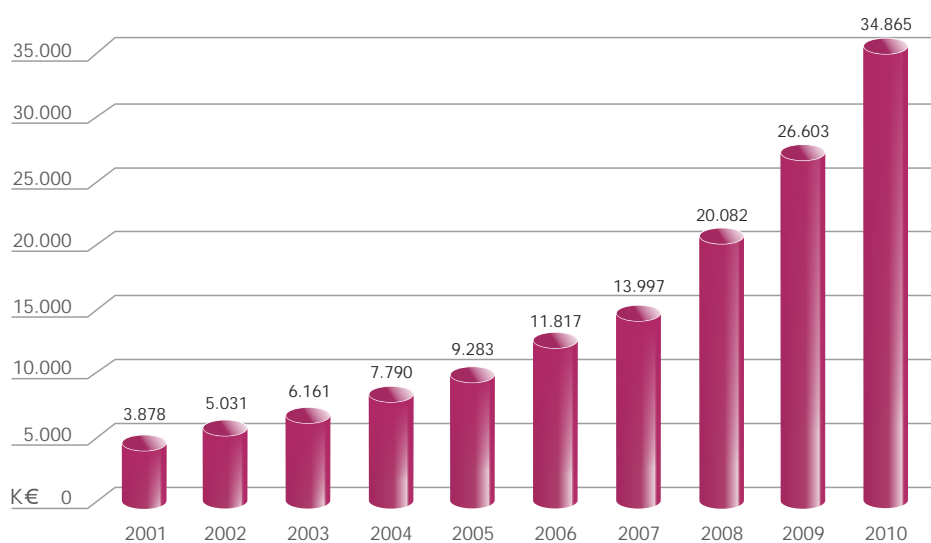
KEY RESULTS IN 2010

- Implementation of intellectual property policy at CRP-Santé.
- Making standard documents available for the exchange of material (material transfer agreements) and information (non-disclosure agreements).
- Securing several patent applications and active management of the CRP-Santé patent portfolio.

