ACTIVITY 2011





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ADMINISTRATION BOARD

The Chairman's message

Dear reader,

On third of October the whole country in general but especially all members of CRP-Santé felt honoured by the press release that the Nobel Prize in Physiology or Medicine 2011 was awarded to Jules A. Hoffmann «for his discoveries concerning the activation of innate immunity».

Professor Hoffmann was in fact not only born in Echternach, a small town in eastern Luxembourg, but Jules A. Hoffmann is also a member of the Board of Administration and President of the Scientific Board of CRP-Santé. In these two important roles, he contributed largely to the still ongoing restructuration of CRP-Santé as well as to the Luxembourgish initiative to develop outstanding biomedicine projects in our country in collaboration with a wide range of international institutional and private partners.

In my quality as President of the Board of Administrators, I have the privilege and the exceptional honour to warmly congratulate Professor Jules A. Hoffmann on his brilliant success concerning the activation of innate immunity. I am deeply convinced that this Nobel Prize awarded to a researcher with Luxembourgish origins who still has very strong links to the country and local scientific community will sustainably catalyse outstanding research at national level and especially at CRP-Santé.

2011 with this outstanding event that a member of CRP-Santé won a Nobel Prize, was an excellent year for our research institution. In fact, all the research departments have been able to contribute significantly to the reaching of the aims defined by the second performance contract with the Government for the years 2011 to 2013. The reader will find in this annual report all relevant facts and figures concerning the whole activity of CRP-Santé, but I would like to expressly underline that our researchers did not only fulfill the requirements of the performance contract to a considerable degree. They did even do



much better by publishing more than eighty peer reviewed scientific papers with a high impact factor.

I am deeply convinced that outstanding scientific excellence will be the only sustainable way to meet the challenges in the future. Indeed, during the past year CRP-Santé was

able to create strong and important partnerships and collaborations with both international public and private partners; however this was only possible thanks to the fact that parts of our research activities are internationally recognized as being among the best in their respective fields.

In the recent past CRP-Santé was able to constantly develop its activities in a context of economic growth and a national governmental research policy aiming to increase spending for research and innovation up to 1% of GNP. But in the following years, we will also have to challenge the impact of the international financial and economic crisis and its effect on research in terms of funding, even if the Government still confirms its commitment to consider public research as being one of the priorities of its policy, the impact of the crisis is likely to diminish or make more difficult access to finance for the public research centers. I believe that by merging in the short future activities in order to generate on the one hand economies of scale, but on the other hand mainly in order to create in some strategic domains the critical mass by combining expertise with resources we will be able to face the challenges of the future. Thanks to the recent reforms and restructuring of the Institution, I am confident that CRP-Santé will be more successful in creating national and international collaborations and economical and societal value.

ADMINISTRATION BOARD

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MANAGEMENT BOARD'S MESSAGE



Thomas LENTZ

Marie-Lise LAIR

Jean-Claude SCHMIT

With the start of the second performance contract covering the years 2011 to 2013, CRP-Santé continues its excellent output : last year, our researchers have published 84 peer reviewed scientific papers with an impact factor (IF) above 2, coming from 66 in 2010 (+27%), including 21 publications above IF 5, and 3 outstanding publications above IF 10. Seven PhD students have finished with success their doctoral training in 2011 and CRP-Santé has recruited 10 new PhD students during the same period, joining a pool of about 40 doctoral students in total. Unfortunately, further extension of PhD training is for the moment not possible because of exiguous laboratory space in our current locations.

Building on first successes in 2010, our Clinical Investigation and Epidemiology Center (CIEC) could rapidly expand its activities in 2011. With 16 new studies initiated following ICH-Good Clinical Practices, CIEC reached in only a single year the goals set for the whole 3 years performance contract period. In addition, via CIEC activities CRP-Santé is now a full partner in the ECRIN network (European Clinical

Research Infrastructure Network, EU FP7 program) promoting academic clinical research in Europe. CIEC has also launched in 2011 its new website www.luxclin.lu, as smart way of connecting with clinical investigators and the general public. Finally, our third national clinical research day was a huge success bringing together a till now not reached number of investigators, clinical research staff, private and academic promoters and interested scientists from Luxembourg and the Greater Region.

Our public health activities made also remarkable progress in 2011. This department now has a well established track record in scientific, peer-reviewed publications and contributes to higher education by PhD training. The department was recently able to attract new projects to CRP-Santé, such as the National Cancer Registry and the National Accident Registry.

MANAGEMENT BOARD'S MESSAGE

Following a general trend in research CRP-Santé activities become increasingly multi-disciplinary and international. Close to 50% of our research projects are with collaboration partners, documented by formal collaboration contracts, either national or from outside Luxembourg. In order to sustain this development CRP-Santé had in 2011 formal meetings with the University of Liège (GIGA research center), the University of Reims Champagne Ardenne and the University of Strasbourg, aiming at finding additional areas of collaboration and student training. CRP-Santé researchers are now also members of the PhD school in Life Sciences which was newly created at the University of Luxembourg, and as such contribute actively in the definition and implementation of the PhD program.

CRP-Santé prepares for future challenges by a continuous strategic reflection, which translates into structural and functional improvements of our organization. Based on external audits, we improved the processes in the department of oncology in 2010/11 and are now busy restructuring the department of cardiovascular diseases. Similar audits are planned for the remaining departments over the next years and we believe that this permanent review process is essential for keeping our organization dynamic. In 2011, CRP-Santé created the competence center for Methodology and Statistics (CCMS), building on already existing in-house capabilities which are now coordinated and developed under the leadership of Prof. Stephen Senn, who joined CRP-Santé from the University of Glasgow. CCMS is a service provider to internal (research units) and external clients such as the WHO, the academia and the pharmaceutical industry. A next step, planned for 2012, will be the inception of a health economics research unit for which we have developed a strategic plan together with an international scientific advisory board under the guidance of Prof. Scott Ramsay from the Fred Hutchinson Cancer Research Center in Seattle, and for which we are currently seeking a senior leader. We are also in the process of reassessing our strategy in mental health research with the help of an external expert, in order to better

satisfy the needs of our country in a field which is extremely costly in terms of human suffering and health care expen-

Mr. Thomas Lentz, our new CFO who started to work with us in April 2011, is strongly committed to further improve the quality of administration and technical services. Thereby he continues implementing the idea of the previous CFO that researchers should be relieved from excessive administrative burden and should be able to concentrate efficiently on their core business which is research.

Economical and societal value creation from the research activities remains a priority for CRP-Santé. Even if the economical environment in the biohealth sector is still sparse in and around Luxembourg, CRP-Santé was able to initiate several promising collaborations with private industry partners and filed a patent in 2011.

After many years of waiting, 2012 will be finally the year in which we will start the construction work of our new research building. The planning phase is finished and the authorization processes come to an end. The perspective of new, adequate facilities motivates the employees and management of CRP-Santé to image future growth and development of their institution for the benefit of Luxembourg.

DEPARTMENT OF CARDIOVASCULAR DISEASES



HEAD OF LABORATORYDr. Daniel WAGNER, MD, PhD



ASSOCIATE HEAD OF LABORATORY
Dr. Yvan DEVAUX. PhD

Laboratory of Cardiovascular Research

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

- Organization of the 2011 Benelux Bioinformatics Conference.
- Development of the myocardial infarction drug-target interactome network (My-DTome) to predict cardiovascular effects of non-cardiovascular drugs.
- Large-scale analysis of microRNAs as diagnostic biomarkers of acute myocardial infarction.
- Demonstration of the performance of cloud computing for gene set analysis.
- Completion of one PhD thesis.



RESEARCH DEPARTMENTS / DEPARTMENT OF CARDIOVASCULAR DISEASES / Laboratory of Cardiovascular Research

PUBLICATIONS

- Proteomic analysis of plasma samples from patients with acute myocardial infarction identifies haptoglobin as a potential prognostic biomarker. Haas B, Serchi T, Wagner DR, Gilson G, Planchon S, Renaut J, Hoffmann L, Bohn T, Devaux Y. J Proteomics. 2011;75(1):229-36. Epub 2011 Jul 13.
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- Chemokine receptor 5 polymorphism in myocardial infarction patients from Luxembourg. Rodius S, Lambert C, Devaux C, Schmit JC, Devaux Y, Wagner DR. Bull Soc Sci Med Grand Duche Luxemb. 2011;(1):31-40.
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- Predictive integration of gene functional similarity and co-expression defines treatment response of endothelial progenitor cells. Azuaje FJ, Wang H, Zheng H, Leonard F, Rolland-Turner M, Zhang L, Devaux Y, Wagner DR. BMC Syst Biol. 2011;5:46.
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- Computational discrete models of tissue growth and regeneration. Azuaje F. Brief Bioinform. 2011;12(1):64-77. Epub 2010 May 30.

KEY PARTNERS

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

DEPARTMENT OF IMMUNOLOGY



HEAD OF LABORATORYProf. Claude P. MULLER, MD, MS

Laboratory of Immunology

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, tick-borne 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.



RESEARCH DEPARTMENTS / DEPARTMENT OF IMMUNOLOGY / Laboratory of Immunology

KEY RESULTS

- With the emergence of influenza A viruses (IAV) increasingly resistant against common antiviral drugs, in particular Oseltamivir (Tamiflu) there is an urgent need for new antiviral drugs. We have identified a cellular protein (vacuolar ATPase) as a novel target for inhibition of viral growth and with a potential for the treatment of influenza A virus infections. The novelty of this approach is that it targets cellular proteins that are not susceptible to mutations unlike viral proteins. Brit J Pharmacol 164, 344-357, 2011.
- As part of the worldwide effort to control avian influenza virus (AIV), we have extended surveillance to the wetlands in Northern Nigeria. We found reassortant low-pathogenic AIV H5N2 viruses in wild birds, that were related to highly pathogenic H5N1 strains found a few months earlier in the same bird species and belonged to a group of viruses that have a high risk of becoming highly pathogenic. These viruses contained genes both from European and South-African strains and represent a considerable risk for poultry industry in the region. J Gen Virol 92, 1172-1183, 2011.
- To understand the origin of the swine-origin pandemic influenza virus (pH1N1), we investigated antibodies in Luxembourg swine farmers. More swine farmers had antibodies against swine influenza virus (SIV) and against pH1N1 than the general population. Antibodies against SIV and pH1N1 correlated in swine workers but not in the general population suggesting that swine workers had contact with a pH1N1-like virus but not the general population. Emerging Infectious Diseases 17, 404-1, 2011
- We investigated virus-host interactions of the NS1 protein of highly pathogenic H5N1 virus and compared them to several influenza A viruses. We showed that NS1 of two avian strains, in contrast to NS1 of H1N1/2009 stimulated translation of viral mRNA; NS1 of H5N1 was an effective inhibitor of cellular premRNA polyadenylation, unlike NS1 of H5N2 and H1N1/2009. These differential activities contribute to the higher pathogenicity of the H5N1, and the lower pathogenicity of the other viral strains. J Biol Chem 286, 7239-47, 2011.

