

Biomedical Research



Vrije
Universiteit
Brussel



Universitair Ziekenhuis Brussel



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Biomedical research at the University Medical Center Brussels

Today more than ever, our society is facing many challenges in the field of health. Health research at the University Medical Center Brussels merges scientific expertise of various research teams into 10 specialized clusters. Each cluster consists of several research groups performing basic, pharmaceutical, translational, clinical or medical-sociological research. A main objective is the development of more personalized medicine, with medical decisions, practices, and treatment being tailored to the individual patient.

Nine clusters focus on the following major health challenges:

- **Medical imaging**
- **Cardiovascular disorders**
- **Central nervous system disorders**
- **Development and ageing**
- **Diabetes**
- **Liver disorders**
- **Oncology**
- **Reproduction, genetics and regenerative medicine**
- **Public health**

In addition, one cluster combines all pharmaceutical research associated in the **Pharmaceutical Institute**. Fundamental, translational and clinical research is performed at the **University Medical Center Brussels**, which includes the **Faculty of Medicine and Pharmacy of the Vrije Universiteit Brussel** and the university hospital **UZ Brussel** located nearby. With its 700 beds, nearly 30,000 inpatients and 500,000 outpatients are treated yearly. Moreover, close to 350 clinical studies are performed every year, including both academic and industry sponsored phase I-IV trials. Clinical trials are supported centrally by a **Clinical Trial Center**, which provides assistance in the design, quality control and evaluation of all forms of clinical trials. Furthermore, there is a phase I unit, study nurses service, and a unit of clinical methodology and statistics.

Multidisciplinary health research is also performed in close collaboration with several research teams of the **engineering, sciences and humanities faculties of the Vrije Universiteit Brussel**.

With this brochure, we invite you to discover the world of biomedical research performed at the University Medical Center Brussels. You will find an extensive overview of the research conducted in a whole array of biomedical topics. For any further questions concerning innovation and valorization, we invite you to contact the Technology Transfer Interface of the Vrije Universiteit Brussel or the University Medical Center Research Manager.



Prof. dr. Jacques De Keyser
Vice-Dean Research



Dr. Aude Bonehill
University Medical Center
Research Manager



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Vrije Universiteit Brussel - UZ Brussel

Oncology Research Center

orc.vub.ac.be

The Oncology Research Center (ORC) is a multidisciplinary group in which basic, translational and clinical investigators from the Vrije Universiteit Brussel (VUB) and UZ Brussel collaborate. The ORC provides the opportunity to combine different expertises, conduct studies and share information in the field of oncology. These opportunities optimize and facilitate basic, preclinical, translational, psychosocial, clinical and public health research being performed by scientists at the ORC.

**Personalized Cancer Treatment, Hematology, Multiple Myeloma,
Improve End-of-life Care, Research Palliative Care, Immunotherapy, Radiotherapy**

End-of-Life Care (ZRL)

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Hematology and Immunology (HEIM)

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Laboratory of Medical and Molecular Oncology (LMMO)

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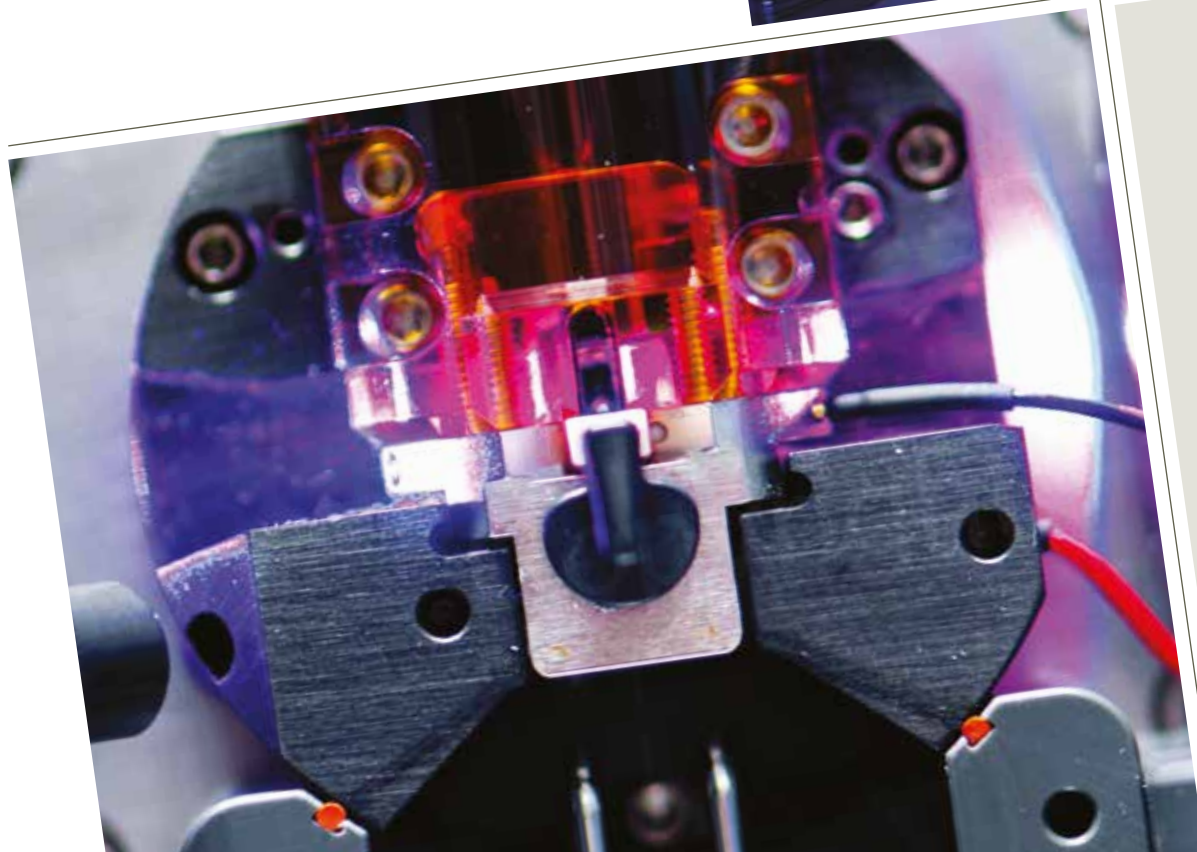
Laboratory of Molecular and Cellular Therapy (LMCT)

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Translational Radiation Oncology, supportive care and Physics (TROP)

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Main study areas

Multiple myeloma

- Cellular and molecular biology of multiple myeloma
- *In vitro* molecular and cellular multiple myeloma studies
- The development of a worldwide validated mouse model for the study of myeloma pathogenesis and preclinical drug development
- Role of immunomodulatory drugs in enhancing the efficacy of an anti-myeloma vaccination strategy
- Phase II-IV clinical trials in myeloma patients

Melanoma

- Messenger RNA based immunotherapy of melanoma
- Inhibitory mechanisms exerted by melanoma cells and their environment
- Relationship between persistent STAT3 activation and myeloid derived suppressor cell-mediated immune suppression in melanoma
- Phase II-III clinical trials involving dendritic cell therapy in melanoma

Cancer Immunology

- Multitargeted therapy: development of novel therapeutic combinations for augmenting the potency of cancer vaccines
- Enhancing tumor immunity by intranodal injection of mRNA encoding tumor antigens and activation stimuli
- Translational research involving dendritic cell therapy and clinical trials for early as well as advanced disease
- Manipulation of the immune system using targeted lentiviral vectors

Cancer genetics and targeted treatment

- Preclinical assessment of anticancer agents with a focus on the HER pathway in BA/F3 cells
- Preclinical siRNA development to specifically inhibit mutant receptors that are resistant to tyrosine kinase inhibitors and investigation of its *in vivo* application
- Genetic cancer with an emphasis on breast/ovarian cancer in relationship to the Familial Cancer Clinic of the Oncology Center

- Genomic biomarker research. Investigator initiated translational studies in following tumor types: lung cancer, brain tumors, melanoma, sarcoma and esophageal cancer.

Palliative care research

- Flanders study to Improve End-of-life Care and Evaluation tools (FLIECE): study promotes better palliative care and end-of-life care by developing tools to guide clinicians and health care institutions
- European Intersectorial and Multidisciplinary Palliative Care Research Training (EUROIMPACT): study develops an educational and research training framework in end-of-life care research in Europe
- International study of Place of Death (iPOD): examines cross-national patterns in place of death using death certificate data
- European Sentinel Network of General Practitioners Study to Monitor End-of-Life Care (EURO SENTIMELC)
- Dying well with dementia aims to promote better palliative care and end-of-life care for patients with dementia in long-term-care settings and to compare the results with other countries
- End-of-life decisions: implications for public health policy
- The practice of terminal sedation: a multiple perspectives study
- Legalization of euthanasia: the 'slippery slope' hypothesis tested in Flanders, Belgium
- Public views on end-of-life care

Other research topics

- Molecular and phenotypic characterization of leukemic cells
- NK cell activity in leukemia, characterization of hematopoietic and mesenchymal stem cells
- Pathogenesis of thrombophilia
- Sponsored and academic studies to assess the tolerability and efficacy of novel systemic treatments of cancer (phase I, II, III); sponsored and academic studies
- Radiobiology of colorectal cancer

Equipment & infrastructure

Cell banks

- Hematopoietic stem cell bank
- Tumor biobank
- Dendritic cell bank

Cell analysis

- FACS ArianIII (High multicolor performance and sorting applications)
- FACS LSR Fortessa (High multicolor performance)
- FACS Canto (High multicolor performance)

Genetic analysis

- Sequencing GS Junior System
- Micro-arrays
- Next Generation Sequencing Platform

Biosafety (C2-C4)

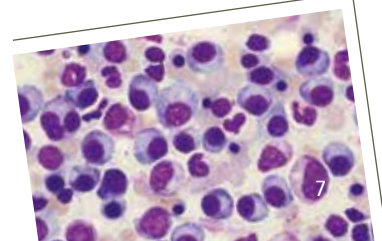
- Retroviruslab
- HIV lab

New radiation techniques

- Vero stereotactic body radiotherapy (SBRT) system. (joint product of Brainlab and MHI)
- Tomotherapy Hi Art system
- Elekta Sli 15 accelerator
- Nucletron HDR Ir 192
- Therapies:
 - Image-guided Radiotherapy
 - Frameless radiosurgery

Industrial collaboration fields

- Preclinical models for cancer (5TMM murine model for multiple myeloma; BA/F3 cell model; Cancer cell lines; Transfected cell lines for the study of the functionality of cancer genes, ...)
- Phase I-III studies in the field of cancer
- Industrial collaborations: Galapagos, Celgene, ISIS Pharmaceuticals, Roche, Pfizer, Centocor, Mundipharma, Merck, Boehringer-Ingelheim, Novo Nordisk, BrainLAB, VERO gmbh, VISHAY, Novartis, Astra Zeneca, Orfit industries.