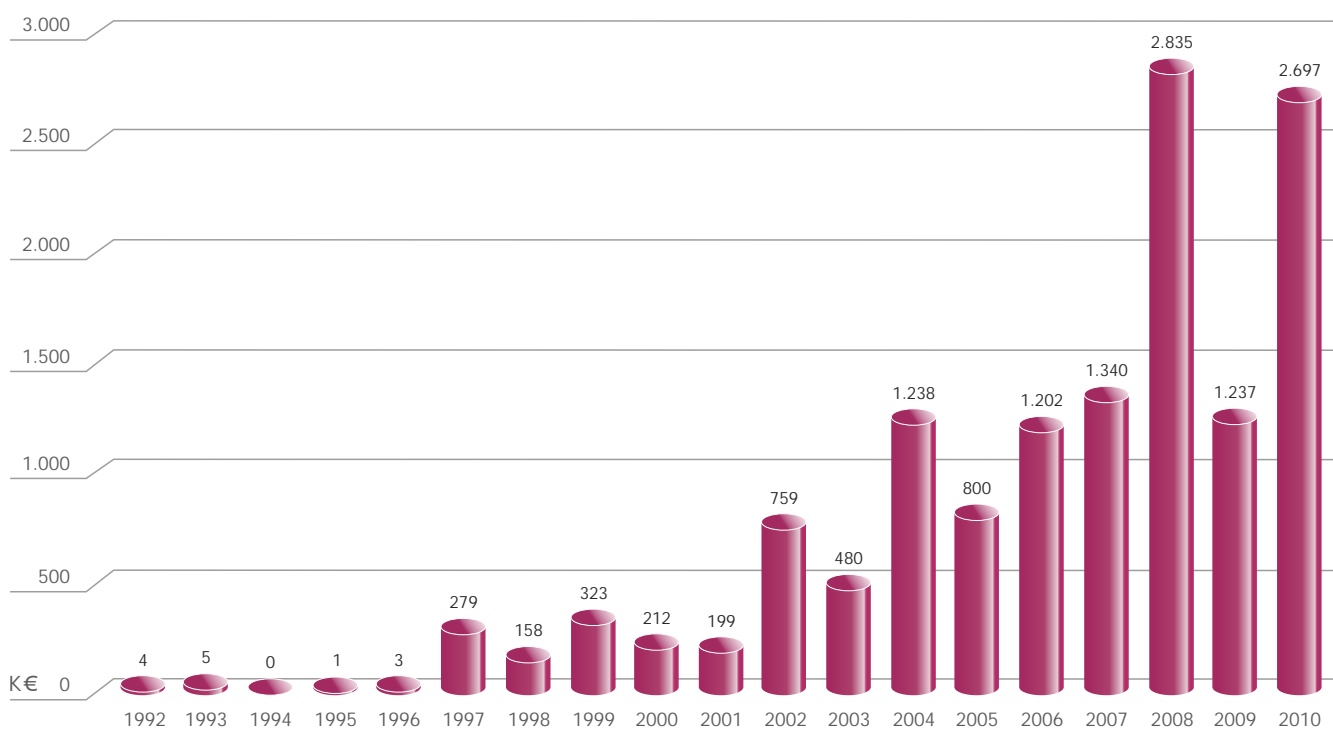


Key Figures

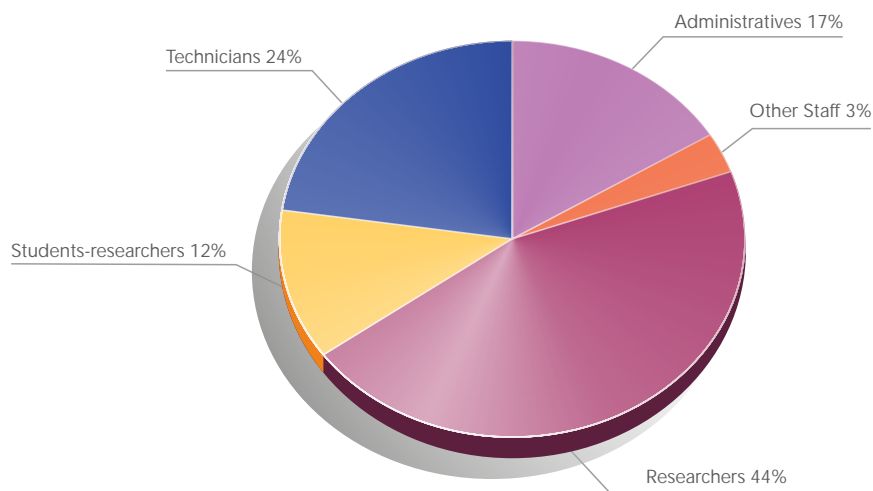
Total yearly budgets (including CAPEX) in kEuros