■ The human glucocorticoid receptor (GR) is the receptor for cortisol, the key stress mediator. We have investigated the structure of the GR gene and dissected GR expression that is modulated by multiple layers of transcriptional and translational complexity including multiple untranslated first exons, each with its own promoter, SNPs and epigenetic methylation. These studies help to understand inadequate responses to psychosocial stress. Human Genetics 129, 533-543, 2011.

PUBLICATIONS

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- Revsin Y, Lin MK, Kranz T, Muller CP, Meyer J. J Nucleic Acid Investigations. 2011;2(1):70-76.
- Measles Rubeola. Kremer JR, Muller CP. In Conn's Current Therapy 2011. Bope ET, Rakel RE and Kellerman RD, eds. Philadelphia, London: Saunders Elsevier, 2011. p.142-144.
- Rubella and congenital rubella. Huebschen JM, Muller CP. In Conn's Current Therapy 2011. Bope ET, Rakel RE, Kellerman RD and Conn HF, eds. Philadelphia, London: Saunders Elsevier, 2011. p.141-142.

- 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
- Informal network of academic and public health laboratories in West and Central Africa, Central Asia and South-East Asia working together on viral pathogens
- COST B28 Consortium "Array Technologies for BSL 3 and 4 Pathogens" including institutions from 24 European countries
- Network of 24 European National Reference Laboratories for Measles and Rubella for which the department is responsible as a WHO Regional Reference Center for Measles and Rubella Research
- VIRIM Network in the Greater Region (Saar-Lor-Lux, Rheinland-Pfalz, Wallonia)
- WHO, CDC Atlanta, ECDC Stockholm, European Union

DEPARTMENT OF ONCOLOGY



HEAD OF DEPARTMENTProf. Rolf BJERKVIG, PhD

MISSION

Created in 2008, the Department of Oncology is currently composed of two research units: the Laboratory of Experimental Hemato-Oncology (LHCE) and the Norlux Neuro-Oncology Laboratory (Norlux).

The department carries out translational research at the cellular and molecular level with a focus on cancers of the brain, lung, blood and metastases. Research strongly relies on patient derived tumor biopsies and is highly active in the development of novel animal models for cancer research. The laboratories apply a wide range of state-of-the art technologies including genomic, transcriptomic, proteomic, and metabolomic analyses, as well as in vitro and in vivo imaging technologies (e.g, flow cytometry, confocal microscopy, in vivo bioluminescence/fluorescence, magnetic resonance imaging [MRI]). The Department is also highly active in training and teaching activities, including the supervision of Master and Ph.D. students through its affiliation with several doctoral schools in Luxembourg and Europe. Prof. Rolf Bjerkvig, Head of the Department, also holds the position of professor of anatomy and cell biology at the University of Bergen in Norway. Prof. Bjerkvig is a member of numerous national and international scientific committees and has been honored with several international awards for his research in neurooncology.



HEAD OF LABORATORYDr. Guy BERCHEM, MD

Laboratory of Experimental Hemato-Oncology

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 carried out fundamental research on autophagy as an important resistance mechanism activated in cancer cells leading to tumor escape from therapies.

KEY RESULTS

- Identification of miRNA signature in B-cell chronic lymphocytic leukemia.
- Identification of autophagy as a new player in non-small cell lung carcinoma.

PUBLICATIONS

- Microenvironmental hypoxia orchestrating the cell stroma cross talk, tumor progression and antitumor response.
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- Centre Hospitalier de Luxembourg (CHL), Service de Pneumologie
- Institut de Cancérologie Gustave Roussy, INSERM U753, 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.



DEPARTMENT OF ONCOLOGY



HEAD OF LABORATORYDr. Simone NICLOU, PhD

Norlux Neuro-Oncology Laboratory

MISSION

The Norlux laboratory aims to understand the biological mechanisms underlying the initiation and progression of malignant brain tumors and to identify novel molecular therapeutic strategies against these incurable cancers. A special focus is on tumor angiogenesis and metabolism, tumor heterogeneity and cell based therapeutic strategies. The laboratory is part of the NorLux Neuro-Oncology network.



RESEARCH DEPARTMENTS / DEPARTMENT OF ONCOLOGY / Norlux Neuro-Oncology Laboratory

KEY RESULTS

- Norlux has generated two major high impact publications in 20122. One in Proc Natl Acad Sci U S A (IF 9.7) and one in CELL STEM CELL (IF 25.4)
- The laboratory has been highly successful in competitive funding: in 2011 44.8 % of the laboratory budget is covered by external competitive grant money.
- S.P. Niclou has been invited to join the Scientific Advisory Board of the European Association for Neuro-Oncology (EANO).
- S. P. Niclou has been elected as council member of the European Association for Cancer Research (EACR), the largest Cancer Research organization in Europe, where she serves as a representative of Luxembourg.
- As a coordinator, the laboratory took the lead in the application for a large European research initiative on brain tumor metabolism, encompassing 8 high rank partners, within the EU FP7-HEALTH program.

PUBLICATIONS

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- Expression of the progenitor marker NG2/CSPG4 predicts poor survival and resistance to ionising radiation in glioblastoma. Svendsen A, Verhoeff JJ, Immervoll H, Brogger JC, Kmiecik J, Poli A, Netland IA, Prestegarden L, Planaguma J, Torsvik A, Kjersem AB, Sakariassen PO, Heggdal JI, Van Furth WR, Bjerkvig R, Lund-Johansen M, Enger PO, Felsberg J, Brons NH,Tronstad KJ, Waha A, Chekenya M. Acta Neuropathol. 2011;122(4):495-510. Epub 2011 Aug 24.

KEY PARTNERS

- 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



HEAD OF UNIT Mrs. Marie-Lise LAIR



ASSOCIATE HEAD OF UNIT Dr. Sophie COUFFIGNAL, MD

Centre for Health **Studies**

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

- Publication for the first time in Luxembourg of European indicators in neonatology
- The Ministry of Health requested the Centre for Health Studies to establish the National Register of Injuries
- The Ministry of Health has commissioned the Centre for Health Studies as responsible for implementing the National Cancer Register
- Publication of the final evaluation of the satisfaction of dependents residing in nursing homes
- Signing of two contracts with WHO-TDR for the management of study data on neglected diseases

PUBLICATIONS

- The cost of headache disorders in Europe: the Eurolight project. Linde M, Gustavsson A, Stovner LJ, Steiner TJ, Barre J, Katsarava Z, Lainez JM, Lampl C, Lanteri-Minet M, Rastenyte D, Ruiz de la Torre E, Tassorelli C, Andree C. Eur J Neurol. 2011. [Epub ahead of print].
- Simultaneous determination of nicotine and PAH metabolites in human hair specimen: A potential methodology to assess tobacco smoke contribution in PAH exposure. Appenzeller BM, Mathon C, Schummer C, Alkerwi A, Lair ML. Toxicol Lett. 2011. [Epub ahead of print].

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- Antimalarial drug safety information generated through routine monitoring in a rural health centre in South-Western Senegal. Olliaro P, Brasseur P, Badiane M, Cisse M, Agnamey P, Vaillant M. Trop Med Int Health. 2011;16(Suppl 1):103.
- Evidence of the influence of physical activity on the metabolic syndrome and/or on insulin resistance in pediatric populations: a systematic review. Guinhouya BC, Samouda H, Zitouni D, Vilhelm C, Hubert H. Int J Pediatr Obes. 2011;6(5-6):361-88. Epub 2011 Aug 18.
- The Eurolight project: the impact of primary headache disorders in Europe. Description of methods. Andree C, Stovner LJ, Steiner TJ, Barre J, Katsarava Z, Lainez JM, Lanteri-Minet M, Mick G, Rastenyte D, Ruiz de la Torre E,

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- Dietary, behavioural and socio-economic determinants of the metabolic syndrome among adults in Luxembourg: findings from the ORISCAV-LUX study. Alkerwi A, Donneau AF, Sauvageot N, Lair ML, Albert A, Guillaume M. Public Health Nutr. 2011:1-11. [Epub ahead of print].
- Hypoxia modulates the effect of dihydroartemisinin on endothelial cells. D'Alessandro S, Basilico N, Corbett Y, Scaccabarozzi D, Omodeo-Sale F, Saresella M, Marventano I, Vaillant M, Olliaro P, Taramelli D. Biochem Pharmacol. 2011;82(5):476-84. Epub 2011 Jun 13.
- L'écriture de nous, autobiographie collective contre les fictions sociales de stigmate. Absil G, Vandoorne C, Fond-Harmant L. In Récits et fictions dans la société contemporaine. Paris: L'Harmattan, 2011. p.151-173. (Logiques sociales).
- Changing patterns of malaria during 1996-2010 in an area of moderate transmission in Southern Senegal. Brasseur P, Badiane M, Cisse M, Agnamey P, Vaillant MT, Olliaro PL. Malar J. 2011;10(1):203.
- Psychosocial risk and protective factors of secondary school dropout in Luxembourg: the protocol of an exploratory case-control study. Esch P, Bocquet V, Pull C, Couffignal S, Graas M, Lair ML, Lehnert T, Fond-Harmant L, Ansseau M. BMC Public Health. 2011;11(1):555.



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- Who Is a Typical Patient with Visceral Leishmaniasis? Characterizing the Demographic and Nutritional Profile of Patients in Brazil, East Africa, and South Asia. Harhay MO, Olliaro PL, Vaillant M, Chappuis F, Lima MA, Ritmeijer K, Costa CH, Costa DL, Rijal S, Sundar S, Balasegaram M. Am J Trop Med Hyg. 2011;84(4):543-550.