Vrije Universiteit Brussel - UZ Brussel

C4N, Center for Neurosciences

www.c4n.be

The Center for Neurosciences coordinates neuroscience-related research activities, and especially aims a lasting collaborative research program among basic and clinical neuroscientists, allowing research from bench to bed.

Neuroprotection, Neuromodulation, Astrocyte-neuron interactions, Stroke, Epilepsy, Multiple Sclerosis, Mental functions & fatigue

Experimental Pharmacology (EFAR)

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Neurology (NEUR)

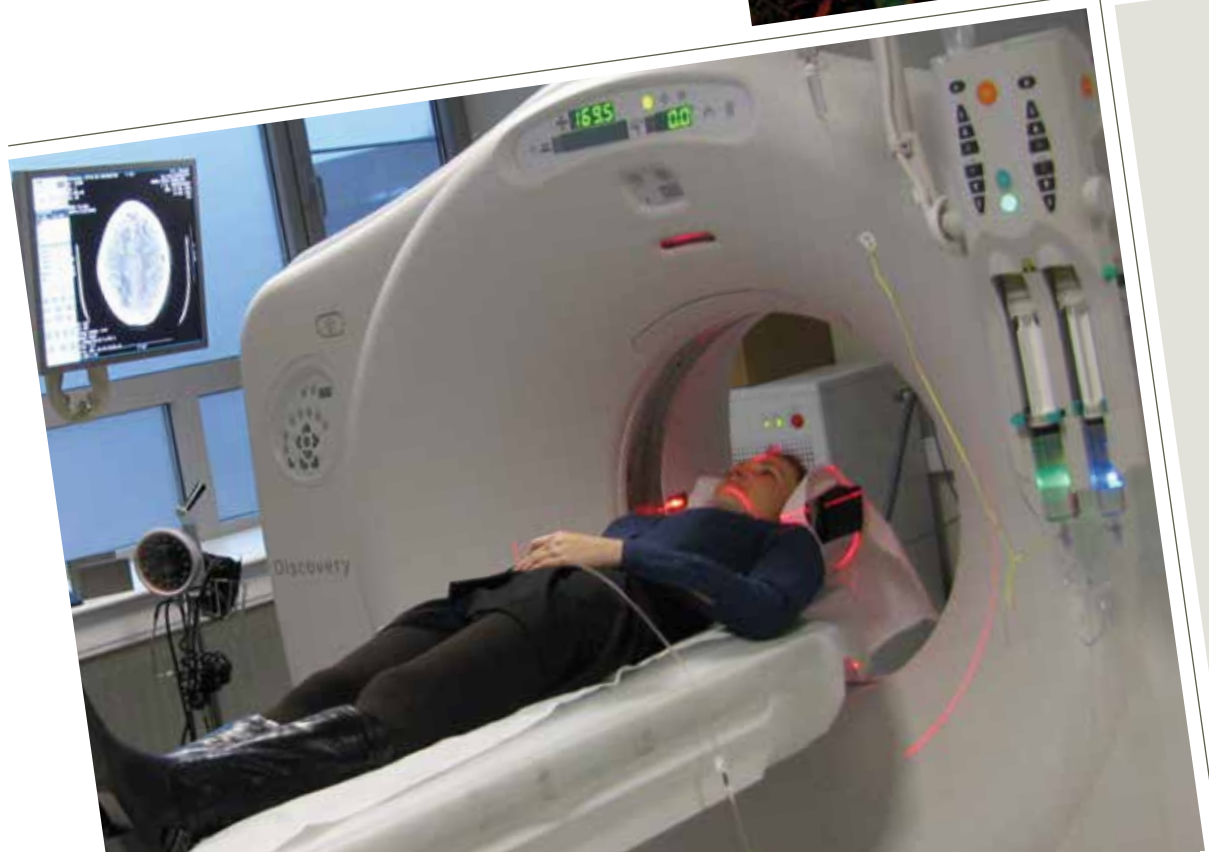
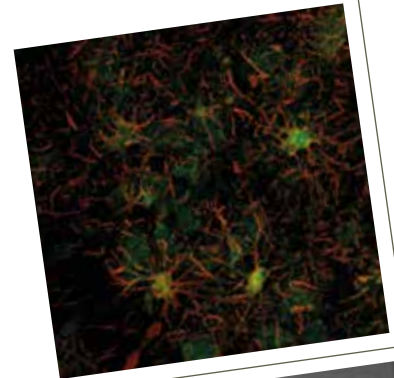
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Pharmaceutical Biotechnology and Molecular Biology (MICH)

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Cerebral Resuscitation Research Group (CRRG)

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Main study areas

- Development of innovative new anti-epileptic drugs, that are more effective, produce less side effects, and improve cognition. Development of drugs that prevent epileptogenesis. Main targets: astrocytes, monoamines, neuropeptides, glutamate transporters.
- Acute management of stroke, with focus on revascularisation, neuroprotective interventions (IGF-1, monoamines), the role of the sympathetic nervous system, and telemedicine.
- Multiple sclerosis and other neurodegenerative disorders such as Parkinson's disease: pathophysiology (main target: the role of astrocytes, monoamines, glutamate transporters, IGF-1), factors that affect disease progression, and new therapeutic interventions.
- Neuromodulation of affective disorders, autonomic nervous system (effects on the immune system and systemic disorders), and blood pressure.
- The pathophysiology and management of fatigue and cognition in neurological disorders.
- Development of high-throughput analytical methods for monoamines, amino acids, neuropeptides and drugs.

Equipment & infrastructure

Methods & equipment:

- Broad range of rodent models:
 - Chemical and electrical models for epileptic seizures and chronic epilepsy
 - Models for Parkinson's disease: 6-hydroxydopamine and lactacystin model
 - Endothelin-1 model for focal transient cerebral ischemia
 - Several genetic models e.g. astrocyte-specific beta2 adrenergic receptor knockout mouse
- Rodent behavioural unit:
 - Locomotor activity: open field, rotational behaviour (Rotometer), neurological deficit score, Rotarod
 - Spatial memory: Morris water maze for rats and mice; Y maze for mice
 - Anti-depressant-like activity: forced

- swim test, tail suspension test
- Stereotaxic surgery (rat and mouse) and in vivo microdialysis
- Telemetry-based 24h video-EEG monitoring units for rodents
- Radiotelemetric cardiac monitoring units
- Broad range of analytical equipment:
 - Liquid chromatography with electrochemical, fluorescence or ultraviolet detection for the quantification of neurotransmitters and drugs
 - Nano liquid chromatography coupled to tandem mass spectrometry for the determination of neuropeptides and drugs
 - Capillary electrophoresis
 - Size exclusion chromatography
- Protein and DNA/RNA electrophoresis
- Doppler flowmetry
- Cell cultures (growth of neuroviruses, cell infections, quantification) and transfection
- Immunobiotechnological techniques: (immuno)histochemistry, Western blotting, ELISA
- Brain histology, fluorescence microscopy
- Nanobodies
- Molecular biology techniques, DNA microarrays, real-time PCR

Clinical facilities:

- Clinical neurophysiology (EEG, MEP, visual, auditory and somatosensory evoked potentials, event-related potentials, EMG, EEG-video monitoring)
- Doppler (transcranial, cervical)
- Stroke unit with monitoring
- MR scanning of the brain (MR spectroscopy, perfusion)
- PET and SPECT scan of the brain
- Magstim super rapid stimulator for repetitive transcranial magnetic stimulation and neuronavigation system
- Electroconvulsive therapy
- Nervus vagus stimulation
- Transcranial direct stimulation system
- Multiple exercise equipment (ergometers, treadmill, rotarod)
- Eye-tracking equipment
- Climatic chamber for exercise & clinical testings (high & low temperature, humidity)
- EEG 64 channel equipment

- Nexus 10 psychophysiological monitoring
- Life shirt (HRV, core temperature,...)
- Core and skin temperature measurement
- Reaction time test
- Attention and learning tests
- Neurocognitive test batteries
- Dual belt treadmill (spinal cord, MS, stroke patients testing)

Industrial collaboration fields

- Preclinical models for neuroprotection and neuromodulation, especially in the field of epilepsy, stroke, Parkinson's disease and multiple sclerosis
- Phase I – III studies in the field of stroke and multiple sclerosis
- Telemedicine
- Consultancy support in the field of stroke, epilepsy and multiple sclerosis
- Preclinical and clinical studies on vagus nerve stimulation
- Repetitive transcranial magnetic stimulation
- Neurophysiological studies in the field of exercise, fatigue and cognition



Vrije Universiteit Brussel – UZ Brussel

Liver and Cell Biology & Toxicology

Yearly, 60,000 European citizens die due to liver failure, and at least ten times more are chronically affected and disabled by liver disorders. There is currently no curative treatment, and liver transplantation often becomes the ultimate solution, which is only available to a small fraction of patients due to shortage of donors. The cluster Liver and Cell Biology and Toxicology endeavors to find new and better treatment options by investigating mechanisms regulating the function of liver cells in health and disease. Specifically, finding of new drug targets for the treatment of acute and chronic liver conditions is one of the cluster's main goals. At the same time, liver cell therapy options based on hepatic progenitors and postnatal stem cells are explored. Stem cell-derived liver cells, as well as primary hepatic cells, could also be used to construct *in vitro* liver models for toxicity testing of new drug candidates and chemicals in general. Such systems could potentially replace or at least reduce the use of experimental animals in safety studies, but more importantly, contribute to more accurate prediction of hepatotoxic potential of new drug candidates and alike. The latter remains an important socio-economical problem being the most frequent safety related reason of post-marketing drug withdrawal and an important cause of acute liver failure. Consequently, development of metabolically-competent *in vitro* liver models applicable in the industrial settings is one of the most prominent research domains within the Liver and Cell Biology & Toxicology cluster.