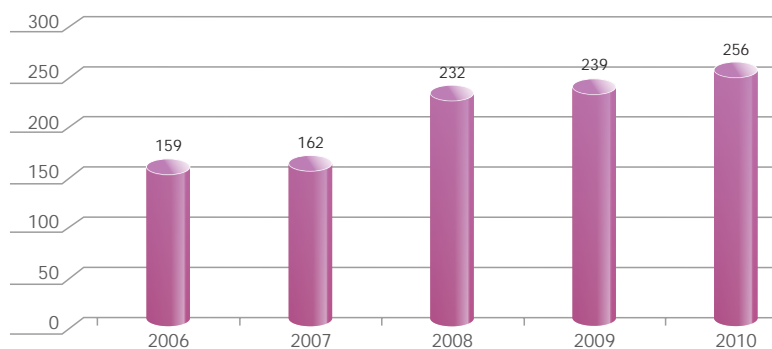
Investments at CRP-Santé



Categories of professional staff of CRP-Santé



Staff evolution over the years



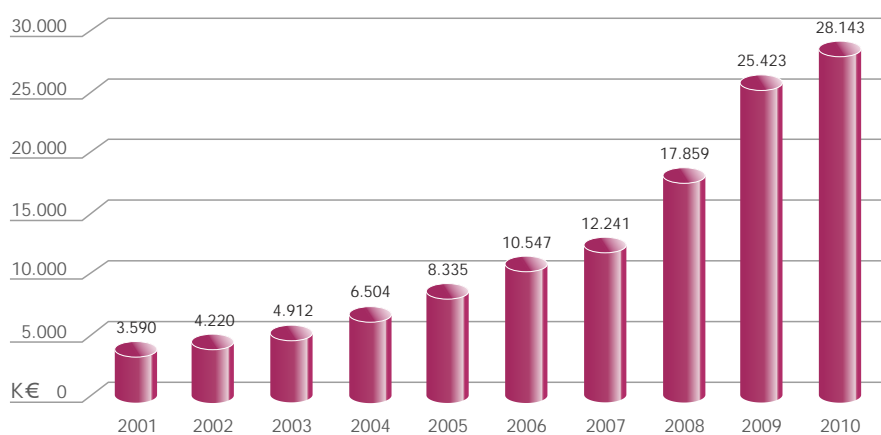
Employees from 29 nationalities work at CRP-Santé

December 2010
Nationalities

Nationalities	Total
Albanian	0,39%
Belarussian	0,39%
Belgian	18,75%
British	0,39%
Bulgarian	0,39%
Chinese	1,95%
Congolese	0,39%
Corean	0,78%
Dutch	0,39%
French	34,78%
German	8,98%
Greek-Danish	0,39%
Indian	0,78%
Italian	1,17%
Kenyan	0,39%
Lebanese	0,39%
Luxembourgish	22,67%
Malaisian	0,39%
Norwegian	0,39%
Polish	0,78%
Portuguese	1,56%
Romanian	0,39%
Russian	0,39%
Rwandan	0,39%
Serbian	0,39%
Swedish	0,39%
Swiss	0,78%
Tunisian	0,39%
Venezuelan	0,39%

Grand Total 100,00%

R & D charges at CRP-Santé



* Those amounts include costs, Operating costs and Travel costs

* Investments, Depreciation of equipments, Interests, Taxes and Non-recurring expenses are excluded

La comptabilité financière et analytique a été réalisée au CRP-Santé. Les comptes ont été vérifiés par KPMG Audit Sarl, réviseurs d'entreprise agréés, et approuvés par le Conseil d'Administration lors de sa séance du 30/03/2011



BILAN AU 31 DECEMBRE 2010

(en Euros)

ACTIF	31.12.2010	31.12.2009
A. CAPITAL SOUSCRIT NON VERSE		
B. FRAIS D'ETABLISSEMENT		
C. ACTIF IMMOBILISE		
I. Immobilisations incorporelles	268.598,70	162.709,42
2. Concessions, brevets, licences, marques, ainsi que droits et valeurs similaires		
a) acquis à titre onéreux	268.598,70	162.709,42
b) créés par l'entreprise		
II. Immobilisations corporelles	4.476.730,30	1.360.389,85
2. Installations techniques et machines	0,00	0,00
3. Autres installations, outillage et mobilier	4.476.730,30	1.360.389,85
4. Acomptes versés et immobilisations corporelles en cours	0,00	0,00
III. Immobilisations financières	1.262.394,68	1.012.394,68
3. Participations	1.262.394,68	1.012.394,68
TOTAL DE L'ACTIF IMMOBILISE	6.007.723,68	2.535.493,95
D. ACTIF CIRCULANT		
I. Stocks	0,00	0,00
II. Créances		
1. Créances résultant de ventes et prestations de services	329.508,37	239.529,39
a) dont la durée résiduelle est inférieure ou égale à un an	329.508,37	239.529,39
b) dont la durée résiduelle est supérieure à un an		
2. Créances sur partenaires	1.530.350,48	1.978.621,79
3. Créances sur des entreprises avec lesquelles la société a un lien de participation	189.268,52	24.038,77
4. Autres créances	782.616,42	852.336,04
a) dont la durée résiduelle est inférieure ou égale à un an	782.616,42	852.336,04
b) dont la durée résiduelle est supérieure à un an		
III. Valeurs mobilières	0,00	0,00
IV. Avoirs en banque, avoirs en compte de chèques postaux, chèques et en caisse	12.000.731,07	8.550.405,60
TOTAL DE L'ACTIF CIRCULANT	14.832.474,86	11.644.931,59
E. COMPTES DE REGULARISATION	200.508,82	240.007,25
TOTAL DE L'ACTIF	21.040.707,36	14.420.432,79

BILAN AU 31 DECEMBRE 2010

(en Euros)

