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Cédric Blanpain
Université libre de Bruxelles

Stem cells and skin cancers

Our laboratory recently identified the cellular origin of the most frequents skin cancers in patients: the basal cell carcinoma and the squamous cell carcinoma. These cancer stem cells were identified using genetic mouse models. Our project consists in studying the role of stem cells in skin cancer initiation, growth and relapse after therapy. Using transcriptional profiling of skin cancer stem cells, we identified new markers expressed by these cells. Now, we will define the role of these markers in the regulation of cancer stem cells and malignant progression. We will also assess whether these novel biomarkers could be used as prognosis factors and/or as targets for the development of novel therapy for human epithelial cancer.

Alain Chariot
Université de Liège

Deciphering the roles played by IKKεin breast cancer

Breast cancer results in many cases from the constitutive activity of a family of proteins, the kinases. In particular, 15% of breast cancers are characterized by an amplification of the gene coding for the kinase IKKε. Our objective is to understand how the deregulated expression of IKKε leads to breast cancer by generating a mouse model that mimics this upregulation. This model will allow, among other things, identifying proteins that interact with IKKε. Our objective is to identify potential targets to design new therapeutic drugs to treat breast cancer.

Jean-François Collet
Université catholique de Louvain

Protein folding and protein repair in the cell envelope of Gram-negative bacteria

The cell envelope of Gram-negative bacteria, including several pathogenic species that are harmful to humans, is a permeability barrier which protects bacteria from various stresses, such as antimicrobial drugs. We still have a poor understanding of the mechanisms which govern envelope biogenesis and maintain its integrity. Our project consists in understanding the mechanisms by which envelope proteins are assembled. The proteins that are involved in envelope biogenesis are also attractive targets for the design of new antibiotics and anti-inflammatory drugs. Developing new antibiotics against Gram-negative bacteria is critical due to the rapidly rising number of antibiotic-resistant bacterial strains.

Pierre Coulie
Université catholique de Louvain

Functions of intratumoral lymphocytes.

Tumors often contain white blood cells called lymphocytes, which are the main players of our immune system. Some of these lymphocytes specifically recognize cancer cells and should kill them. But in many cases there is no killing, and this project aims at understanding the reasons for this defect. It can be particularly important for a new modality of anticancer treatment called 'immunotherapy', which increases the number and activity of antitumour lymphocytes, for example through vaccinations. The lymphocytes will be studied directly within samples of human tumours, or inside small tumour nodules reconstructed in the laboratory. In addition there will be a detailed analysis of a specialized subgroup of lymphocytes whose main function is to suppress the activity of neighbouring lymphocytes. Here the focus will be on the mechanism of this inhibition.

Carine Maenhaut
Université libre de Bruxelles

Molecular characterization of the physiopathology and progression of thyroid cancers.

Thyroid cancers comprise several well defined types, presenting different histologies and with variable rates of growth and biological aggressiveness. Our project aims at characterizing at the molecular level the physiopathology and progression of these different types of cancers. For this, we will integrate data from two complementary high throughput methodologies: gene expression profiles obtained by microarray and transcriptome sequencing. This molecular characterization will allow for defining new molecular markers for diagnosis, prognosis, response to treatment, and to identify novel potential therapeutic targets or individualized therapeutic approaches.

Pierre Maquet
Université de Liège

Characterization of genetic determinants of the individual variations in sleep and resilience to sleep loss in humans.

Numerous lifestyle and socioeconomic factors prevailing in industrialized societies promote the extension of working hours, shift work and jet lags and consequently tend to increasingly curtail or disrupt sleep periods. Daytime sleepiness becomes a frequent complaint and has important consequences not only in terms of quality of life, but also in relation to education, public health (traffic accidents, obesity and cardiovascular accidents) and economics. To come up with principled and optimal solutions to these issues, our research work aims at specifying certain genetic determinants of sleep/wake regulation and resilience to sleep deprivation.

Laurent Nguyen
Université de Liège

Molecular regulation of cerebral cortical neurogenesis.

The development of the cerebral cortex occurs in several stages including, neural proliferation, neuroblast migration and neuronal differentiation. Disruption of these steps often causes cortical malformations that lead to severe learning disabilities, mental retardation or epilepsy. Thus, untangling the mechanisms that control these cellular steps during the formation of the cortex is critical to understand the pathological events that contribute to the onset or the progression of some neurological disorders. The objective of our project is to elucidate new molecular pathways that regulate cerebral cortical neurogenesis with an emphasis on the contribution of cell–cycle independent properties of Cip/Kip proteins and specific postranscriptional/postranslational modifications of cytosolic substrates.

Etienne Pays
Université libre de Bruxelles

Cellular functions and medical applications of apolipoproteins L.

We propose to investigate the cellular functions and medical potential of a family of proteins termed apolipoproteins L. Two distinct perspectives are considered. On one hand, we will investigate the biological processes mediated by apolipoproteins L, focusing in particular on the role of apolipoproteins L1 in renal function. This could result in useful applications regarding end-stage renal disease. On the other hand, we have generated apolipoproteins L1 mutants that are able to efficiently kill the two pathogens Trypanosoma gambiense and T. rhodesiense, responsible for sleeping sickness in human and nagana in cattle. We propose to investigate the potential of this breakthrough in terms of both understanding the mechanism of resistance of T. gambiense to human serum, and fighting against both human and animal diseases caused by these parasites.