***In vitro* toxicology, alternative 3R methods, stem cells, primary hepatocytes, cosmetic safety, chronic liver disease, hepatic stellate cell, liver progenitor cell, liver regeneration, autoinflammation, autoallergy, immunomodulation, stem cells, immunotherapy**

In Vitro Toxicology and Dermato-Cosmetology (IVTD)

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ivtd-fafy.be

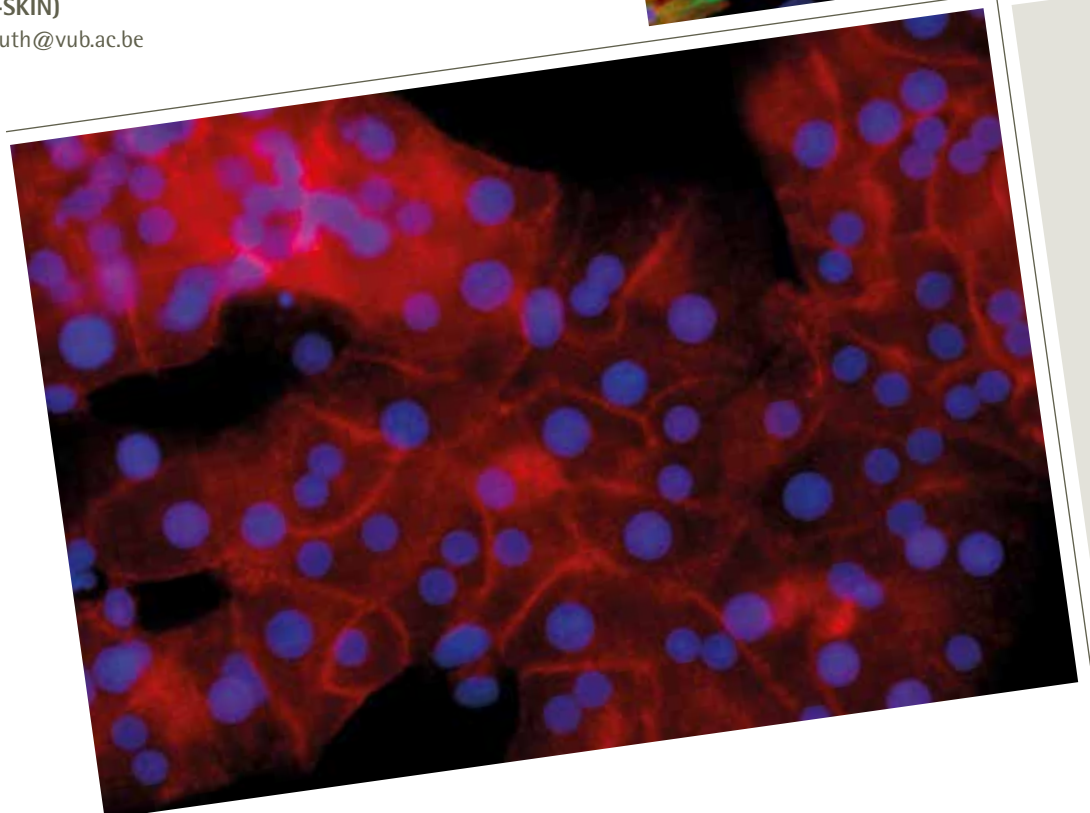
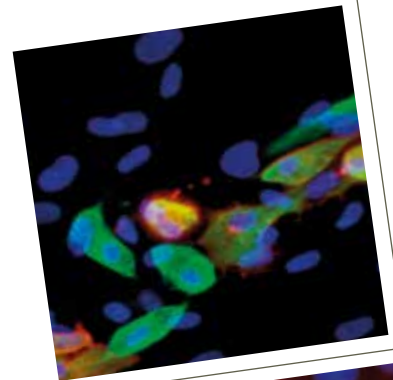
Liver Cell Biology Lab (LIVR)

Leo van Grunsven – lvgrunsv@vub.ac.be

cyto.vub.ac.be

Immunology of the Skin (I-SKIN)

Jan Gutermuth – jan.gutermuth@vub.ac.be



Main study areas

In Vitro Toxicology and Dermato-Cosmetology (IVTD)

- *In vitro* toxicology:
 - Development of metabolically-competent *in vitro* liver models based on:
 - Primary hepatocytes by (i) exploring epigenetic mechanisms of gene regulation i.e. histone acetylation, DNA methylation, microRNAs (ii) and (iii) immortalization of primary hepatocytes
 - Stem cells isolated from various human postnatal tissues, i.e. skin, adipose tissue and Wharton's jelly, by (i) careful characterization, (ii) *in vitro* expansion and (iii) differentiation towards the hepatic phenotyp,
 - A coating substratum and 3D cell cultivation scaffold derived from decellularized liver matrix
 - Safety assessment of dermato-cosmetic substances based on non-invasive bioengineering and *in vitro* methodology
- Clinical research:
Targeting intercellular communication in the treatment of acute and chronic liver diseases and potential use of stem cells in end-stage liver disorders

Liver Cell biology Lab (LIVR)

- Investigation of mechanisms involved in hepatic stellate cell activation *in vitro* and *in vivo*; studies on autophagy, ER stress, histone modifications and miRNA involvement
- The hepatic progenitor cell niche under experimental conditions and in human liver disease

I-SKIN Lab

- Functional characterization of stem cells for immunomodulatory capacities (Dendritic cell-T cell-stem cell coculture system)
- Development of preclinical models of asthma, eczema and autoimmunity
- Evaluation of the therapeutic potential of stem cells in preclinical models
- Evaluation of the adipose tissue derived stem cells in chronic ulcers

Equipment and infrastructure

In Vitro Toxicology and Dermato-Cosmetology (IVTD)

- Biosafety level 2 laboratory and culture facilities
- Organ perfusion unit
- Scintillation counter (TriCarb 2810 TR; Perkin Elmer)
- Fluorescence microscope (Nikon Eclipse Ti)
- 2 RTqPCR thermal cyclers (Step One Plus; Applied Biosystems, iQ5; Bio-Rad)
- Microplate reader (Victor3; Perkin-Elmer)
- Micro-volume UV spectrophotometer (NanoDrop 2000c; Thermo SCIENTIFIC)

Liver Cell biology Lab (LIVR)

- Protein and DNA/RNA electrophoresis
- Cell sorter, FACSaria (Becton Dickinson)
- Biosafety level 2 cell culture facility
- Liver histology lab with Cryostat microtome
- 2 Fluorescence microscopes (Zeiss)

Cell/Molecular biology lab including Elisa plate reader (iMark/Biorad), UV spectrophotometer (GeneQuant), RTqPCR (ABI 7500) and Chemical analyzer (Spotchem EZ)

I-SKIN lab and Department of Dermatology

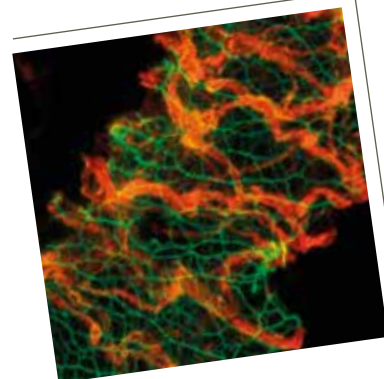
- Histology lab with cryostat and microtome (Microm HM525 and HM325, respectively)
- *In vivo* image station (4000MM, Kodak)
- Western blot system (iBlot, Invitrogen)
- In- and outpatient care, clinical studies

Industrial application fields

- *In vitro* models closely reflecting liver function are urgently needed in:
 - The cosmetic industry, where animal testing and marketing bans have become final in March 2013, irrespective of the availability of alternative nonanimal tests
 - The pharmaceutical industry, where *in vitro* methods become key for early decision making in the drug development process due to their speed, high

throughput and cost-effectiveness

- The chemical industry, where safety testing under REACH regulation is associated with substantial financial costs and high animal consumption
- *In vitro* dendritic and T cell function assays, as well as preclinical animal models, can be used for the identification of new therapy options for diseases with a strong inflammatory component.



Vrije Universiteit Brussel - UZ Brussel

Research Center for Cardiovascular Diseases

www.chvz.be

The CHVZ research center includes different research groups, all interested in the field of cardiovascular diseases. In parallel, a Center for Cardiovascular Diseases is embedded in the patient care of the University Hospital UZ Brussel, providing a unique opportunity to optimize translational research within the field of cardiovascular disease.

Atherosclerosis, valvulopathy, cardiovascular imaging, ion channel disorders, genetic cardiac diseases, atrial fibrillation, clinical cardiovascular pharmacology, integration of clinical pathways in the EMD, linking the EMD with the data medical warehouse

Center for Cardiovascular Diseases (CHVZ)

Guy Van Camp - guy.vancamp@uzbrussel.be

Health Informatics (KWSB)

Rudi Van De Velde - rudi.van.de.velde@vub.ac.be

Clinical Pharmacology & Clinical Pharmacy (KFAR)

Alain Dupont - alain.dupont@vub.ac.be

Micro CT



Main study areas

Cardiac imaging – G. Van Camp

Cooperation is organised with the SAL (Small Animal Lab) of the MIMA research group from the Medical Imaging and Physical Sciences research cluster.

- Elucidate the mechanisms of "drug induced valvulopathy"
- Define the determining factors for the evolution from aortic valve sclerosis to aortic valve stenosis
- Imaging of the vulnerable plaque using nanobodies and fluorescence techniques in an animal model, with the option of implementing it in the clinic

Ion channel disorders – P. Brugada

- The study of heart rhythm disorders, together with ventricular tachycardia and the risk of sudden death
- The study of genetic defects, more specifically the Brugada Syndrome, and the potential link between ion channel disorders and neurological disorders
- Examine whether morphological and functional abnormalities present in the Brugada Syndrome, can help in the diagnosis and determination of the prognosis of patients with Brugada Syndrome

Clinical Pharmacology – A. Dupont

- Optimization of the medicine policy in the hospital through research within the CHVZ. The results of this research can be translated to other departments of the hospital

Health Informatics – R. Van De Velde

- Optimisation of the integration of IT in the electronic patient file. One of the first projects will consist of incorporating the clinical "heart failure" path in the electronic patient file

Equipment & infrastructure

Centrum Hart- en Vaatziekten UZ Brussel (CHVZ)

- GE and Philips Healthcare ultrasound systems
- Software application tools Echopac and

Excellera for post-processing of GE- and Philips Healthcare ultrasound images

- Digital biplane and monoplane flat panel coronary angiography systems
- All diagnostic interventional tools as fractional flow reserve, intracoronary echocardiography,...
- All modalities for electrophysiological and ablation techniques including a magnetic navigation system

Small Animal Lab of MIMA research group

- GE Vivid 7 echosystem with dedicated post-processing software system and probes adapted for small animal imaging
- SPECT imaging
- Micro CT
- Immunofluorescence system
- Development of nano body imaging systems

Industrial application fields

- Well-developed clinical pharmacological research Phase III & Phase IV studies with all pharmaceutical companies



Vrije Universiteit Brussel – UZ Brussel

Public Health

gf.vub.ac.be/public-health.php

The cluster Public Health joins together 4 research groups, performing basic, translational and medical-sociological research in health economics, health care organization, eHealth and family medicine.