PASSIF	31.12.2010	31.12.2009
A. CAPITAUX PROPRES		
I. Capital souscrit	99.157,41	99.157,41
IV. Réserves	2.126.881,09	0,00
V. Résultats reportés	653.191,37	620.148,52
VI. Résultat de l'exercice	229.033,54	33.042,85
VII. Subventions d'investissement	5.996.249,74	2.523.881,26
TOTAL DES CAPITAUX PROPRES	9.104.513,15	3.276.230,04
B. PROVISIONS POUR RISQUES ET CHARGES		
3. Autres provisions	340.301,91	539.895,46
TOTAL DES PROVISIONS	340.301,91	539.895,46
C. DETTES		
1. Emprunts obligataires	0,00	0,00
2. Dettes envers des établissements de crédit	0,00	0,00
3. Acomptes reçus sur commandes	0,00	0,00
4. Dettes sur achats et prestations de services	1.614.551,74	1.717.267,56
a) dont la durée résiduelle est inférieure ou égale à un an	1.614.551,74	1.717.267,56
b) dont la durée résiduelle est supérieure à un an		
5. Dettes représentées par des effets de commerce	0,00	0,00
6. Dettes envers des entreprises liées	0,00	0,00
7. Dettes envers des entreprises avec lesquelles la société a un lien de participation	0,00	0,00
8. Dettes fiscales et dettes au titre de la sécurité sociale	980.962,41	831.591,57
a) Dettes fiscales	444.625,58	384.451,86
b) Dettes au titre de la sécurité sociale	536.336,83	447.139,71
9. Autres dettes	94.735,15	97.520,37
a) dont la durée résiduelle est inférieure ou égale à un an	78.115,15	80.900,37
b) dont la durée résiduelle est supérieure à un an	16.620,00	16.620,00
TOTAL DES DETTES	2.690.249,30	2.646.379,50
D. COMPTES DE REGULARISATION	8.905.643,00	7.957.927,79
TOTAL DU PASSIF	21.040.707,36	14.420.432,79

**COMPTE DE PROFITS ET PERTES POUR L'EXERCICE ALLANT DU
1 JANVIER 2010 AU 31 DECEMBRE 2010**

(en Euros)

	2010 (01.01.10-31.12.10)	2009 (01.01.09-31.12.09)
A. CHARGES		
1. Réduction du stock de produits finis et en cours de fabrication		
2. a) Consommation de marchandises et de matières premières et consommables	2.894.949,64	3.482.113,56
b) Autres charges externes	4.226.606,88	7.014.960,27
3. Frais de personnel		
a) Salaires et traitements	14.818.059,54	12.696.402,95
b) Charges sociales couvrant les salaires et traitements	1.942.185,95	1.721.372,37
4. a) Corrections de valeur sur frais d'établissement et sur immobilisations corporelles et incorporelles	4.822.165,46	360.110,83
b) Corrections de valeur sur éléments de l'actif circulant		
5. Autres charges d'exploitation	928.231,46	1.220.579,01
6. Corrections de valeur sur immobilisations financières et sur valeurs mobilières faisant partie de l'actif circulant		
7. Intérêts et charges assimilées		
b) Autres intérêts et charges	6.645,60	6.356,99
10. Charges exceptionnelles	5.226.405,86	101.326,80
13. Résultat de l'exercice (bénéfice de l'exercice)	229.033,54	33.042,85
TOTAL DES CHARGES	35.094.283,93	26.636.265,63
B. PRODUITS		
1. Montant net du chiffre d'affaires	735.349,91	384.189,10
2. Augmentation du stock de produits finis et en cours de fabrication		
3. Travaux effectués par l'entreprise pour elle-même et portés à l'actif		
4. Contributions et Fonds	28.725.146,47	25.967.588,70
5. Produits de participations		
6. Produits d'autres valeurs mobilières et de créances de l'actif immobilisé		
7. Autres intérêts et produits assimilés		
b) Autres intérêts et produits assimilés	66.046,53	114.108,29
9. Produits exceptionnels	5.567.741,02	170.379,54
10. Résultat de l'exercice (perte de l'exercice)	0,00	0,00
TOTAL DES PRODUITS	35.094.283,93	26.636.265,63



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CENTRE DE RECHERCHE PUBLIC

ACTIVITY REPORT 2010

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