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- Comparison of short-course multidrug treatment with standard therapy for visceral leishmaniasis in India: an open-label, non-inferiority, randomised controlled trial. Sundar S, Sinha PK, Rai M, Verma DK, Nawin K, Alam S, Chakravarty J, Vaillant M, Verma N, Pandey K, Kumari P, Lal CS, Arora R, Sharma B, Ellis S, Strub-Wourgaft N, Balasegaram M, Olliaro P, Das P, Modabber F. Lancet. 2011;377(9764):477-86. Epub 2011 Jan 20.
- Reduced sympathetically driven heart rate variability during sleep in Parkinson's disease: a case-control polysomnography-based study. Sauvageot N, Vaillant M, Diederich NJ. Mov Disord. 2011;26(2):234-40. Epub 2011 Jan 31.
- Prevalence of the metabolic syndrome in Luxembourg according to the Joint Interim statement definition estimated from the ORISCAV-LUX study. Alkerwi A, Donneau AF, Sauvageot N, Lair ML, Scheen A, Albert A, Guillaume M. BMC Public Health. 2011;11(1):4.
- Programmes de lutte contre le diabète dans 6 pays européens et le Canada. Fond-Harmant L. Santé publique. 2011;23(1):41-53.
- Cryptosporidium contamination of surface and water supplies in haiti. Brasseur P, Agnamey P, Emmanuel E, Pape JW, Vaillant M, Raccurt CP. Arch Environ Occup Health. 2011;66(1):12-7.

- 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



DEPARTMENT OF PUBLIC HEALTH



EXTERNAL EXPERT Dr. Jean-Louis ROBERT

European Medicines Agency -Luxembourg **Focal Point**

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

- 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.

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



DEPARTMENT OF PUBLIC HEALTH



EXTERNAL EXPERT Mr. Alain ORIGER

European **Monitoring Centre** for Drugs and Drug addiction -Luxembourg **Focal Point**

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

KEY RESULTS

- Epidemiological surveillance of problem drug use and validation of applied methodologies. The national RELIS surveillance system does produce EU comparable drug-related data and provides indispensable input for targeted research.
- Peer-reviewed publications on hepatitis B (HBV), hepatitis C (HCV) and HIV infections in problem drug users (PDU) and intravenous drug users (IDU) in Luxembourg.
- New results from a serial, multi-methods PDU/IDU prevalence estimation study. (in press)
- Methodological research on drug-use surveillance systems and indirect epidemiological indicators. (in press)

RESEARCH DEPARTMENTS / DEPARTMENT OF PUBLIC HEALTH / European Monitoring Centre for Drugs and Drug addiction – Luxembourg Focal Point

PUBLICATIONS

- Origer A, Schmit J.-C. Prevalence of hepatitis B and C and HIV infections among problem drug users in Luxembourg: self-report versus serological evidence. J Epidemiol Community Health 2011;66:64-68.
- Removille N, Origer A, Couffignal S, Vaillant M, Schmit JC, Lair ML. A hepatitis A, B, C and HIV prevalence and risk factor study in ever injecting and non-injecting drug users in Luxembourg associated with HAV and HBV immunisations. BMC Public Health. 2011:19;11(1):351.
- Origer A, Lopes Da Costa S, Diederich C. Annual national report on the state of the drugs problem - Grand Duchy of Luxembourg, EMCDDA Focal Point, Luxembourg. EMCDDA Focal Point - CRP-SANTE, Luxembourg 2011.

- Inpatient & outpatient treatment centres (CTM, Jugend an Drogenhellef, Arcus, Solidarité-Jeunes)
- Psychiatric departments of national hospitals
- Low threshold agencies (Abrigado, CNDS)
- Services in prison (Programme Tox, Centre Pénitenciaire Luxembourg)
- Law enforcement agencies (Police Judiciaire)



DEPARTMENT OF PUBLIC HEALTH



HEAD OF UNITDr. Charles PULL, MD, MA

Laboratory of Emotional Disorders

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 LATE is the use of virtual reality.



RESEARCH DEPARTMENTS / DEPARTMENT OF PUBLIC HEALTH / Laboratory of Emotional Disorders

KEY RESULTS

- 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

- Psychosocial risk and protective factors of secondary school dropout in Luxembourg: the protocol of an exploratory case-control study. Esch P, Bocquet V, Pull C, Couffignal S, Graas M, Lair ML, Lehnert T, Fond-Harmant L, Ansseau M. BMC Public Health. 2011;11(1):555.
- Gray Matter Volume Decreases in Elderly Patients with Schizophrenia: A Voxel-based Morphometry Study. Schuster C, Schuller AM, Paulos C, Namer I, Pull C, Danion JM, Foucher JR. Schizophr Bull. 2011. [Epub ahead of print].
- Assessment of body-image perception and attitudes in obesity. Pull CB, Aguayo GA. Curr Opin Psychiatry. 2011;24(1):41-8.

- 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, Québec, Canada
- Universitat Jaume I, Castellon, Spain

DEPARTMENT OF PUBLIC HEALTH



HEAD OF LABORATORYProf. Daniel THEISEN, PhD

Sports Medicine Research Laboratory

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 2011 was to pursue our ongoing studies, to start new research projects and to disseminate first scientific results.



RESEARCH DEPARTMENTS / DEPARTMENT OF PUBLIC HEALTH / Sports Medicine Research Laboratory

KEY RESULTS

- Five new research projects have been launched, involving collaborations with 3 universities in Germany, Maastricht and Belgium and 2 private companies.
- Two new PhD students and one post-doctoral fellow have received an AFR grant from the National Research Fund and have integrated our team.
- Within the framework of a research project, a clinical pathway has been implemented at the Centre Hospitalier de Luxembourg Clinique d'Eich to optimize clinical intervention after knee soft tissue injuries.
- Sports injury surveillance has been pursued at a broad level across different sport federations on behalf of the Ministry of Sport and the National Olympic Committee (COSL).
- Our laboratory was involved in the organization of 11 national conferences, 1 national workshop and 1 international congress. Our results were presented at 9 scientific meetings and congresses.

PUBLICATIONS

- Association between preseason functional tests and injuries in youth football: A prospective follow-up. Frisch A, Urhausen A, Seil R, Croisier JL, Windal T, Theisen D. Scand J Med Sci Sports. 2011;21(6):e468-76. Epub 2011 Aug 18
- Cardiovascular determinants of exercise capacity in the paralympic athlete with spinal cord injury. Theisen D. Exp Physiol. 2011. [Epub ahead of print].
- Muscle strength and hop performance criteria prior to return to sports after ACL reconstruction. Thomee R, Kaplan Y, Kvist J, Myklebust G, Risberg MA, Theisen D, Tsepis E, Werner S, Wondrasch B, Witvrouw E. Knee Surg Sports Traumatol Arthrosc. 2011;19(11):1798-805. Epub 2011 Sep 20.
- Cardiovascular evaluation of middle-aged/senior individuals engaged in leisure-time sport activities: position stand from the sections of exercise physiology and sports cardiology of the European Association of Cardiovascular Prevention and

Rehabilitation. Borjesson M, Urhausen A, Kouidi E, Dugmore D, Sharma S, Halle M, Heidbuchel H, Bjornstad HH, Gielen S, Mezzani A, Corrado D, Pelliccia A, Vanhees L. Eur J Cardiovasc Prev Rehabil. 2011;18(3):446-458.

KEY PARTNERS

- 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
- Université catholique de Louvain, Louvain-la-Neuve, Belgium

DEPARTMENT OF VIROLOGY, ALLERGOLOGY AND IMMUNITY



HEAD OF LABORATORYDr. François HENTGES, MD

Laboratory of Immunogenetics and Allergology

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

- A new dog allergen, Can f 6, has been isolated. 61% of the patients allergic to dogs react to Can f 6. The new allergen cross-reacts with Fel d 4, a cat allergen. These findings have to be taken into account when interpreting positive skin or in vitro IgE tests to dog or cat dander.
- Parvalbumins are major allergens of fish. They are highly conserved and fish allergic patients generally react to several fish species. Using different parvalbumins isolated by our laboratory, we could establish patient-specific sensitization profiles leading to personalized diagnostic implications.
- The humoral and cellular immune response of BALB/c mice to the main cat allergen Fel d 1 varies markedly when different adjuvants (AL[OH]3, LPS, CpG) are used in immunization mixtures. These findings will be used to modulate allergy-like induced immune reponses to Fel d 1 in mice.
- NK cell trogocytosis in TAP-deficient individuals was shown. NK cell phenotyping was performed with 13 color flow cytometry.
- The anti-inflammatory role of neurturin in an asthma model was confirmed. NK cells were investigated as a potential target in glioblastoma treatment.

RESEARCH DEPARTMENTS / DEPARTMENT OF VIROLOGY, ALLERGOLOGY AND IMMUNITY / Laboratory of Immunogenetics and Allergology

PUBLICATIONS

- Identification of a new major dog allergen highly cross-reactive with Fel d 4 in a population of cat- and dog-sensitized patients. Hilger C, Swiontek K, Arumugam K, Lehners C, Hentges F. J Allergy Clin Immunol. 2011. [Epub ahead of print].
- Chronic papular urticaria due to pigeon ticks in an adult. Manzotti G, Hilger C, Heffler E, Rolla G. Eur J Dermatol. 2011;21(6):992-3.
- Expression of the progenitor marker NG2/CSPG4 predicts poor survival and resistance to ionising radiation in glioblastoma. Svendsen A, Verhoeff JJ, Immervoll H, Brogger JC, Kmiecik J, Poli A, Netland IA, Prestegarden L, Planaguma J, Torsvik A, Kjersem AB, Sakariassen PO, Heggdal JI, Van Furth WR, Bjerkvig R, Lund-Johansen M, Enger PO, Felsberg J, Brons NH, Tronstad KJ, Waha A, Chekenya M. Acta Neuropathol. 2011;122(4):495-510. Epub 2011 Aug 24.
- Fish Allergy: A Comprehensive Review of Recent Developments in Fish Allergy Diagnosis and Fish Allergen Detection. Kuehn A., Hilger C., Hentges F. . In Food allergies: Symptoms, diagnosis, and treatment. Rodgers PM, ed. New York: Nova Science Publishers Inc, 2011. p.51-78.
- Evaluation of two new recombinant guinea-pig lipocalins, Cav p 2 and Cav p 3, in the diagnosis of guinea-pig allergy. Hilger C, Swiontek K, Kler S, Diederich C, Lehners C, Vogel L,

Vieths S, Hentges F. Clin Exp Allergy. 2011;41(6):899-908. Epub 2011 Apr 25.

- Increased Th2 cytokine secretion, eosinophilic airway inflammation, and airway hyperresponsiveness in neurturindeficient mice. Michel T, Theresine M, Poli A, Domingues O, Ammerlaan W, Brons NH, Hentges F, Zimmer J. J Immunol. 2011;186(11):6497-504. Epub 2011 Apr 20.
- Inhaled mammalian allergens: Lipocalins and serum albumins. Hilger C, Kleine-Tebbe J. Allergo Journal. 2011;20(3):142-144.
- Clinical monosensitivity to salmonid fish linked to specific lgE-epitopes on salmon and trout beta-parvalbumins. Kuehn A, Hutt-Kempf E, Hilger C, Hentges F. Allergy. 2011;66(2):299-301. Epub 2010 Aug 30.