Health economic evaluations, Health care payment systems, Financial equity in health care, Health services research, Health policy, Innovations in health care, Evaluation research, Social inequalities, Integrated care, Chronic disease, Diabetes, COPD, Heart failure, E-health, Medical informatics, Biostatistics, Data-mining

Interuniversity Center for Health Economics Research (I-CHER)

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Organisation, Policy and Inequalities in Health (OPIH)

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Family Medicine (HUIS)

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Biostatistics & Medical Informatics (BISI)

Ronald Buyl - rbuyl@vub.ac.be

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Main study areas

Interuniversity Center for Health Economics Research (I-CHER)

- Cost-effectiveness studies in health care
Examples are : cost-effectiveness studies on pharmacist-led information technology intervention for medication errors in primary care, health promotion interventions in kindergarten, enhanced women-centred care in prenatal care, health promotion in mental health care
- Cost-of-illness studies
Examples are: cost-of-illness studies of acute stroke care, direct medical costs of traffic injuries
- Health impact studies of traffic policies (analytic modelling in the evaluation of traffic policies)

Organisation, policy and social inequalities in health care (OPIH)

- Evaluation of policy reforms in health care
- Evaluation of reforms in mental health care in Belgium
- Assessing the needs for health services
Developing a method to assess the needs for mental health services in the Brussels area
- Health care innovations
 - Effectiveness, efficiency and acceptability of innovations in health care organisation models, including the implementation of technologies
 - Inter-organisational networks and collaboration models in a changing health care landscape
 - The use of internet by patients and citizens
 - Developments in participation models in health care
- Socio-economic and sociocultural disparities in health services use

Family Medicine (HUIS)

- Integrated health care delivery
Integrated care has been defined by the World Health Organization (WHO) as: "The management and delivery of health services such as that people receive a continuum of health promotion, disease prevention, diagnosis, treatment, disease management, rehabilitation and palliative care services, through the dif-

ferent levels and sites of care within the health system, and according to their bio-psycho and social needs throughout the life course" (WHO, 2012).

- Research priorities:
 - Integrated care programmes and multifaceted intervention strategies for patients with (multiple) chronic care conditions
 - 'Transmural care' (from hospital to home care, and vice versa) for patients with multi-morbidity.
 - Quality indicators for integrated healthcare delivery
 - Development of a conceptual framework on multi-morbidity including a complexity analysis at the level of the patient, caregiver and health system.
- Other research topics:
 - Health services accessibility for socio-economically disadvantaged groups
 - Sexual behaviour and dysfunctions in gay men

E-health, Medical Informatics (BISI):

- Introduction of Information and Communication Technology (ICT) in the health system
- Electronic Messaging of Health Data
- Medical prescriptions and medical record systems
- ICT for (continuous) medical education
- ICT for development (ICT4D): ICT in education and in the medical sector.

Biostatistics, Data-mining:

- The development of new algorithms for statistical data mining and pattern recognition
- Adaptive wavelet methods for mining signal data bases, such as Mass Spectra in proteomics and different versions of multivariate decision tree methods for information discovery and modelling of complex medical and pharmaceutical data bases
- Design and (multivariate) statistical analysis of clinical trials

Equipment & infrastructure

E-Health, Medical Informatics:

- Data center and computer infrastruc-

ture for medical applications

- Virtual computer-room infrastructure supporting education and research on the University Medical Center Brussels

Biostatistics, Data-Mining:

- Apart from the availability of diverse advanced statistical software tools (SPSS, SAS, R,...) the FIDO software platform forms a very powerful environment for fast prototyping and development of pharmaceutical and medical data technology applications tailored to specific users eg. mass spectrometry data analysis in proteomics

Industrial application fields

- Expertise in health economic evaluations
- Supporting health services in implementing organisational health care innovation strategies (knowledge brokering of evidence)
- Data mining and modelling consultancies with focus on medical and pharmaceutical applications.
- New multivariate Consensus tree approach was able to discern specific risk patient groups that were not discovered using traditional statistical methods.
- Latest research in collaboration with WIV, and supported by INNOVIRIS, involves the development of multivariate time series models in an epidemiological context for monitoring acute respiratory health problems in relation to air pollution in the Brussels region.
- Consultancy regarding ICT in the health- and education systems.
- Expertise in university development cooperation, project selection and evaluation



Vrije Universiteit Brussel - UZ Brussel

Medical Imaging and Physical Sciences

Different research teams collaborate in an interdisciplinary research effort which encompasses the development and validation of innovative core technologies, their applications in preclinical translational research and the introduction of these emerging technologies into clinical diagnostic imaging practice.

Cellular and molecular imaging, nuclear medicine, radiology, image-guided radiotherapy, frameless radiosurgery, radiobiology

Medical Imaging (MIMA)

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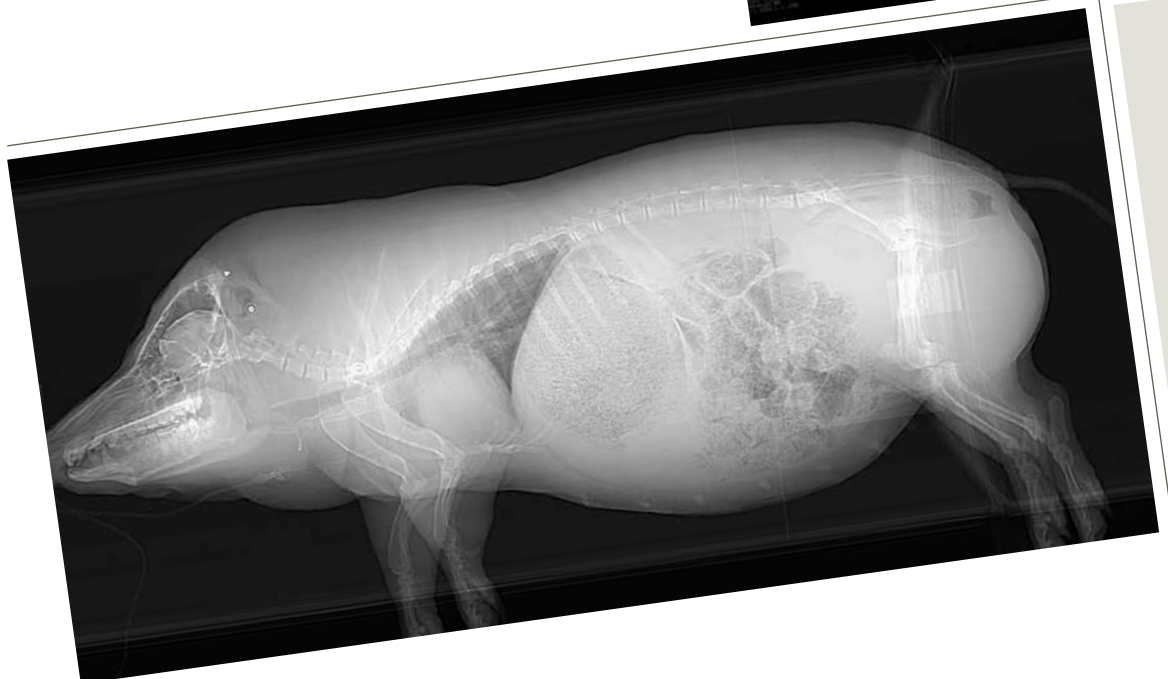
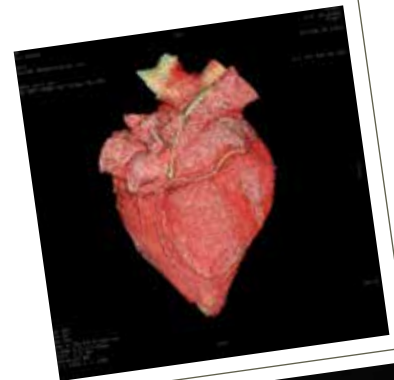
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www.icmibrussels.be

Translational Radiation Oncology and Physics (TROP)

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Mark De Ridder - mark.deridder@uzbrussel.be



Main study areas

Medical Imaging (MIMA)

- Introducing nanobodies as a generic method for pre-clinical and clinical molecular imaging
- Developing imaging strategies for serial quantitative monitoring of transplanted cell populations
- Cardiac imaging for the monitoring of cardiotoxic effects of drugs and for the imaging of the sympathetic innervation of the heart
- Development of algorithms for the efficient compression of TOF-PET data and for the reconstruction for truncated CT-image data
- Pinhole tomography for small-animal imaging
- Perfusion imaging
- Optimization and quality control of micro-CT systems
- Radiation dosimetry, quality control and radiation protection (low dose CT scanning)
- Spectral CT applications
- Valorisation of CT contrast agents in animal models
- Digital breast tomosynthesis (DBT)
- Advanced MRI applications (fMRI, DTI, perfusion)
- Concordance between high resolution imaging and human anatomy
- Hip prosthesis imaging research program
- Shoulder imaging research program.

Translational Radiation Oncology and Physics (TROP)

- Radiosensitization of hypoxic tumor cells by nitric oxide produced intratumorally by tumor cells, tumor-associated immune cells or hepatocytes
- High-precision radiotherapy by following tumor motion during radiation
- Ablative stereotactic radiotherapy for the treatment of colorectal cancer.

Equipment & infrastructure

Medical Imaging (MIMA)

- Radiochemistry unit for the production of new radiolabeled molecules for the diagnosis and therapy of various diseases and for the routine production of

clinical PET and SPECT radiopharmaceuticals.

- Nanobody generation unit
- MicroSPECT: E.Cam 180 Siemens
- MicroCT: SkyScan 1178 High-Throughput MicroCT
- Bioluminescence Imaging: Photo Imager Biospace
- Fluorescence Imaging: Fluorescence Molecular Tomograph FMTTM2500 LX (Perkin Elmer)
- Ultrasound Imaging: General Electric
- Dual energy CT scanner with iterative reconstruction module: General Electric 750 HD
- Prototype Digital Breast Tomosynthesis unit: General Electric
- Hard- and software for fMRI and DTI experiments (TMS coil, DTI studio, MedINRIA)
- Radiation dosimetry lab: TLD reader, humanoid and technical phantoms

Translational Radiation Oncology and Physics (TROP)

- Vero stereotactic body radiotherapy (SBRT) system. (joint product of Brainlab and MHI)
- Tomotherapy Hi Art system
- Elekta Sli 15 accelerator
- Nucletron HDR Ir 192

Industrial application fields

Medical Imaging (MIMA)

- Clinical imaging services (all modalities, including fMRI experiments and spectral CT)
- Radiation dosimetry services
- Animal models for imaging
- Preclinical Imaging Services (optical, SPECT, CT, Ultrasound, FMT)
- Clinical PET/CT and SPECT (Phase I, II and III studies)

Translational Radiation Oncology and Physics (TROP)

- Cf. Oncology Research Center (ORC) page 7



Vrije Universiteit Brussel – UZ Brussel

Diabetes Research Center

The Diabetes Research Center (DRC) develops cell therapeutic strategies for the prevention and treatment of diabetes. It undertakes a translational program for the preservation and replacement of insulin-producing beta cells, which are known to be depleted in type 1 diabetes. A sufficient beta cell mass is needed to improve metabolic control of the patients and to avoid the devastating disease complications. The DRC uses a cell biologic platform to design and monitor methods for preclinical testing and clinical trials.