Pierre Roger
Université libre de Bruxelles

Regulation of CDK4 and CDK6 kinases in cell proliferation and cancer.

Cancer may result from abnormal control of cell proliferation. The various phases of the cell division cycle are orchestrated by a family of kinases, the cyclin-dependent kinases (CDKs). Our project aims at understanding novel mechanisms that control CDK4 and CDK6 which are critical in the regulation of the division cycle of normal and cancer cells. Our results have the potential (i) to identify new drug targets, (ii) to understand mechanisms of resistance to CDK-inhibitory drugs currently in clinical trials, and (iii) to improve the specificity of treatments and thus reduce their toxicity.

Stéphane Schurmans
Université de Liège

Analysis of the tumor suppressor potential of a new gene implicated in acute leukemia

We generated a mouse model of acute leukemia by genetically suppressing a new gene of interest in the laboratory. Our hypothesis is that this gene is a tumor suppressor, and that alterations in its structure or expression can lead to the development of hematopoietic and extra-hematopoietic tumors. Our objective is to analyze the tumor suppressor potential of this gene and to investigate if it represents a new tumoral marker and/or a new target for the treatment of cancer. For this, we will first generate additional genetically-modified mice to extend our preliminary results to extra-hematopoietic tissues. Second, we will analyze human tumor samples to detect alterations in gene structure and expression.

Benoît Van den Eynde
Université catholique de Louvain

Mechanistic studies of antigen processing and characterization of novel proteasome subtypes.

Cancer cells display on their surface specific markers, called antigens, which allow the immune system to distinguish them from normal cells in order to reject them. These markers are the targets of therapeutic cancer vaccines currently tested in patients. These antigens are displayed on the surface of cancer cells by specialized presenting molecules (HLA molecules) and derive from proteins located inside the cell. In our project, we will study how these antigens are extracted from the parental protein and are transported to the cell surface to be presented to the immune system. We will study various actors involved in this antigen processing pathway and, in particular, the proteasome, a particle responsible for intracellular protein degradation.

Pierre van der Bruggen
Université catholique de Louvain

Regulatory roles of galectins in the immune response.

We are trying to better understand why specialized cells of our immune system, the T lymphocytes, do not destroy cancer cells. Cancer cells often produce a molecule, named galectin-3, which sticks to T lymphocytes, thereby impeding their proper functioning. We have succeeded in treating inactive lymphocytes with “sugars”, which trap the galectin-3 and therefore release the receptors of T lymphocytes. One of these “sugars” will soon be tested in a clinical trial with cancer patients. In our project, we will test if, in addition to galectin-3, other galectins block the proper functioning of T lymphocytes, and we will try to find strategies to counteract the negative effects of galectins. We will also examine if the T lymphocytes that are inactive in other human diseases can be treated, and thus reactivated, with the same “sugars”.

Emile Van Schaftingen
Université catholique de Louvain

Faulty metabolite repair, a new view on enzyme specificity.

Enzymes of metabolism are less specific than usually thought. They may sometimes act on intracellular metabolites that resemble their physiological substrate and convert these metabolites to 'faulty' metabolites. In some cases, a faulty metabolite may be reconverted to a useful metabolite by a 'metabolite repair enzyme', preventing it to cause toxic effects such as serious neurological disorder. The goal of our project is to identify new metabolite repair enzymes and to establish their role. This will lead to a new vision of intermediary metabolism, and to an understanding of the role of enzymes with enigmatic function and of (neuro)metabolic disorders in which non classical metabolites accumulate.

Pierre Vanderhaeghen
Université libre de Bruxelles

Mechanisms of brain development and diseases using pluripotent stem cell technology.

The cerebral cortex is the most complex structure in our brain. It is the center of most higher brain functions, but also the target of many neurological diseases. In this project, we will study the mechanisms of cortical development in health and diseases, using novel pluripotent stem cell technologies developed in our laboratory. Our objectives are (i) to identify novel genes involved in cortical development, (ii) to use cortical neurons generated in the laboratory, in an experimental model of cell therapy for cortical disease, and (iii) to generate and study cellular models of human neurological diseases.

Miikka Vikkula
Université catholique de Louvain

Identification of new lymph/angiogenic genes by using next generation sequencing.

Vascular anomalies affect >10% of infants. The lesions are randomly localized (on the skin, intestines, brain etc), and may cause various functional deficiencies, be non-esthetic, and even cause bleeding. In our project, we will perform genetic analyses on vascular anomalies following the hypothesis that genetic changes play a role in the development of these lesions. For this, we will use the novel technique called next generation sequencing (NGS) to study the genome within surgically resected vascular anomaly lesions. The high resolution of the technology provides an efficient and rapid tool towards discovering predisposing genetic mechanisms and novel diagnostic markers.