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



DEPARTMENT OF VIROLOGY, ALLERGOLOGY AND IMMUNITY



HEAD OF LABORATORYDr. André STEINMETZ. PhD

Laboratory of Plant Molecular Biology

MISSION

Understand the molecular mechanisms of biological processes in human diseases, with a particular focus on the actin cytoskeleton and bioactive compounds from medicinal plants.

KEY RESULTS

■ We have previously established that the two LIM domain-containing proteins (LIMs) are important regulators of the actin cytoskeleton organization. Novel functional analyses demonstrate that one LIM, namely WLIM2, shuttles into the nucleus, binds to specific DNA sequences and activates histone gene expression. These sets of data indicate that LIMs are part of a cytoskeletal-nuclear crosstalk involved in the control of gene expression



RESEARCH DEPARTMENTS / DEPARTMENT OF VIROLOGY, ALLERGOLOGY AND IMMUNITY / Laboratory of Plant Molecular Biology

- In the frame of the HUMCRP CORE project (FNR), we provide evidence that the three LIMs of the human cysteine-rich protein (CRP) family display direct actin-stabilizing and -bundling activities. We found that these activities are not altered by six point mutations previously associated with cardiomyopathies. However, two point mutants exhibit significant modifications in their actin regulatory activities and are currently investigated in greater details to test their possible implication in heart disease.
- A manuscript describing an atypical subclass of actin-depolymerizing factors (ADFs) has been published in FEBS Letters. We provide evidence that both ADF5 and ADF9 do not enhance actin filament turnover as most of ADFs/cofilins do, but instead promote actin filament stabilization and bundling. We are currently investigating the underlying molecular mechanisms, which might help to understand the formation of actin rods in degenerative diseases such as Alzheimer's disease.
- We have purified and identified a plant component that induces apoptosis in leukemia cells and has cytostatic effects on non-leukemia cancer cell lines.
- The Retrovirology and Plant Molecular Biology laboratories have been awarded by FNR for their contribution to FNR's Researchers' Night 2010 ("Outstanding Promotion of Scientific Culture"). They organized a science café on "Science in Advertisements: Use and Misuse", as well as a workshop on "Experimental cosmetics Use of local medicinal herbs"

PUBLICATIONS

- Analysis of the transcriptome of *Panax notoginseng* root uncovers putative triterpene saponin-biosynthetic genes and genetic markers. Luo H, Sun C, Sun Y, Wu Q, Li Y, Song J, Niu Y, Cheng X, Xu H, Li C, Liu J, Steinmetz A, Chen S. BMC Genomics. 2011;12(Suppl 5):S5.
- Sesquiterpenoids and triterpenoids from *Abies holophylla* and their bioactivities. Xia JH, Zhang SD, Li YL, Wu L, Zhu ZJ, Yang XW, Zeng HW, Li HL, Wang N, Steinmetz A, Zhang WD. Phytochemistry. 2011. [Epub ahead of print].

- 454 EST analysis detects genes putatively involved in ginsenoside biosynthesis in *Panax ginseng*. Chen S, Luo H, Li Y, Sun Y, Wu Q, Niu Y, Song J, Lv A, Zhu Y, Sun C, Steinmetz A, Qian Z. Plant Cell Rep. 2011;30(9):1593-601. Epub 2011 Apr 12.

 Anti-cancer effects of 20(S)-protopanoxadiol on human
- Anti-cancer effects of 20(S)-protopanoxadiol on human acute lymphoblastic leukemia cell lines Reh and RS4;11. Sun L, Wang Q, Liu X, Brons NH, Wang N, Steinmetz A, Lv Y, Liao Y, Zheng H. Med Oncol. 2011;Epub 2010 Mar 31.
- Arabidopsis actin-depolymerizing factors (ADFs) 1 and 9 display antagonist activities. Tholl S, Moreau F, Hoffmann C, Arumugam K, Dieterle M, Moes D, Neumann K, Steinmetz A, Thomas C. FEBS Lett. 2011;585(12):1821-7. Epub 2011 May 11.
- Protective effect of dammarane sapogenins against chemotherapy-induced myelosuppression in mice. Yang Y, Xu S, Xu Q, Liu X, Gao Y, Steinmetz A, Wang N, Wang T, Qiu G. Exp Biol Med (Maywood). 2011;236(6):729-35.

KEY PARTNERS

- University of Bergen, Department of Biomedicine, Bergen, 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



HEAD OF LABORATORYDr. Jean-Claude SCHMIT, MD, PhD, MBA



ASSOCIATE HEAD OF LABORATORY
Dr. Carole DEVAUX, PhD

Laboratory of Retrovirology

MISSION

Chronic viral infections caused by HIV and HCV are an evergrowing 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

- Engineering of a set of chimeric CXCR4/CXCR7 chemokine receptors and their preliminary characterization for HIV-1 entry and chemokines binding
- Prediction of the tridimensional structures of the HIV-1 co-receptors CCR5 and CXCR4 and identification of new peptides inhibiting HIV-1 entry and neutralizing CXCL12 chemokine binding
- Validation of a recombinant viral assay for phenotypic HIV tropism evaluation highlighted subtype-related discordances with the Geno2Pheno-coreceptor genotypic prediction tool currently recommended by European Guidelines for HIV-infected patient management
- Validation and uncertainty assessment of three HIV-1 DNA real-time PCRs for early diagnosis in infants and total cell associated HIV-1 DNA quantification
- Developement and validation of an upgraded version of the COMET software for HCV genotyping and subtyping.

RESEARCH DEPARTMENTS / DEPARTMENT OF VIROLOGY, ALLERGOLOGY AND IMMUNITY / Laboratory of Retrovirology

PUBLICATIONS

- Association of haptoglobin phenotypes with the development of Kaposi's sarcoma in HIV patients. Speeckaert R, Colebunders B, Boelaert JR, Brochez L, Van Acker J, Van Wanzeele F, Hemmer R, Speeckaert MM, Verhofstede C, De Buyzere M, Arendt V, Plum J, Delanghe JR. Arch Dermatol Res. 2011;303(10):763-9. Epub 2011 Jul 12.
- Rescue of HIV-1 long-time archived X4 strains to escape maraviroc. Baatz F, Struck D, Lemaire M, De Landtsheer S, Servais JY, Arendt V, Schmit JC, Perez Bercoff D. Antiviral Res. 2011;92(3):488-92. Epub 2011 Oct 13.
- Identification of a new major dog allergen highly cross-reactive with Fel d 4 in a population of cat- and dog-sensitized patients. Hilger C, Swiontek K, Arumugam K, Lehners C, Hentges F. J Allergy Clin Immunol. 2011; [Epub ahead of print].
- Engineering and screening the N-terminus of chemokines for drug discovery. Chevigne A, Fievez V, Schmit JC, Deroo S. Biochem Pharmacol. 2011;82(10):1438-56. Epub 2011 Jul 30.
- High correlation between the Roche COBAS(R) AmpliPrep/COBAS(R) TaqMan(R) HIV-1, v2.0 and the Abbott m2000 RealTime HIV-1 assays for quantification of viral load in HIV-1 B and non-B subtypes. Karasi JC, Dziezuk F, Quennery L,

- Forster S, Reischl U, Colucci G, Schoener D, Seguin-Devaux C, Schmit JC. J Clin Virol. 2011;52(3):181-6. Epub 2011 Aug 3.
- Concordance between HIV-1 genotypic coreceptor tropism predictions based on plasma RNA and proviral DNA. Verhofstede C, Brudney D, Reynaerts J, Vaira D, Fransen K, De Bel A, Seguin-Devaux C, De Wit S, Vandekerckhove L, Geretti AM. HIV Med. 2011;12(9):544-52. Epub 2011 Apr 25.
- Selection of a CXCR4 antagonist from a human heavy chain CDR3-derived phage library. Chevigne A, Fischer A, Mathu J, Counson M, Beaupain N, Plesseria JM, Schmit JC, Deroo S. FEBS J. 2011;278(16):2867-78. Epub 2011 Jun 27.
- The HIV/AIDS epidemic in sub-Saharan Africa: thin-king ahead on programmatic tasks and related operational research. Zachariah R, Van Damme W, Arendt V, Schmit JC, Harries AD. J Int AIDS Soc. 2011;14 (Suppl 1):S7.
- Impact of the HIV-1 env genetic context outside HR1-HR2 on resistance to the fusion inhibitor enfuvirtide and viral infectivity in clinical isolates. Baatz F, Nijhuis M, Lemaire M, Riedijk M, Wensing AM, Servais JY, van Ham PM, Hoepelman AI, Koopmans PP, Sprenger HG, Devaux C, Schmit JC, Perez Bercoff D. PLoS One. 2011;6(7):e21535. Epub 2011 Jul 8.



- Arabidopsis actin-depolymerizing factors (ADFs) 1 and 9 display antagonist activities. Tholl S, Moreau F, Hoffmann C, Arumugam K, Dieterle M, Moes D, Neumann K, Steinmetz A, Thomas C. FEBS Lett. 2011;585(12):1821-7. Epub 2011 May 11.
- Chemokine receptor 5 polymorphism in myocardial infarction patients from Luxembourg. Rodius S, Lambert C, Devaux C, Schmit JC, Devaux Y, Wagner DR. Bull Soc Sci Med Grand Duche Luxemb. 2011;(1):31-40.
- Evaluation of saliva as an alternative matrix for monitoring plasma Zidovudine, Lamivudine and nevirapine concentrations in Rwanda. Gras A, Schneider S, Karasi JC, Ternes AM, Sauvageot N, Karasi-Omes C, Henry AP, Schmit JC, Seguin-Devaux C, Arendt V. Curr HIV Res. 2011;9(4):223-8.
- A hepatitis A, B, C and HIV prevalence and risk factor study in ever injecting and non-injecting drug users in Luxembourg associated with HAV and HBV immunisations. Removille N, Origer A, Couffignal S, Vaillant M, Schmit JC, Lair ML. BMC Public Health. 2011;11(1):351.
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- Prediction of response to antiretroviral therapy by human experts and by the EuResist data-driven expert system (the EVE study). Zazzi M, Kaiser R, Sonnerborg A, Struck D, Altmann A, Prosperi M, Rosen-Zvi M, Petroczi A, Peres Y, Schulter E, Boucher CA, Brun-Vezinet F, Harrigan PR, Morris L, Obermeier M, Perno CF, Phanuphak P, Pillay D, Shafer RW, Vandamme AM, van Laethem K, Wensing AM, Lengauer T, Incardona F. HIV Med. 2011;12(4):211-8. Epub 2010 Aug 19.