The **DRC is composed of 3 research units** spanning cell biological, preclinical and clinical activities, 4 core facilities (functional cytomics, gene expression, confocal microscopy, preclinical models) and a diabetes biobank with human cells, tissue, blood and data. It hosts over 100 scientific, technical and administrative collaborators. The DRC has integrated extramural collaborations into an international consortium, the Center for Beta Cell Therapy in Diabetes with an R&D platform, a clinical network, reference centers and bioindustrial partners.

Diabetes, Pancreas, Beta cell mass, Acinar cells, Embryonic stem cells, Proliferation, Reprogramming, Transdifferentiation, Regeneration, Animal models, Biomarkers, Prediction, Prevention, Beta cell transplantation, Immunotherapy

Diabetes Pathology and Therapy (DIAB)

Frans Gorus – frans.gorus@uzbrussel.be

Cell Differentiation (DIFF)

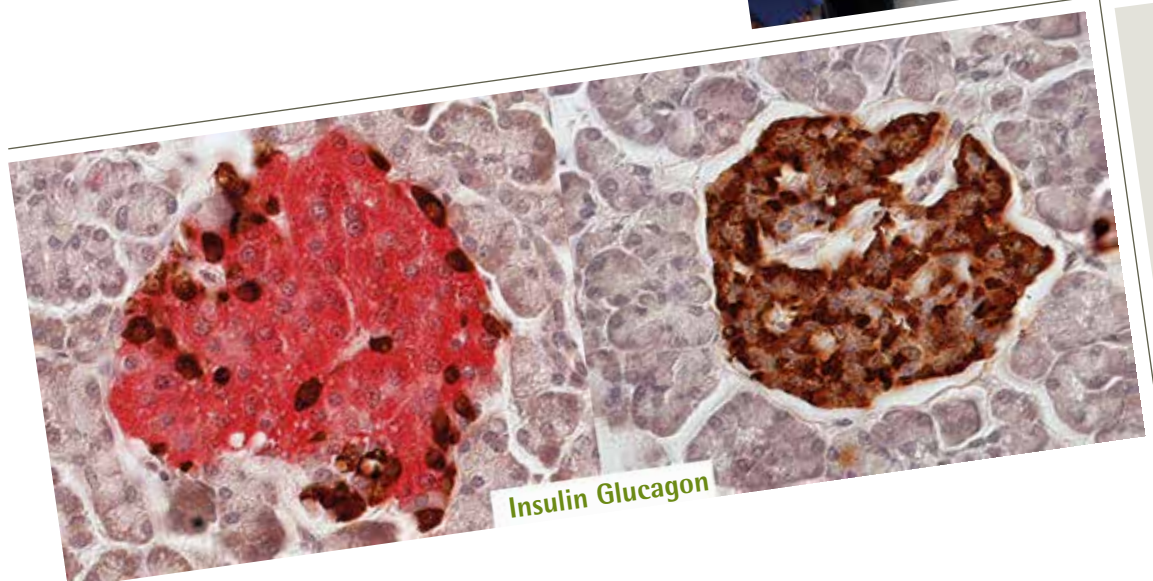
Luc Bouwens – lucbo@vub.ac.be – diff.vub.ac.be

Beta Cell Neogenesis (BENE)

Harry Heimberg – harry.heimberg@vub.ac.be – bene.vub.ac.be

Center for Beta Cell Therapy in Diabetes

Daniël Pipeleers – daniel.pipeleers@vub.ac.be – www.betacelltherapy.org



Main study areas

Cell Biological basis

Diabetes Pathology and Therapy (DIAB)

- Assessment of functional beta cell mass in situ
- Identification of (pre)beta cell phenotypes and their markers
- Regulation of insulin producing capacity

Cell Differentiation (DIFF)

- Reprogramming of pancreatic exocrine acinar cells to endocrine beta cells
- Directed differentiation of embryonic stem cells to pancreatic cells

Beta Cell Neogenesis (BENE)

- Generation of a functional beta cell mass by differentiation, proliferation, maturation and survival: identification of the necessary extra- and intracellular factors
- *In vitro* expansion of non-beta cells from mouse and human pancreas and differentiation to functional beta cells
- Identification and isolation of beta cell stem/progenitor cells from pancreas of mouse and man

Translational development

Diabetes Pathology and Therapy (DIAB)

- Studies to select biological markers for detecting and monitoring disease progression and assessing intervention strategies in preclinical models and clinical trials:
 - Clinical biology platform for development and validation of genetic, hormonal and autoantibody markers of diabetes
 - Beta cell proteomics and transcriptomics to identify novel biomarkers of beta cell damage
 - Access to Diabetes Biobank (blood samples, data) for (inter)national studies on the epidemiology and biology of type 1 diabetes
 - Stratification of type 1 diabetic patients according to disease state and of relatives according to disease risk: selection and composition of study groups for clinical trials
 - Detection of beta cell death and monitoring of functional beta cell mass during disease and following interventions: surrogate endpoints for clinical trials

- Access to Diabetes Biobank (pancreas tissue) to assess functional beta cell mass and inflammation in the pancreas and their relation to circulating biomarkers (antibodies, genes)
- Preclinical models to identify cells and/or compounds to help replace a functional beta cell mass through cell transplantation or beta cell regeneration:
 - Development of a confined implant site that can be monitored and modulated in order to improve metabolic outcome of a human beta cell graft
 - Comparison of outcome of primary human beta cell grafts with that of grafts prepared from alternative sources (human embryonic stem cell-derived grafts, reprogrammed human adult differentiated cells, perinatal porcine cells) with the use of various immune-isolation devices
 - Determination of beta cell numbers in the pancreas of normal and diabetic NOD mice with and without anti-T lymphocyte treatment (anti-CD3)
 - Effect of compounds on the regeneration of beta cells in the diabetic pancreas

Cell Differentiation (DIFF)

- Stimulation of beta cell regeneration in diabetes with growth factors, cytokines, or phytochemicals
- Noninvasive imaging of the pancreatic beta cell mass with biomarkers

Beta Cell Neogenesis (BENE)

- Development of experimental models to study proliferation and survival of beta cells and (re)programming of non-beta to beta cells

Clinical trials

Diabetes Pathology and Therapy (DIAB)

- Cell transplantation to restore a functional beta cell mass in type 1 diabetes patients
- Arrest of the disease process in early (pre)clinical stages of type 1 diabetes. More info see www.betacelltherapy.org
 - www.bdronline.be

Infrastructure and (major) equipment

Diabetes Pathology and Therapy (DIAB)

- Functional cytomics core facility
 - Flow cytometers: FACS Vantage, FACStar Plus (n=2), FACSAria (Becton Dickinson)
 - Pathway imaging modules (Becton Dickinson – Atto Biosciences) for simultaneous detection and sensitive quantification (in space and time) of 8 fluorophores in living cells
- Preclinical model core facility
 - Fully equipped labs for animal dissection, transplantation, organ- and



islet isolation, cell culture, histology, immunocytochemistry, fluorescence microscopes, microtomes, molecular biology, clinical biology

- Electron microscope and microtome core facility
 - Fully equipped histopathology platform with transmission EM Philips Tecnai 10 and Scanning EM-SEM 505 electron microscopes and 9 microtomes
- Diabetes Biobank
 - Sample- and databank from diabetic patients and risk groups with 23 ultralow freezers (-80°C) and protected confidential database
 - Beta Cell Bank in UZ Brussel: GMP facility with 2 fully equipped clean rooms for preparation of clinical grade grafts
 - Pancreatic tissue bank
- Clinical biology platform
 - Fully equipped clinical biology lab in UZ Brussel with automated (immunoassay) analyzers, liquid scintillation counters, gamma counters, DNA extraction robot
- Metabolic unit in UZ Brussel with Phase I clinical trial facility

Cell Differentiation (DIFF)

- Confocal microscopy core facility
 - Leica DMIRBE confocal laser scanning microscope TCS-SP1
- Fully equipped rooms for histology, fluorescence light microscopy, cell & tissue culture, RNA and protein analysis

Beta Cell Neogenesis (BENE)

- Gene expression core facility
 - Equipment for RNA and DNA analysis: DNA sequencer, Nanodrop, BioAnalyzer, Real time PCR thermal cycler, conventional thermal cyclers, gel electrophoresis
- Fully equipped rooms for (i) recombinant adeno- and lentivirus production, (ii) in vivo transduction experiments with adeno- and lentivirus, (iii) islet isolation from mouse pancreas, (iv) isolation and culture of embryonic pancreas, and (v) culturing primary cells and immortalized cell lines

ples and epidemiological, clinical and biological data from >8000 patients and >9000 relatives aged under 40 years for recruitment of patients for clinical trials and for companies with which DRC collaborates (TolerX, GSK, Peptor, Andromeda)

- Development of Drug Screening Platform for testing the potential of compounds to stimulate beta cell growth and differentiation
- Preclinical testing of beta cell grafts (with or without alginate encapsulation) derived from perinatal porcine pancreata, produced by a DRC spin-off (Beta Cell nv), in preparation of clinical phase I and II trials
- Preclinical testing of human embryonic stem cell-derived grafts (with or without Encaptra™-immuno-isolation device) (Via-Cyte)

Cell differentiation (DIFF)

- Screening of chemicals for their protective, mitogenic, and other effects relating to beta cell number in the pancreas

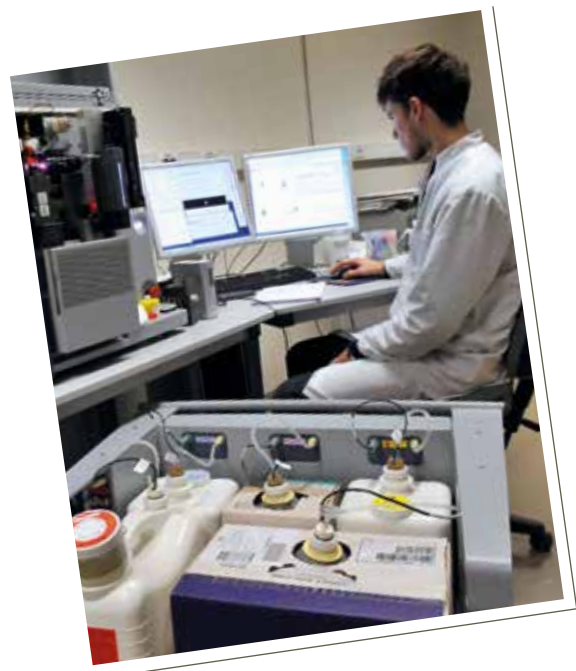
Beta Cell Differentiation (BENE)

- Definition of a minimal set of signals that drive the generation and preservation of functional beta cells

Industrial application fields

Diabetes Pathology and Therapy (DIAB)

- Diabetes Biobank (included in CMI-Biobank) comprising >70000 bloodsam-



Vrije Universiteit Brussel – UZ Brussel

Pharmaceutical Research and Data Technology

www.vub.ac.be/farmacie/research/Research.html

The Center for Pharmaceutical Research (CePhaR) consists of four research groups involved in various stages of pharmaceutical R&D, from early lead selection to the assessment of efficacy and safety of finished products. Innovation is the driving force. Our goal is to deal with key bottlenecks in the pharmaceutical R&D process of today, including rational method development, adequate data mining, search for appropriate biomarkers and the development of better *in vivo* and *in vitro* models for human health and disease.

Analytical Chemistry, Chirality, Chemometrics, Experimental design, Pharmaceutical analysis, Neurochemistry, Neuropharmacology, Pharmacokinetics, Microdialysis, Behaviour, Neurovirology, Antiviral compounds, Poliovirus, TMEV, Multiple sclerosis, *In vitro* toxicology, Alternative 3R methods, Stem cells, Primary hepatocytes, Cosmetic safety

Analytical Chemistry and Pharmaceutical Technology (FABI)

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www.vub.ac.be/fabi/

Associated group 1: Experimental Pharmacology (EFAR)

Yvette Michotte – ymichot@vub.ac.be

www.vub.ac.be/farmacie/research/fasc.html

Associated group 2: Pharmaceutical Biotechnology and Molecular Biology (MICH)

Bart Rombaut- brombaut@vub.ac.be

www.vub.ac.be/MICH/

Associated group 3: In Vitro Toxicology and Dermato-Cosmetology (IVTD)

Vera Rogiers- vrogiers@vub.ac.be

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Main study areas

Analytical Chemistry and Pharmaceutical Technology (FABI)

- Evaluation of “the rational use of new developments in separation techniques”. The separation techniques considered are liquid chromatography, capillary electrophoresis and capillary electrochromatography.
- Chiral separations: definition and update of separation strategies by means of different electrophoretic and chromatographic separation techniques.
- Fingerprint development for herbal extracts and their data handling
- Drug impurity profiling
- Introduce analytical separation techniques in virology
- All data analysis of experimental results, for instance, multivariate calibration aspects on fingerprint data, classification of different plant species.

Experimental Pharmacology (EFAR)

- Studying pathophysiological changes in the brain in order to define new strategies for drug development and drug testing. The group is particularly interested in epilepsy and its comorbidities (e.g. cognitive decline and depression), Parkinson's disease and focal transient brain ischemia.
- *In vivo* microdialysis is used to sample different neurotransmitters and neuromodulators such as dopamine, serotonin, noradrenaline, glutamate, GABA, D-serine and various neuropeptides from specific brain areas in freely moving rodents. The neurochemical data thus obtained are supported by behavioural and immunobiological techniques.
- The group has a strong analytical background and is specialized in the development of miniaturized LC methods, coupled to fluorescence, electrochemical or tandem mass spectrometric (MS/MS) detection, for the quantification of neurotransmitters and neuromodulators in microdialysates. In addition, we have a large experience in the development and validation of analytical methods for the determination of drugs in

drug products and biological samples with capillary electrophoresis, LC-UV, LC-fluorescence and LC-MS/MS. For some drugs such as anti-epileptics, the microdialysis technique is also applied to study their pharmacokinetics and brain distribution.

Pharmaceutical Biotechnology and Molecular Biology (MICH)

- Fundamental research on the replication cycle of poliovirus, research concentrates on the first steps of the cycle (adsorption, uncoating) and the last step (assembly);
- Development of new poliovaccines (also biotech vaccines);
- Fundamental research on antiviral compounds (in collaboration with Janssen Research Foundation);
- Viruses on the origin of multiple sclerosis?
- Theiler's murine encephalitis virus (TMEV), a mouse model for multiple sclerosis.

In Vitro Toxicology and Dermato-Cosmetology (IVTD)

- *In vitro* toxicology:
 - Development of metabolically-competent *in vitro* liver models based on:
 - a) Primary hepatocytes by (i) exploring epigenetic mechanisms of gene regulation i.e. histone acetylation, DNA methylation, microRNAs (ii) investigation of the role of intercellular communication and (iii) immortalization of primary hepatocytes,
 - b) Stem cells isolated from various human postnatal tissues, i.e. skin, adipose tissue and Wharton's jelly, by (i) careful characterization, (ii) *in vitro* expansion and (iii) differentiation towards the hepatic phenotype,
 - c) A coating substratum and 3D cell cultivation scaffold derived from decellularized liver matrix.
 - Safety assessment of chemato-cosmetic based on non-invasive bioengineering and *in vitro* methodology.
- Clinical research:
Targeting intercellular communication in

the treatment of acute and chronic liver diseases and potential use of stem cells in disorders of the central nervous system.

Equipment & infrastructure

Analytical Chemistry and Pharmaceutical Technology (FABI)

- Ultrahigh pressure liquid chromatography system coupled to mass spectrometer
- Shimadzu gradient ultrafast liquid chromatography (UFLC) system with diode array detection
- Supercritical fluid chromatography system with diode array detection Thar Method station II
- ELSD detector Alltech ELSD 2000
- Merck-Hitachi Lachrom Elite Gradient HPLC system with diode array detection
- Capillary electrophoresis Agilent HP3DCE system with diode array detection
- 2 x Merck-Hitachi Lachrom gradient HPLC systems with UV detection
- 2 x Capillary electrophoresis Beckman P/ACE MDQ systems with diode array detection and Laser induced fluorescence detection
- NIR spectrophotometer Bran+Luebbe InfraAlyzer 500
- Ecocell 111 liter incubator
- Pressurized capillary electrochromatography system Unimicro-Trisep 2100 GV
- UV/Vis spectrophotometer Shimadzu UV-2101PC
- Nitrogen generator Permea CPA1
- Plasma cleaner/sterilizer Harrick Plasma

Experimental Pharmacology (EFAR)

- Broad range of rodent models:
 - Chemical and electrical models for epileptic seizures and chronic epilepsy
 - 6-hydroxydopamine model for Parkinson's disease: striatal, MFB and nigral lesioning
 - Endothelin-1 model for focal transient cerebral ischemia
- Rodent behavioural unit:
 - Locomotor activity: open field, rotational behaviour (Rotometer), neurological deficit score, Rotarod

- Spatial memory: Morris water maze for rats and mice; Y maze for mice
- Anti-depressant-like activity: forced swim test, tail suspension test
- Stereotaxic surgery (rat and mouse) and *in vivo* microdialysis
- Telemetry-based 24h video-EEG monitoring units for rodents
- PK/PD modelling
- Broad range of analytical equipment:
 - Liquid chromatography with electrochemical, fluorescence or ultraviolet detection for the quantification of neurotransmitters and drugs
 - Nano liquid chromatography coupled to tandem mass spectrometry for the determination of neuropeptides and drugs
 - Capillary electrophoresis
 - Size exclusion chromatography
- Doppler flowmetry
- Immunobiotechnological techniques: (immuno)histochemistry, Western blotting, ELISA

Pharmaceutical Biotechnology and Molecular Biology (MICH)

- Biologic duoflow (Fast Protein Liquid Chromatography) with IMAC-purification, size exclusion and hydrophobic interchange column)
- Biosafety level 2(+) laboratories
- Cell culture facilities
- Virus culture facilities
- Liquid handling system (robot) Perkin Elmer Multiprobe II with gripper
- Liquid handling system (robot) Perkin Elmer Multiprobe II with shaking
- Spectrofotometer Nanodrop ND 1000 UV-Vis
- Liquid scintillation counter Wallac1409
- Biotek Microplate Fluorescence Reader FL600
- Asys Microplate Reader Expert 96
- Luminescent Image Analyzer ImageQuant LAS4000
- Capillary electrophoresis system Beckman Coulter P/ACE MDQ system with Diode array detector (FABI)
- Shaking incubator (Barnstead MaxQ 5000) - max 6 x 2l
- Ultracentrifugation (swingout and fixed angle)
- PCR Perkin Elmer GeneAmp PCR system 2400

- Immunobiotechnological techniques: Western blotting, ELISA, affinity capture assay
- Standard virological techniques: plaque titration, infectivity assays

In Vitro Toxicology and Dermato-Cosmetology (IVTD)

- Biosafety level 2 laboratory and culture facilities
- Organ perfusion unit
- Scintillation counter (TriCarb 2810 TR; Perkin Elmer)
- Fluorescence microscope (Nikon Eclipse Ti)
- 2 RTqPCR thermal cyclers (Step One Plus; Applied Biosystems, IQ5; Bio-Rad)
- Microplate reader (Victor3; Perkin-Elmer)
- Micro-volume UV spectrophotometer (NanoDrop 2000c; Thermo SCIENTIFIC)

Industrial application fields

Analytical Chemistry and Pharmaceutical Technology (FABI)

- Chiral screening approaches/protocols
- Data analysis (classification, modelling) of any kind of experimental results
- Quality control of herbal extracts
- Fast separations
- Impurity profiling/orthogonal systems

Experimental Pharmacology (EFAR)

- Predictive neuropharmacology:
 - Screening of new chemical entities in different animal models for neurological diseases
 - Evaluation of clinically used drugs
 - Unravelling pathophysiological processes
 - Unravelling new potential mechanisms of action, drug targets
 - Prediction and modulation of blood-brain-barrier passage and active efflux systems
- Biomarkers:
 - Determination of disease-related biomarkers: neurotransmitters, neuropeptides, etc
 - Mechanism-based pharmacokinetic and pharmacodynamic modelling using neurotransmitters as biomark-

ers for predicting drug effects in the brain and drug efficacy based on drug plasma concentrations

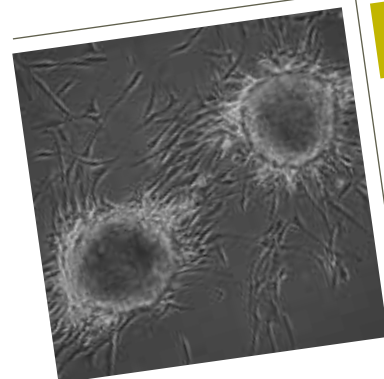
Pharmaceutical Biotechnology and Molecular Biology (MICH)

- Development of new poliovaccines (also biotech vaccines)
- Fundamental research on antiviral compounds
- Fundamental research on and development of nanobodies

In Vitro Toxicology and Dermato-Cosmetology (IVTD)

Assessment of hepatotoxic potential of new chemical entities is an essential and hence legally required step in the development of safe cosmetic, pharmaceutical and chemical products. Therefore, *in vitro* models closely reflecting liver function are urgently needed in:

- The cosmetic industry, where animal testing and marketing bans have become final in March 2013, irrespective of the availability of alternative non-animal tests,
- The pharmaceutical industry, where *in vitro* methods become key for early decision making in the drug development process due to their speed, high throughput and cost-effectiveness,
- The chemical industry, where safety testing under REACH regulation is associated with substantial financial costs and high animal consumption.