- European recommendations for the clinical use of HIV drug resistance testing: 2011 update. Vandamme AM, Camacho RJ, Ceccherini-Silberstein F, de Luca A, Palmisano L, Paraskevis D, Paredes R, Poljak M, Schmit JC, Soriano V, Walter H, Sonnerborg A. AIDS Rev. 2011;13(2):77-108.
- Global trends in molecular epidemiology of HIV-1 during 2000-2007. Hemelaar J, Gouws E, Ghys PD, Osmanov S, Karasi JC, on behalf of the WHO-UNAIDS Network for HIV Isolation and Characterisation. AIDS. 2011;25(5):679-8
- Predicting significant fibrosis in hepatitis C patients in Luxembourg using serological markers. Mossong J, Bill S, Hawotte K, Gilson G, Knolle U, Weber J, Roskams T, Arendt V. Bull Soc Sci Med Grand Duche Luxemb. 2011;(1):19-30.

- EuroSIDA, EuroHIV, Euresist, European Society for Antiviral Resistance (ESAR)
- PMEs: Complix, Ghent, Belgium, ABL, Luxembourg, Institut für Immunologie und Genetik, Kaiserslautern
- Service National des Maladies Infectieuses, Centre Hospitalier de Luxembourg
- AIDS Reference Laboratories of Belgium
- University Medical Center Utrecht, The Netherlands



CLINICAL AND EPIDEMIOLOGICAL INVESTIGATION CENTER (CIEC)



HEAD OF COMPETENCE CENTERDr. 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.



COMPETENCE CENTERS / CLINICAL AND EPIDEMIOLOGICAL INVESTIGATION CENTER (CIEC)

KEY RESULTS

- Initiation of 16 clinical trials: 8 pharma driven (drug&medical devices), 7 investigator initiated or academic (in coll. with IBBL, CRP-Santé research departments, University hospitals St. Luc) in various therapeutic areas (oncology,orthopedics,inf ectious diseases,pulmonology, diabetes,allergy,...)
- CIEC officially joined ECRIN (European clinical research infrastructures) and has as such contributed to the feasibility of 5 new projects financed by the FP7 framework program
- On April 1st 2011, CIEC launched www.luxclin.lu, the first webpage in Luxembourg dedicated to clinical research not only accessible to investigators and health care professionals but also to the public
- In October the 3rd Clinical Research Day took place with an increased number (140) of participants (36 posters are presented)
- To mark the International Day of Clinical Trials on May 20th 2011, the CIEC opened its doors to the public to give insight in its research projects, methods and daily practices.

PUBLICATIONS

■ Prevalence and treatment of anaemia in cancer patients in Luxembourg. Gantenbein M, Untereiner M, Chioti A, Rauh S, Berchem G, Jacob F, Plawny L, Dewilde S, Burie D, Frederick B. Poster Presentation at the 26th General Meeting of the Belgian Hematological Society, Liège, January 28-29, 2011

KEY PARTNERS

- Luxembourg Hospitals
- National Centre for Radiotherapy (Centre François Baclesse), CRP-Tudor, IBBL
- Spanish Lung Cancer Group, UCL-Cliniques Universitaires, St. Luc, ULB-Oncology Centre
- Pharma:Alexion,AstraZeneca,Amgen,Gilead,Celgene,GSK, J&J,MoxiMed,Novartis,Pfizer,Roche,Sanofi,Stryker
- ECRIN, EFGCP

COMPETENCE CENTERS LUXEMBOURG BIOMEDICAL RESEARCH RESOURCES (LBR2)



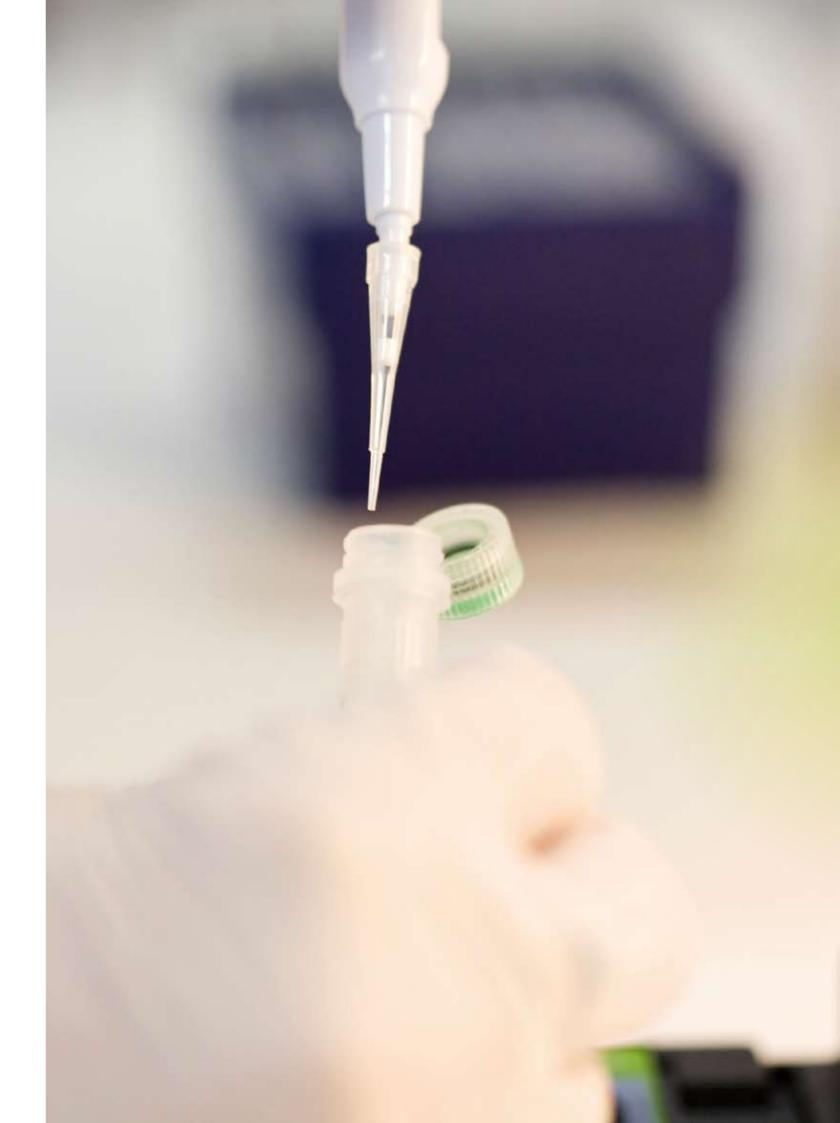
HEAD OF COMPETENCE CENTER Prof. Bruno DOMON, PhD

MISSION

The Luxembourg Biomedical Research Resources (LBR2) provides cutting-edge technical support to researchers at CRP-Santé as well as external users. The LBR2 is focused on translational research, with the specific aim of bridging biomedical research to clinical application, namely the development of assays towards personalized medicine. The center has built expertise in specific areas, including microarray, clinical proteomics, flow cytometry and confocal microscopy; in addition the center has a biomonitoring laboratory and an animal facility.

The specific missions of LBR2 center include:

- Maintain state-of-the-art technology platforms
- Contribute and support CRP-Santé research projects
- Provide services and expertise to external public and private partners, with an emphasis on high added-value projects.



COMPETENCE CENTERS LUXEMBOURG BIOMEDICAL RESEARCH RESOURCES (LBR2)



HEAD OF ANIMAL FACILITY Dr. Simone NICLOU, PhD

Animal Facility

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).





LUXEMBOURG BIOMEDICAL RESEARCH RESOURCES (LBR2)



HEAD OF CONFOCAL MICROSCOPY
Dr. Céline HOFFMANN, PhD

Confocal Microscopy

MISSION

The microscopy platform provides support to scientists for high quality cell imaging. The facility offers assistance at all levels, from specimen preparation through microscope operation and image analysis. Two main techniques are available, confocal microscopy for three dimensional analysis and TIRF (Total Internal Reflection Fluorescence) microscopy for observations in the cortex, near plasma membrane plane. 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

- We imaged the different behavior of two Actin Depolymerization Factors; ADF1 and ADF9, and showed their antagonist activities (Tholl *et al.*, 2011).
- A confocal picture presenting the actin cytoskeleton in BY2 cells decorated by ADF9-GFP has been selected for the cover of FEBS Letters (June issue, Tholl *et al.*).
- We implemented a new powerful technique based on evanescent wave illumination: Total Internal Reflection Fluorescence (TIRF) microscopy. This technique generates high contrast images with a strong reduction of out of focus background (especially in the cortical area for vesicles, receptors or actin observation).
- The platform was invited to the first meeting on Cell Imaging Techniques in the "Grande Région" (Nancy; October 3, 2011) to promote collaboration between institutions of the 3 borders area.

COMPETENCE CENTERS / LUXEMBOURG BIOMEDICAL RESEARCH RESOURCES (LBR2) / Confocal Microscopy

PUBLICATIONS

- Arabidopsis actin-depolymerizing factors (ADFs) 1 and 9 display antagonist activities. Tholl S, Moreau F, Hoffmann C, Arumugam K, Dieterle M, Moes D, Neumann K, Steinmetz A, Thomas C. FEBS Lett. 2011;585(12):1821-7.
- Blocking hypoxia-induced autophagy in tumors restores cytotoxic T-cell activity and promotes regression. Noman MZ, Janji B, Kaminska B, Van Moer K, Pierson S, Przanowski P, Buart S, Berchem G, Romero P, Mami-Chouaib F, Chouaib S. Cancer Res. 2011 Sep; 71 (18):5976-86.
- Transforming growth factor beta receptor 1 is a new candidate prognostic biomarker after acute myocardial infarction. Devaux Y, Bousquenaud M, Rodius S, Marie PY, Maskali F, Zhang L, Azuaje F, Wagner DR. BMC Med Genomics. 2011; Dec, 4:83.
- The acquisition of resistance to TNFalpha in breast cancer cells is associated with constitutive activation of autophagy as revealed by a transcriptome analysis using a custom microarray. Moussay E, Kaoma T, Baginska J, Muller A, Van Moer K, Nicot N, Nazarov PV, Vallar L, Chouaib S, Berchem G, Janji B. Autophagy. 2011 Jul. 7 (7):760-70.