Vrije Universiteit Brussel – UZ Brussel

Reproduction, Genetics and Regenerative Medicine

rgrg.vub.ac.be

The research cluster Reproduction, Genetics and Regenerative medicine consists of 7 research groups and is linked to the Center for Medical Genetics, the Center for Reproductive Medicine and the Department of Pediatrics of the UZ Brussel, allowing to perform basic, translational and clinical research.

Human preimplantation embryo, Human embryonic stem cell, Neuro-paediatrics, Children follow-up, Cardiogenetics, Spermatogonial stem cell, Spermatogenesis, Male infertility, Fertility preservation, Implantation, Endometrium, Embryo, Immunology, Preterm birth, Fetal fibronectin, Bacterial vaginosis, Cytomegalovirus, prenatal diagnosis and prediction of sequellae, Hereditary Neurological Disorders, Mitochondrial Cytopathies, Malformations of Cortical Development, Gene therapy, iPS, Hereditary disease, Genetics, Regenerative medicine

Reproduction and Genetics (REGE)

Karen Sermon – ksermon@vub.ac.be

Biology of the Testis (BITE)

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Follicular Biology (FOBI)

Johan Smits – jsmits@uzbrussel.be

Reproductive Immunology and Implantation (REIM)

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Mother and Child (MOKI)

Gilles Faron – gilles.faron@uzbrussel.be

Neurogenetics (NEGE)

Linda De Meirleir – ldmeirle@uzbrussel.be

Gene Therapy and Regenerative Medicine (GTRM)

Thierry VandenDriessche – thierry.vandendriessche@vub.ac.be

Marinee Chuah – marinee.chuah@vub.ac.be



Main study areas

Reproduction and Genetics (REGE)

- Mitochondrial diseases and malformations of the cortical development and their causes
- Genetic aspects of male infertility
- Preimplantation genetic diagnosis (PGD) both for monogenic diseases and chromosomal aberrations
- Assessing the safety of ART techniques: research project on the epigenetics of human development
- Mechanisms that underlie totipotency in human preimplantation embryos
- Long-term follow-up of children born after Assisted Reproductive Technology
- Research on human embryonic stem cells and induced pluripotent stem cells
- Research project on cardiogenetics focused on Brugada syndrome in close collaboration with the Research Center for Cardiovascular Diseases of the UMC

Biology of the Testis (BITE)

- Feasibility of storing spermatogonial stem cells (SSCs) either as a suspension or as whole tissue
- Transplantation of SSCs by infusion of a cell suspension or by tissue grafting
- Strategies for optimizing the regeneration of spermatogenesis from SSCs
- Feasibility and safety of reproduction with gametes obtained after transplanting SSCs
- Strategies for preventing the loss of germ cells by gonadotoxic treatments
- Strategies for preventing the loss of germ cells in genetic diseases, eg Klinefelter's syndrome.
- Generation of sperm cells in-vitro
- Use of SSCs in regenerative medicine

Follicular Biology (FOBI)

- Storage of ovarian tissue via freezing
- Research into molecular indicators of egg cell quality
- Research into safety of *in vitro* methods to mature gametes
- Research on In Vitro Maturation (IVM) of human oocytes retrieved from small follicles
- Research Bioassays

Reproductive Immunology and Implantation (REIM)

The research group studies the different aspects of early implantation, especially endometrial - embryo interaction and processes involved in successful natural and IVF cycles.

- Endometrial study areas
 - Endometrial morphology in natural and IVF cycles in relation to receptivity
 - Molecular pathways in endometrial receptivity with microarray and subsequent RT-PCR
 - Key role of the COX-2 pathway in the endometrium of IVF cycles with subsequent ongoing pregnancy
 - Specific endometrial gene clusters involved in different IVF stimulation protocols in oocyte donors
 - Endometrial immune system in repeated implantation failure
 - Distribution and function of uterine dendritic cells and their derived cytokines from endometrial tissue and fluid aspirates to an in-vitro model
 - Endometrial natural killer cells and their killer cell immunoglobulin like receptors in endometrial from patients with recurrent implantation failure, miscarriage and pre-eclampsia
- Embryo study areas
 - Expression of HLA in embryo's and follicle fluid, more specifically HLA-C, G and E and combinations of HLA and their KIR receptors
 - Expression of HLA-G in embryo's and embryonic stem cells
 - Soluble HLA and cytokines in embryonic culture supernatant and follicle fluid
 - HLA-G function in human embryonic stem cells
 - HLA genotyping of embryo's in recurrent miscarriage
 - Cross-talk between the embryo and the endometrium
 - Development of a standard implantation model for embryo attachment and early invasion in an Ishikawa cell line
 - Investigation of implantation regulators in the human embryo

Mother and Child (MOKI)

- Screening of preterm birth
 - Fetal fibronectin test as a screening tool in a low-risk population: does recent coitus interfere with its interpretation. Comparative prospective study.
 - Ureaplasma: does the sampling location matter? Prospective study.
 - Does the PCR test predict better preterm birth than the Ureaplasma culture? Prospective study.
 - Is there a link between these different screening tools? Comparative prospective study.
- Urinary infection during pregnancy: When is it more appropriate to screen for asymptomatic bacteriuria: during the first or during the second trimester? A prospective comparative study.
- Cytomegalovirus(CMV) and pregnancy
 - Prenatal diagnosis of CMV:
 - Prediction of sequelae in congenitally infected children (viral load in amniotic fluid, contribution of ultrasound, fetal MRI)
 - In twin pregnancies
 - Elaboration of a screening model for CMV infections during pregnancy

Neurogenetics (NEGE)

- The development of diagnostic, biochemical and molecular methods; the prevention; and the study of treatment of mitochondrial cytopathies
- The identification of genes involved in the regulation of neuronal migration and the study of the functional consequences of mutations in these genes by combining patient-driven molecular genetic studies and comparative genetic research in zebrafish models

Gene Therapy and Regenerative Medicine (GTRM)

Convincing evidence continues to emerge from clinical trials that gene therapy is yielding therapeutic effects in patients suffering from a wide range of diseases. The Department of Gene Therapy and Regenerative Medicine (GTRM) continues to build on our 20 years' experience in this field and focuses primarily on the development and validation of gene and (stem) cell therapy for major health- and life-

threatening genetic disorders, including hemophilia and neuromuscular disorders (Duchenne and myotonic dystrophy). We are actively conducting translational gene therapy studies in small and large animal models, in anticipation of moving forward towards clinical trials. To achieve this goal we have consolidated a broad state-of-the-art technology platform based on the latest viral vectors (retroviral, lentiviral, AAV), non-viral vectors (PB and SB transposons), genome engineering systems (designer nucleases -TALEN) and stem cell technologies (progenitor stem cells and iPS).

Equipment & infrastructure

Reproduction and Genetics (REGE)

- State-of-the-art IVF center (CRG) with more than 5000 cycles per year, providing scarce patient material for research. This includes sperm, oocytes, embryos surplus to IVF treatment and donated by the patients, and embryos created for research.
- Fully equipped medical genetics center, with infrastructure such as a cytogenetics lab, microarray and sequencing facilities, standard molecular biology infrastructure, and a large collection of archived patient material. This includes extracted DNA, skin fibroblast cultures, prenatal tissue cultures and EBV-transformed lymphoblast cell lines.
- Research lab closely integrated with the two previous labs, with separate culture rooms for human and animal work, confocal and fluorescent microscopy and molecular biology facilities. More than 28 hESC lines are available for other researchers through an MTA

Biology of the Testis (BITE)

The BITE laboratory is part of the medical genetics department. We have two cell culture rooms (one for mouse and one for human cells) with one horizontal flow and incubator in each room. We share the pre- and post-PCR room, the staining room (with vertical flow), the imaging room (with two confocal and one fluorescence microscope) and the cold room with the REGE and the FOBI lab. There is also space available for a -20°C freezer, the mQ water

dispenser and two sterilization ovens. Access to FACS, ultrasound-guided injections and imaging and tissue sectioning and paraffin embedding.

Follicular Biology (FOBI)

- Diagnostics: molecular biology tests: oocyte quality testing
- Cell culture media companies: oocyte maturation media
- Pharmaceutical companies: reprotoxicity testing

Mother and Child (MOKI)

- RapidFFN test Analyser kit

Neurogenetics (NEGE)

- Histology and immunohistochemistry facility
- qRT-PCR facility
- Microarray
- Next Generation Sequencing
- Biochemical analysis in collaboration with UZ Gent (Prof. R. Van Coster)
- Zebrafish morpholino knockdown models in collaboration with KUL (Prof. P. De Witte)

Gene Therapy and Regenerative Medicine (GTRM)

Fully equipped P2 laboratory suites and molecular biology laboratories equipped with laminar flows, ultra-centrifuges, incubators, quantitative PCR, fluorescence microscopes. Access to FACS and confocal core facilities, etc.

Industrial application fields

Reproduction and Genetics (REGE)

- Pharma in the field of fertility drugs: CRG conducts large studies with several partners
- Products for the IVF lab: CRG IVF lab conducts large studies with several partners

Biology of the Testis (BITE)

The UZ Brussel already started the banking of testicular tissue from prepubertal patients. The testicular tissue banking has a non-profit character. Since this testicular tissue bank is unique in Flanders, the UZ

Brussel could act as a reference lab with the intention that also other institutes can benefit from our knowledge. Being a reference lab will not only attract Belgian patients, but also patients from other countries, stressing the role of Flanders and Belgium as a medical reference region. The system for in-vitro spermatogenesis could be developed further into a patentable screening assay for studying the pharmacotoxicological properties of existing or new chemical molecules. Such a system could possibly reduce or replace animal testing. Furthermore, in-vitro spermatogenesis may enhance our knowledge about regulatory mechanisms during spermatogenesis, giving a boost to the development of male contraceptives.

Reproductive Immunology and Implantation (REIM)

- Development of a standard test for endometrial receptivity
- Development of a standard test for embryonic implantation capacity

Gene Therapy and Regenerative Medicine (GTRM)

- Development and validation of Advanced Therapy Medicinal Products (ATMPs)
- Gene therapy
- Functional genomics
- Regenerative medicine
- Induced pluripotent stem cells (iPS)
- Genome engineering (TALEN, transposons)



Vrije Universiteit Brussel – UZ Brussel

Development, Ageing and Pathology

gf.vub.ac.be/development-ageing-and-pathology.php

The research of the cluster Development, Ageing & Pathology focuses on 3 major research niches:

- Developmental aspects
- Environmental aspects
- Degenerative & age-related aspects

The priority research lines of this cluster are mainly linked to the specificity of its 7 research groups.

Internal Medicine Specializations (INTG)

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Nephrology: Christian Tielemans - christian.tielemans@uzbrussel.be

Pneumology: Sylvia Verbanck - sylvia.verbanck@uzbrussel.be

Research Methodology and Rheumatology: Patrick Haentjens - patrick.haentjens@uzbrussel.be

Intensive Medicine: Herbert Spapen - herbert.spapen@uzbrussel.be

Frailty in Ageing (FRIA)

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Microbiology (MIPI)

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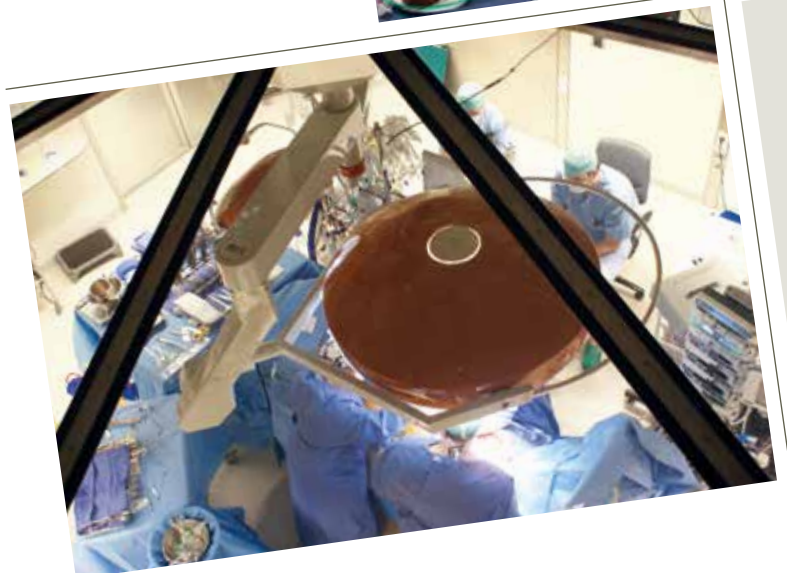
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Main study areas

Internal Medicine Specializations (INTG)

- **Endocrinology:** Thyroid disorders and infertility
- **Nephrology:** Hemodialysis, kidneylithiasis and medication injuries of the podocytes and proteinuria
- **Pneumology:** Lungmodels and ventilationdistribution, lungsaving radiation after breast amputation and nanoparticles in the context of aerosoltherapy
- **Research methodology and rheumatology:** Meta-analyses of hipfractures and European Male-Ageing study
- **Intensive medicine:** renal failure and renal function replacement therapy, indirect calorimetry for optimalisation of the nutrition policy in intensive care (IC) and new ventilation techniques in IC

The **Frailty in Ageing Research (FRIA)** department conducts a comprehensive research program to untangle the underlying mechanisms and to develop interventions for prevention and rehabilitation of frailty in the ageing.

- Effect of physical training on immunosenescence (inflammation, senescent cells), sarcopenia (age-related muscle atrophy), dynapenia (age-related muscle weakness) and cognition: Senior PROject Intensive Training (SPRINT)
- Effect of inflammation on sarcopenia and muscle weakness: intervention with anti-inflammatory products, role of infections in the elderly, role of Advanced Glycation End products (AGE).
- Identification and characterization of senescent cells: T-lymphocytes, influence of chemotherapy, influence of corticoids
- Motivational aspects of physical exercise and active ageing
- Early detection of dementia and mild cognitive impairment

The Research Group on **Emergency and Disaster Medicine (ReGEDiM-URGE)** conducts a research program focused on different aspects of both emergency and disaster medicine :

- **Emergency Medicine:** training, quality assessment and quality improve-

ment, Information Technology (IT)-applications, data-management and process-analysis, outcome predictors in emergency medicine, cardiopulmonary resuscitation, developments in medical imaging techniques, patient satisfaction and patient information, geriatric & pediatric emergency care (EC).

- **Disaster Medicine:** evidence-based disaster medicine, modelling and simulation of disasters and disaster medical management, disaster medical management, disaster mental health, disaster ethics.

Pediatrics (GRON)

- **Pediatric pneumology:** epidemiology/microbiology in otherwise healthy children (community acquired pneumonia (CAP) and persistent wheezing, CAP complicated with empyema) and in cystic fibrosis patients (CF) (Biofilm formation, *S. aureus*, Burkholderia cepacia, respiratory viruses), immunological response (Pertussis and Tuberculosis), new diagnostics in CF (Nasal potential differentials), new treatments in CF, and pharmacological studies (asthma medication, CF new treatments, evaluation of vaccines), and participation in several multicentric studies (infectiology, CF)
- **Pediatric gastroenterology:** milk allergy, gastro-oesophageal reflux and Crohn's disease
- **Pediatric hematology-oncology and immunology:** cooperation in international intervention studies in childhood cancers, studies concerning supportive care aspects in childhood cancer, studies in a coagulation disorders/immunoglobulin substitution therapy phase II trial, cooperation with several international partners for patient based research in primary immunodeficiencies, defects in the innate immune system, management of invasive fungal infections
- **Deontology & Ethics:** deontological, ethical and legal implications of the care for minors
- **Pediatric Nephrology:** study for Aliskiren in pediatric patients with hypertension
- **Neonatology:** cooperation in multicenter interventional randomized con-

trolled studies (e.g. SToP-BPD trial), cooperation with international studies on pharmacokinetics and pharmacodynamics of drugs in newborn infants (e.g. Pharmacool study), involvement in the international Cochrane Collaboration (meta-analysis, individual patient data meta-analysis)

MIPI - Microbiology and Infection Prevention:

- **Microbiology:** Diagnosis, treatment and epidemiology of infectious diseases, especially pertussis, diphtheria, legionellosis, Verotoxin-producing *E. coli* infections, new bacterial identification techniques, Burkholderia cepacia complex in cystic fibrosis patients, anaerobic infections & antibiotic sensitivity, HIV infection and AIDS, and congenital infections (cytomegalovirus (CMV), toxoplasmosis)
- **Infection Prevention:** surveillance and prevention of nosocomial infections
- **Ear, nose and throat:** Hearing loss and congenital CMV infection, sinusitis, assessment of the influence of nasal versus oral breathing on the craniofacial development.

The department of **Surgery (HEEL)** works in close collaboration with the Diabetes Center of the UZ Brussel:

- Neural influence in the resolution of type 2 diabetes mellitus after Roux-en-Y gastric bypass in patients with morbid obesity
- Clinical application of beta cells transplantation in type 1 diabetes
- Nutrition and cancer
- Research into the neurogenic influence through the nervus vagus on oxidative stress at the periphery (o.a. adipose tissue) and chronic inflammation in the metabolic syndrome
- Lymphedema & breastcancer
- Gastrointestinal Tumors (GIST): Analysis gene-mutation/ Open versus laparoscopic intervention

The department of **Anesthesiology and Perioperative Medicine (ANES)** conducts both experimental and clinical studies with respect to pathophysiology of pain, other inflammatory pathways (induced by

ischaemia, infarction, surgery, hypothermia) and pharmacokinetic and -dynamic studies of anesthetics.

- TRPV receptors on the aortamodel and in an in vivo model (animal research)
- Xenon anesthesia (in the context of inflammation experimental research and later clinical)
- Online lung aeration in ventilated patients (various protocols running consecutively)
- Thoroscopic ablation and postoperative pain
- Adjuvantia in local anesthetics
- Acute renal insufficiency (AKI) in postoperative patients
- Thoracic epidural analgesia and cardiac function in 1- and 2-lung ventilation
- Pharmacokinetics and pharmacodynamics of anesthetics

collaborations between research groups in specific projects

- Interaction of thyroid disorders with reproduction and pregnancy: INTG and GRON
- Infection in cystic fibrosis patients: INTG, GRON and MIPI
- Muscle weakness as a parameter at the arrival in EC: INTG, URGE and FRIA
- Lung models and ventilation distribution: age-related changes and pathology: INTG, GRON and FRIA
- Influence of medical and surgical treatment of pituitary disorders: INTG, HEEL and FRIA
- Pulmonary function in elderly participants of the Senior Project Intensive Training (SPRINT): FRIA and INTG
- Renal function in high risk surgery: INTG and ANES
- Influence of anti-inflammatory products on perioperative intervention: HEEL and FRIA
- Outcome of geriatric patients who needed endotracheal intubation in the pre-hospital and in-hospital setting: FRIA and URGE
- Connection between drug use and the functional status of the geriatric patient at the EC: URGE and FRIA
- Respiratory infections in children: MIPI and GRON
- Medication history reconciliation by

clinical pharmacists in patients admitted to the emergency department. (+ FARC): URGE and MIPI

- A philosophical and ethnographic study of medical diagnostics. Literature meets practice (INTG and URGE)
- Assessing and improvement of drawing procedure of blood cultures in the emergency department. (MIPI and URGE)
- Drug use review: empiric antibiotic therapy in the emergency department. (+FARC) : MIPI and Urge
- Pediatric aspects in emergency medicine: URGE and GRON
- Treatment of acute pain in the ER: URGE and ANES

Equipment & infrastructure

FRIA: Laboratory facilities and knowhow for

- Determination of markers of inflammation: circulating (cytokines, chemokines, heat shock proteins, ...), intracellular (heat shock proteins, senescence markers), surface markers in peripheral blood mononuclear cells
- Cell cultures
- Muscle biopsies
- Surface EMG
- Muscle performance
- Physical performance, reaction-time and cognitive testing

ReGEDiM-URGE: simulation and video-conference room for conducting modelling and simulation exercises and applied research in disaster medical management (hardware and software)

GRON: expertise and a fully equipped lungfunction laboratory for measurements of lungfunction in children, expertise and material for flexible and rigid bronchoscopy in children

MIPI: a full equipped laboratory for the different aspects of microbiology is available, including cell cultures for virology, molecular biology, L3 security lab for tuberculosis, MALDI-TOF mass spectrometry for identification of bacteria. For Ear, Nose and Throat research purposes, exten-

sive audiometrical equipment is present. Also, access to Cone-beam CT is available and close collaboration with the colleagues of the department of Orthodontics (SOPA) and their equipment is possible

HEEL: metabolic unit, indirect calorimetric measurements and most recent laproscopic techniques

ANES: PulmoVista 500 to evaluate ventilation adequacy at the bedside, availability of an anesthesia machine equipped to deliver Xenon

Industrial application fields

FRIA: Physical training programs specially designed for elderly persons

ReGEDiM-URGE: the research on simulation and modelling performed by the reseachgroup resulted in the industrial development of different software programs (ISEE®, XVR®, Victim Base®) who are distributed worldwide to emergency rescue services dealing with the acute medical response in mass casualty and disaster settings





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