KEY PARTNERS

- 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
- Plateforme d'Imagerie Cellulaire et Tissulaire, Dr Dominique Dumas, Faculté de médecine, Nancy, France

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LUXEMBOURG BIOMEDICAL RESEARCH RESOURCES (LBR2)



HEAD OF FLOW CYTOMETRYMr. René BRONS

KEY RESULTS

- Critical appraisal of the side population assay in stem cell and cancer stem cell research. Golebiewska A, Brons NH, Bjerkvig R, Niclou SP. Cell Stem Cell. 2011;8(2):136-47.
- Expression of the progenitor marker NG2/CSPG4 predicts poor survival and resistance to ionising radiation in glioblastoma. Svendsen A, Verhoeff JJ, Immervoll H, Brogger JC, Kmiecik J, Poli A, Netland IA, Prestegarden L, Planaguma J, Torsvik A, Kjersem AB, Sakariassen PO, Heggdal JI, Van Furth WR, Bjerkvig R, Lund-Johansen M, Enger PO, Felsberg J, Brons NH, Tronstad KJ, Waha A, Chekenya M. Acta Neuropathol. 2011;122(4):495-510. Epub 2011 Aug 24.
- Increased Th2 cytokine secretion, eosinophilic airway inflammation, and airway hyperresponsiveness in neurturindeficient mice. Michel T, Theresine M, Poli A, Domingues O, Ammerlaan W, Brons NH, Hentges F, Zimmer J. J Immunol. 2011;186(11):6497-504. Epub 2011 Apr 20.
- Anti-cancer effects of 20(S)-protopanoxadiol on human acute lymphoblastic leukemia cell lines Reh and RS4;11. Sun L, Wang Q, Liu X, Brons NH, Wang N, Steinmetz A, Lv Y, Liao Y, Zheng H. Med Oncol. 2011. Epub 2010 Mar 31.

Flow Cytometry

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 FACSA-ria cell sorter and a FACSCanto analyser. It is an open facility accessible for personnel from CRP-Santé as well as external researchers.

PUBLICATIONS

- Critical appraisal of the side population assay in stem cell and cancer stem cell research. Golebiewska A, Brons NH, Bjerkvig R, Niclou SP. Cell Stem Cell. 2011;8(2):136-47.
- Increased Th2 cytokine secretion, eosinophilic airway inflammation, and airway hyperresponsiveness in neurturindeficient mice. Michel T, Theresine M, Poli A, Domingues O, Ammerlaan W, Brons NH, Hentges F, Zimmer J. J Immunol. 2011;186(11):6497-504. Epub 2011 Apr 20.

- Dutch Flowgroup / Dutch Society for Cytometry
- Luxembourg Cytometry Association (LCA)
- Integrated Biobank of Luxembourg (IBBL)
- Complix
- University of Luxembourg
- BectonDickinson
- Translational Genomics Institute (TGen), Phoenix, USA



LUXEMBOURG BIOMEDICAL RESEARCH RESOURCES (LBR2)



LABORATORY COORDINATORDr. Brice APPENZELLER, PhD

Laboratory of Analytical Human Biomonitoring

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.



COMPETENCE CENTERS / LUXEMBOURG BIOMEDICAL RESEARCH RESOURCES (LBR2) / Laboratory of Analytical Human Biomonitoring

KEY RESULTS

- First determination of polycyclic aromatic hydrocarbon metabolites concentration in brain tissue
- Setting up of highly sensitive analytical methods based on hair analysis allowing the biomonitoring of multi-exposure to environmental levels of pollutants

PUBLICATIONS

- Simultaneous determination of nicotine and PAH metabolites in human hair specimen: A potential methodology to assess tobacco smoke contribution in PAH exposure. Appenzeller BM, Mathon C, Schummer C, Alkerwi A, Lair ML. Toxicol Lett. 2011. [Epub ahead of print]. Determination of farm workers' exposure to pesticides by hair analysis. Schummer C, Salquebre G, Briand O, Millet M, Appenzeller BM. Toxicol Lett. 2011. [Epub ahead of print].
- Simultaneous analysis of pesticides from different chemical classes by using a derivatisation step and gas chromatography-mass spectrometry. Raeppel C, Nief M, Fabritius M, Racault L, Appenzeller BM, Millet M. J Chromatogr A. 2011;1218(44):8123-9. Epub 2011 Sep 10.
- Hair analysis for biomonitoring of environmental and occupational exposure to organic pollutants: State of the art, critical review and future needs. Appenzeller BM, Tsatsakis AM. Toxicol Lett. 2011;[Epub ahead of print].
- Determination of PAHs and OH-PAHs in rat brain by gas chromatography tandem (triple quadrupole) mass spectrometry. Grova N, Salquebre G, Schroeder H, Appenzeller BM. Chem Res Toxicol. 2011;24(10):1653-67. Epub 2011 Oct 3.
- Hair analysis to document human exposure to agricultural and non-agricultural pesticides. Appenzeller BMR, Schummer C, Salquebre G, Millet M, Briand O. Toxicol Lett. 2011;205, (Supplement):S71.
- Impact of hair-care products on FAEE hair concentrations in substance abuse monitoring. Gareri J, Appenzeller B, Walasek P, Koren G. Anal Bioanal Chem. 2011;400(1):183-8. Epub 2011 Feb 8.

KEY PARTNERS

- Centre of Toxicology Sciences and Research, Division of Morphology, Medical School, University of Crete, Greece
- Hospital for Sick Children, Division of Clinical Pharmacology & Toxicology, Toronto, Canada
- University of Toronto, Canada
- Institut de Veille Sanitaire, Département Santé Environnement, Hôpital Saint-Maurice, Saint-Maurice, France.
- Université Henri Poincaré, Faculté des Sciences & Techniques, Vandoeuvre Les Nancy, France

Equipe de Physico-Chimie de l'Atmosphère, Strasbourg, France

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LUXEMBOURG BIOMEDICAL RESEARCH RESOURCES (LBR2)



HEAD OF LABORATORYProf. Bruno DOMON, PhD



ASSOCIATE HEAD OF LABORATORY
Dr. Yeoun Jin KIM. PhD

Luxembourg Clinical Proteomics Center

MISSION

The main objective of the Luxembourg Clinical Proteomics Center is creating an internationally competitive translational research unit that bridges the basic biomedicinal researches to clinical applications:

- Evaluating protein biomarkers for diagnosis, prognosis of diseases and monitoring drug responses.
- Building robust proteomic platforms based on state-ofthe-art mass spectrometry technology.
- Developing workflows of targeted proteomics leveraging novel instrumentation.

KEY RESULTS

- The evaluation of the new mass spectrometry techniques for targeted proteomics was continued. LCP has had early access to a novel quadrupole-orbitrap instrument in the framework of collaboration with ThermoFisher Scientific. The quantification capabilities of this new technology was evalutated in the context of targeted proteomics.
- The second phase of the lung cancer project in the Partnership of Personalized Medicin (PPM) program was structured focusing on immediate clinical needs. With the increased efforts in Luxembourg, the experiments on human lung tissue started to guide subsequent analysis of proteome in human plasma.
- The development of quantification workflow was expanded by the second generation-quantification standards enabling accurate quantification of peptides in biological samples. The workflow was applied to clinical samples including human urine and plasma.
- The first peer-reviewed (fully produced in the laboratory) were published. Two PhD programs were approved for AFR grant, and a total of three PhD programs were initiated. Research proposals submited to the CORE and post-doc AFR were successfully approved. We have actively parti-

COMPETENCE CENTERS / LUXEMBOURG BIOMEDICAL RESEARCH RESOURCES (LBR2) / Luxembourg Clinical Proteomics Center

cipated in education programs: teaching a full proteomics module at the University of Luxembourg in the systems biology master program, participation in the EUROKUP COST action, and the organization of a workshop on targeted proteomics in Luxembourg.

PUBLICATIONS

- 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, B. Domon. Mol. Cell. Proteomics, 10: M110.002931 (2011).
- Toward a standardized urine proteome analysis methodology. M. Court, N. Selevsek, M. Matondo, Y. Allory, J. Garin, C.D. Masselon, B. Domon. Proteomics, 11: 1160-71 (2011).
- Selected reaction monitoring applied to proteomics. S. Gallien, E. Duriez, B. Domon. J. Mass Spectrom., 46: 298-312 (2011).
- Systematic quantification of peptides/proteins in urine using selected reaction monitoring. N. Selevsek, M. Matondo, M. Sanchez Carbayo, R. Aebersold, B. Domon. Proteomics, 11: 1135-47 (2011).
- Recommendations for Mass Spectrometry Data Quality Metrics for Open Access Data (Corollary to the Amsterdam Principles). C.R. Kinsinger, H.J. Rodriguez, et al. J. Proteome Res., 11: 1412-9 (2012); Mol. Cell. Proteomics, 10: O111.015446 (2011); Proteomics, 12: 11-20 (2012).
- The human proteome project: current state and future direction. P. Legrain, et al. Mol. Cell. Proteomics, 10: M111.009993 (2011).

- Lung Cancer Statistics in Luxembourg from 1981 to 2008. P.G. Thill, P. Goswami, G. Berchem, B. Domon. Bull. Soc. Sci. Med. Grand Duche Luxemb., 43-55 (2011).
- Mass Spectrometry Based Detection and Quantification of Plasma Glycoproteins Using Selective Reaction Monitoring. Y.J. Kim, Z. Zaidi, S. Gallien, B. Domon.

Nature Protocols (2012), in press.

Highly multiplexed targeted proteomics using precise control of peptide retention time. S. Gallien, S. Peterman, R. Kiyonami, J. Souady, E. Duriez, A. Schoen, B. Domon. Proteomics (2012), in press.

- University of Luxembourg
- ThermoFisher Scientific, USA
- Commissariat à l'Énergie Atomique (CEA), France
- Institut Curie (IC), France
- Fred Hutchinson Cancer Research Center (FHCRC), USA
- Translational Genomics Institute (TGen), USA
- Univeristy of Ghent, Belgium
- Integrated BioBank of Luxembourg (IBBL)



LUXEMBOURG BIOMEDICAL RESEARCH RESOURCES (LBR2)



HEAD OF LABORATORYDr. Laurent VALLAR, PhD

Microarray Center

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, Next-Generation sequencing, biostatistics and bioinformatics.



COMPETENCE CENTERS / LUXEMBOURG BIOMEDICAL RESEARCH RESOURCES (LBR2) / Microarray Center

KEY RESULTS

- Microarray Center participated in 28 research projects funded either by the Fonds National de la Recherche (5), CRP-Santé (10), University of Luxembourg (5) or foreign institutions (8). The laboratory also coordinated a FNR CORE project focused on the study of alternative splicing in lung cancer.
- Christelle Ghoneim, post-doctoral researcher at MC, was rewarded the best and most outstanding poster at the Oncotrans conference held in September 2011 in Nancy, France. Dr Ghoneim introduced new genomic signatures specific for two types of non small cell lung cancer.
- Komal Baig, a graduate student from University of Luxembourg, successfully completed her Master degree in Systems Biology after having conducted part of her research project in the laboratory. Gina Youcef started her PhD under the cosupervision of MC and the INSERM/UMRS 961 from Nancy. Her project is funded by an AFR grant from FNR.
- With the implementation of a Roche 454 GS Junior sequencing platform, MC has significantly expanded its offer of services which now covers the various application areas permitted by Next-Generation Sequencing technology.
- The laboratory also implemented a high-throughput real time PCR platform. The system is particularly useful for fast validation in large series of samples of expression data obtained from whole genome analyses.

PUBLICATIONS

■ The acquisition of resistance to TNFalpha in breast cancer cells is associated with constitutive activation of autophagy as revealed by a transcriptome analysis using a custom microarray. Moussay E, Kaoma T, Baginska J, Muller A, Van Moer K, Nicot N, Nazarov PV, Vallar L, Chouaib S, Berchem G, Janji B. Autophagy. 2011;7(7):760-70. Epub 2011 Jul 1.

- MicroRNA as biomarkers and regulators in B-cell chronic lymphocytic leukemia. Moussay E, Wang K, Cho JH, van Moer K, Pierson S, Paggetti J, Nazarov PV, Palissot V, Hood LE, Berchem G, Galas DJ. Proc Natl Acad Sci U S A. 2011;108(16):6573-8. Epub 2011 Apr 1.
- Prognostic transcriptional association networks: a new supervised approach based on regression trees. Nepomuceno-Chamorro I, Azuaje F, Devaux Y, Nazarov PV, Muller A, Aguilar-Ruiz JS, Wagner DR. Bioinformatics. 2011;27(2):252-8. Epub 2010 Nov 21.

KEY PARTNERS

- 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

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METHODOLOGY AND STATISTICS (CCMS)



HEAD OF COMPETENCE CENTERProf. Stephen SENN, PhD

MISSION

The Competence Center for Methodology and Statistics was established in March 2010 in order to meet the methodological and statistical needs of all CRP-Santé laboratories. It also aims to develop contractual public health data management, and 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 statistical methods which guarantee the highest quality of the results.

KEY RESULTS

- Support for and collaboration with researchers in the CES: (On many occasions this has led to joint publications, some of which are mentioned in the section reporting activities of the CES)
- Collaborative work with WHO/TDR (special programme for training and research) in investigating treatments for Neglected Tropical Diseases (NRDs): leishmaniasis, shistosomiasis, Tuberculosis, HAT, Malaria



COMPETENCE CENTERS / METHODOLOGY AND STATISTICS (CCMS)

- Support for the Eurolight project (EPHEA sponsored)
- Doctoral thesis submitted by Laurence Renard (successfully defended in 2012)
- Support for work at CRP-Sante on HIV resistance
- Advice and training for various external bodies including statistics courses given for the Royal Statistical Society (London), Roche Pharmaceuticals (Basle) and trainee nurses in Metz and Thionville

PUBLICATIONS

- The cost of headache disorders in Europe: the Eurolight project. Linde M, Gustavsson A, Stovner LJ, Steiner TJ, Barre J, Katsarava Z, Lainez JM, Lampl C, Lanteri-Minet M, Rastenyte D, Ruiz de la Torre E, Tassorelli C, Andree C. Eur J Neurol. 2011. [Epub ahead of print].
- Psychosocial risk and protective factors of secondary school dropout in Luxembourg: the protocol of an exploratory case-control study. Esch P, Bocquet V, Pull C, Couffignal S, Graas M, Lair ML, Lehnert T, Fond-Harmant L, Ansseau M. BMC Public Health. 2011;11(1):555.
- A Multicentre Randomized Controlled Trial of the Efficacy and Safety of Single-Dose Praziquantel at 40 mg/kg vs. 60 mg/kg for Treating Intestinal Schistosomiasis in the Philippines, Mauritania, Tanzania and Brazil. Olliaro PL, Vaillant MT, Belizario VJ, Lwambo NJ, Ouldabdallahi M, Pieri OS, Amarillo ML, Kaatano GM, Diaw M, Domingues AC, Favre TC, Lapujade O, Alves F, Chitsulo L. PLoS Negl Trop Dis. 2011;5(6):e1165. Epub 2011 Jun 14.
- An algorithm to identify patients with treated type 2 diabetes using medico-administrative data. Renard LM, Bocquet V, Vidal-Trecan G, Lair ML, Couffignal S, Blum-Boisgard C. BMC Med Inform Decis Mak. 2011;11:23.
- Effect of artesunate and mefloquine in combination on the Fridericia corrected QT intervals in Plasmodium falciparum infected adults from Thailand. Krudsood S, Looareesuwan S, Wilairatama P, Leowattana W, Tangpukdee N, Chalermrut K, Ramanathan S, Navaratnam V, Olliaro P, Vaillant M, Kiechel JR, Taylor WR. Trop Med Int Health. 2011 Apr;16(4):458-6.

- Comparison of short-course multidrug treatment with standard therapy for visceral leishmaniasis in India: an open-label, non-inferiority, randomised controlled trial. Sundar S, Sinha PK, Rai M, Verma DK, Nawin K, Alam S, Chakravarty J, Vaillant M, Verma N, Pandey K, Kumari P, Lal CS, Arora R, Sharma B, Ellis S, Strub-Wourgaft N, Balasegaram M, Olliaro P, Das P, Modabber F. Lancet. 2011;377(9764):477-86. Epub 2011 Jan 20.
- Reduced sympathetically driven heart rate variability during sleep in Parkinson's disease: a case-control polysomnography-based study. Sauvageot N, Vaillant M, Diederich NJ. Mov Disord. 2011;26(2):234-40. Epub 2011 Jan 31.
- Discriminant analyses of peanut allergy severity scores. Collignon, JM Monnez, P Vallois et al. *Journal of Applied Statistics*, 2011, 38, 9, 1783–1799;
- Modelling in drug development. Senn S. In Simplicity, Complexity and Modelling. Christie M, Cliffe A, Dawid P and Senn S, eds. Chichester: John Wiley, 2011. p.35-49. (Statistics in Practice).
- You May Believe You Are a Bayesian But You Are Probably Wrong. Senn S. Rationality, Markets and Morals. 2011;2(42):48–66.
- Creating a suite of macros for meta-analysis in SAS®: A case study in collaboration. Senn S, Weir J, Hua TA, Berlin C, Branson M, Glimm E. Statistics & Probability Letters. 2011;81(7):842-851.
- U is for Unease: Reasons for Mistrusting Overlap Measures for Reporting Clinical Trials. Senn S. Stat Biopharm Res. 2011;3(2):302-309.

KEY PARTNERS

- World Health Organization
- Royal Statistical Society, UK
- Department of Statistical Science, University College London, United Kingdom
- Department of Pharmacology and Clinical Pharmacology, University of Auckland, New Zealand
- School of Mathematics and Statistics, University of Cambridge, United Kingdom

TECHNICAL AND ADMINISTRATIVE DEPARTMENT



HEAD OF DEPARTMENTThomas LENTZ. MBA

Communication

The communication unit is headed by Aurélia DERISCHEBOURG

MISSION

Development of the internal and external communication and marketing strategy.

Promotion of the institution's image to the scientific community and to the public.

The unit is also in charge of event management (e.g. conferences, workshops).

KEY RESULTS

- E-marketing strategy linked to the website
- Promotion of the Scientific Culture in partnership with other national institutions and associations (FNR, Télévie, Fondation Cancer, etc.)
- Organization of congresses, workshops, seminars. Call for funding (accompanying measures of FNR) and sponsorship
- Publication of comics, newsletters, flyers, documents of presentation



TECHNICAL AND ADMINISTRATIVE DEPARTMENT

Technical Environment Safety Service

The TESS unit is headed by Jean-Luc KONRAD

MISSION

■ Taking care of all technical issues on buildings used by CRP-Santé including the maintenance and the supervision of technical installations, waste handling and energy optimization.

Striving for excellence in environmental, health and safety performance involving all employees and facilities.

KEY RESULTS

- Acquisition of 'green' electricity for the entire CRP-Santé
- Setup of the final design and planning of the new building of CRP-Santé
- Rearrangement of offices to improve the use of surfaces and an ergonomic environment
- Carry out of a preventive maintenance program to improve performance and extend the life of building equipment, furniture and interior finishes
- Integration of the maintenance program for IBBL and providing support to IBBL for setting up new equipment
- Improvement of individual health surveillance and risk assessment by inventory of risk at work

Finances

The finances unit is headed by Jérémy KLEIN.

MISSIO

Day-to-day management of all financial aspects for the research projects in compliance with legal and contractual requirements.

Preparation of the annual budget together with the head of units.

Active assistance in the preparation of the individual budgets for each project in collaboration with the principal investigators.

Establishment of financial statements for partners, management and the board of administration.

KEY RESULTS

- Integration of the controlling in the financial department
- Redesign of the management dashboard
- Providing accounting services for Complix Luxembourg and IBBL
- Cash flow management optimization
- Cost improvements by centralizing insurance
- Filing and acceptance of a FEDER grant for the extension of the animal facility

Human Resources

The human resource unit is headed by Natacha BEICHT.

MISSION

Providing service and support to all employees regarding HR matters and assist management in the development of HR strategy in compliance with the performance contract.

Performing as the social secretariat for CRP-Santé and Complix Luxembourg.

Taking care of recruitment, development and training of CRP-Santé staff.

KEY RESULTS

- Continuous progress in the implementation of the HR strategy related to the European Charter for Researcher
- Implementation of a new time management system
- Improve the offer of training courses to the employees

Information Technologies

The IT unit was lead by Romain GENSON as interim manager followed by Thibaut LENFANT.

MISSION

Guarantying the quality of IT services though a high availability of the IT infrastructure and providing professional advice.

Being on top of the technical evolution and introducing new technologies.

Providing technical support to ensure the successful realization of IT related projects.

KEY RESULTS

- Server consolidation and virtualization based on Blade Server technology running VMware
- Data consolidation on a new high performance storage
- Development and implementation of the new intranet
- Integration of department of Immunology IT infrastructure in the IT network of CRP-Santé

Project Management

The project management unit is headed by Jo SCHROEDER.

MISSION

Transversal management of all research projects and providing support in the application process for competitive projects on national and European levels. Furthermore, watch for new competitive funding opportunities on national and European levels. Additionally, drafting and follow up of contractual agreements related to the various projects and the collaboration with scientific partners. Finally, implementation and maintenance of the protection regulations insurance coverage for research projects and assisting the Technology Transfer Office in the legal protection of intellectual property.

KEY RESULTS

- In 2011, the overall number of projects realized at CRP-Santé grew by 35% and reached 202 projects by the end of the year.
- 10 applications for EU funding programs have been submitted. 4 applications were accepted, 2 are still pending.
- Start setting-up an internal project management training course adapted to CRP-Santé needs for young researchers and AFR beneficiaries
- Consolidation of the legal management of the contractual assets
- Design a streamlined process for the filing of ethic committee applications by researchers

Purchasing

The purchasing unit is headed by Marc WEISEN.

MISSION

Improving the centralized purchasing function to get best quality products and synergies at the lowest cost.

Identifying new supply sources to enhance negotiation levels.

KEY RESULTS

- Negotiation and acquisition of equipment for the new animal facility
- Creating additional value by improved centralization of purchasing
- Increased purchasing support to the laboratories

Quality Management

The quality management unit is headed by Blandine VALET.

MISSION

Supervision and monitoring the development and implementation of the Quality Management System by creating and sustaining a climate of acceptance for continuous improvement.

Targeting to get the main laboratories ISO 9001 certified by end of the current performance contract.

KEY RESULTS

- Creation of process mapping and quality policy / definition of measurable and relevant objectives and indicators.
- Implementation of corrective and preventive actions following the internal audit.
- Preparation of the specifications of a tool such as an Enterprise Resource Planning (ERP) to help with the processes.
- Integration of two additional units into the scope of reporting for ISO 9001 certification.

Technology Transfer

The technology transfer unit is headed by Dr. Françoise LINERS.

MISSION

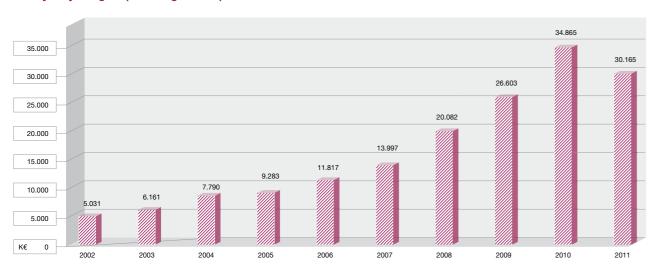
Translation of the biomedical research made in Luxembourg into economic value by securing and pro-actively protecting of intellectual property with commercial potential. Marketing of technology through negotiation of agreements with private companies and institutions as well as facilitating the creation of spin-off companies.

KEY RESULTS

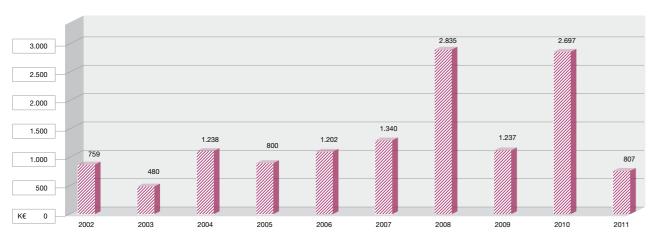
- Finalization of a licensing agreement with Firalis, a French innovative biotech company
- Deposit of one new patent application
- Launching the process of a public/private partnership in the field of sports medicine

KEY FIGURES

Total yearly budgets (including CAPEX)

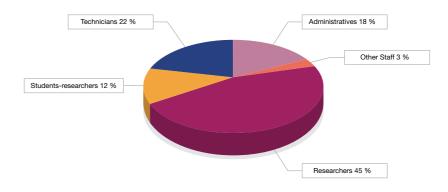


Investments at CRP-Santé

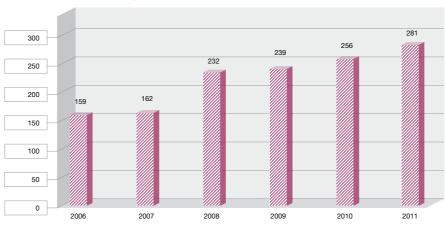


KEY FIGURES

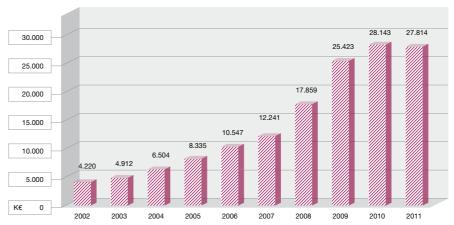
Categories of professional staff of CRP-Santé



Staff evolution over the years



R & D charges at CRP-Santé



^{*} Those amounts include Staff costs, Operating costs and Travel costs

Employees from 30 nationalities work at CRP-Santé

	ecember 201
Ν	lationalities

December 2011 Nationalities	
Albanian	0,36 9
American	0,36 9
Belarussian	0,36 9
Belgian	19,57
Belgian-Luxembourgish	0,36 9
British	0,36
Bulgarian	0,36 9
Canadian	0,36
Chinese	1,41 9
Congolese	0,71 9
Corean	0,71 9
Dutch	0,36
French	34,16
German	7,83 9
Greek	0,36
Greek-Danish	0,369
Indian	1,07 9
Italian	1,41 9
Kenyan	0,36 9
Lebanese	0,71
Luxembourgish	22,06 9
Malaisian	0,36
Norwegian	0,36 9
Polish	1,07 9
Portuguese	1,07 9
Romanian	0,71
Russian	0,36 9
Serbian	0,36 9
Swiss	1,42 9
Tunisian	0,36
Venezuelan	0,36

Grand Total

100,00 %

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

AUDITOR'S REPORT

Bilan au 31 décembre 2011

(en Euros)		
ACTIF	31.12.2011	31.12.2010
A. CAPITAL SOUSCRIT NON VERSE		
B. FRAIS D'ETABLISSEMENT		
C. ACTIF IMMOBILISE		
I. Immobilisations incorporelles	212.178	268.599
2. Concessions, brevets, licences, marques, ainsi que droits et valeurs similaires	0.0.470	
a) acquis à titre onéreux b) créés par l'entreprise	212.178	268.599
II. Immobilisations corporelles	3.585.584	4.476.730
Installations techniques et machines		
3. Autres installations, outillage et mobilier	3.585.584	4.476.730
Acomptes versés et immobilisations corporelles en cours		
III. Immobilisations financières	1.262.395	1.262.395
3. Participations	1.262.395	1.262.395
TOTAL DE L'ACTIF IMMOBILISE	5.060.156	6.007.724
D. ACTIF CIRCULANT I. Stocks		
II. Créances		
1. Créances résultant de ventes et prestations de services	174.666	329.508
a) dont la durée résiduelle est inférieure ou égale à un an	174.666	329.508
b) dont la durée résiduelle est supérieure à un an		
2. Créances sur partenaires	2.198.687	1.530.350
3. Créances sur des entreprises avec lesquelles la société a un lien de participation	182.577	189.269
4. Autres créances	882.557	782.616
a) dont la durée résiduelle est inférieure ou égale à un an	882.557	782.616
b) dont la durée résiduelle est supérieure à un an		
III. Valeurs mobilières		
IV. Avoirs en banque, avoirs en compte de chèques postaux, chèques et en caisse	12.972.966	12.000.731
TOTAL DE L'ACTIF CIRCULANT	16.411.453	14.832.475
E COMPTES DE RECUI ADISATION		
E. COMPTES DE REGULARISATION	299.404	200.509

AUDITOR'S REPORT

Bilan au 31 décembre 2011

en Euros)		
PASSIF	31.12.2011	31.12.2010
A. CAPITAUX PROPRES		
I. Capital souscrit	99.157	99.157
IV. Réserves	1.486.881	2.126.88
V. Résultats reportés	882.225	653.19 ⁻
VI. Résultat de l'exercice	40.886	229.03
VII. Subventions d'investissement	5.048.682	5.996.25
TOTAL DES CAPITAUX PROPRES	7.557.832	9.104.513
B. PROVISIONS POUR RISQUES ET CHARGES		
3. Autres provisions	639.647	340.302
TOTAL DES PROVISIONS	639.647	340.302
C. DETTES		
1. Emprunts obligataires		
2. Dettes envers des établissements de crédit		
3. Acomptes reçus sur commandes		
4. Dettes sur achats et prestations de services	1.246.416	1.614.55
a) dont la durée résiduelle est inférieure ou égale à un an b) dont la durée résiduelle est supérieure à un an	1.246.416	1.614.552
5. Dettes représentées par des effets de commerce		
6. Dettes envers des entreprises liées		
7. Dettes envers des entreprises avec lesquelles la société à un lien de participation		
8. Dettes fiscales et dettes au titre de la sécurité sociale	1.042.616	980.962
a) Dettes fiscales	488.912	444.620
b) Dettes au titre de la sécurité sociale	553.703	536.33
9. Autres dettes	167.664	94.73
a) dont la durée résiduelle est inférieure ou égale à un an b) dont la durée résiduelle est supérieure à un an	151.044 16.620	78.11 16.62
TOTAL DES DETTES	2.456.695	2.690.24
D. COMPTES DE REGULARISATION	11.116.840	8.905.64
		2.222.0
TOTAL DU PASSIF	21.771.013	21.040.707

Compte de profits et pertes pour l'exercice allant du 1^{er} janvier 2011 au 31 décembre 2011

(en Euros)

	2011 (01.01.11-31.12.11)	2010 (01.01.10-31.12.10)
A. CHARGES		
1. Réduction du stock de produits finis et en cours de fabrication		
2. a) Consommation de marchandises et de matières premières et consommablesb) Autres charges externes	3.100.039 5.002.304	2.894.950 4.226.607
Frais de personnel a) Salaires et traitements b) Charges sociales couvrant les salaires et traitements	16.626.528 2.174.873	14.818.060 1.942.186
4. a) Corrections de valeur sur frais d'établissement et sur immobilisations corporelles et incorporelles b) Corrections de valeur sur éléments de l'actif circulant	1.754.634	4.822.165
5. Autres charges d'exploitation	1.499.952	928.231
 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	4.554	6.645
10. Charges exceptionnelles	2.480	5.226.406
13. Résultat de l'exercice (bénéfice de l'exercice)	40.886	229.034
TOTAL DES CHARGES	30.206.251	35.094.284
B. PRODUITS		
1. Montant net du chiffre d'affaires	800.596	735.350
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	29.173.239	38.764.603
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	140.829	66.047
9. Produits exceptionnels	91.588	-4.471.715
10. Résultat de l'exercice (perte de l'exercice)		
TOTAL DES PRODUITS	30.206.251	35.094.284



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ACTIVITY 2011

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Photos: D.R. CRP-Santé

Layout: agacom Imprimerie: Scanlor

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