F.M.R.E.
G.S.K.E.

Séance académique

Academische zitting

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28 mai - mei 2019

Prix scientifiques 2019 de la F.M.R.E.
Wetenschappelijke prijzen 2019 van de G.S.K.E.

→ Ernest Solvay prize – € 25.000

- **Lauréat/Laureaat: Prof. dr. Ir. Simon De Meyer, PhD (KU Leuven-KULAK)**

Neutrophil extracellular traps: novel targets for neuroprotection in stroke

Stroke is one of the leading causes of death and disability worldwide. Ischemic stroke is caused by a blood clot that blocks one or multiple arteries that provide blood to the brain. The sudden loss of blood circulation results in a local deficit of oxygen and nutrients, which leads to brain cell damage and corresponding loss of neurologic function. The main goal of acute treatment is to recanalize the occluded artery in order to reestablish blood flow in the affected brain tissue. Although timely recanalization of the occluded artery is fundamental to salvage threatened ischemic tissue, reperfusion of the ischemic territory can also exacerbate tissue damage, a process called reperfusion injury. Increasing evidence shows that ischemic stroke is "thrombo-inflammatory" disorder, involving a complex interplay between both thrombotic and inflammatory pathways. Our research is focused on neutrophil extracellular traps or NETs, which form an intriguing new link between thrombosis and inflammation. We investigate how NETs are involved in stroke neurodegeneration and how the degradation of already formed NETs, or the prevention of new NETs generation, can contribute to reduced brain damage.

The high medical and social burden of ischemic stroke is in strong contrast to the limited treatment options that are currently available. Our research can lead to novel treatment strategies that allow better removal of the occluding blood clot and better protection against subsequent reperfusion injury, both leading to less neurologic damage in stroke patients.

→ Prix Fonds Elisabeth Vreven prijs – € 15.000

- **Lauréat/Laureaat: Prof. Thomas Voets (KU Leuven)**

Unraveling the role of TRPM3 in neuropathic and inflammatory pain

Recent estimates indicate that about 1 million Belgians suffer from moderate-to-severe chronic pain. Chronic back pain, migraine, diabetic neuropathy, osteo-arthritis, cancer pain and chemotherapy-induced neuropathic pain are just a few examples of common conditions associated with persistent pain, representing a heavy burden for the patients. The analgesic drugs that are currently on the market provide insufficient pain relief in about 50% of patients, and the use of opioid painkillers is associated with a significant risk of tolerance, addiction and potentially fatal overdose. Therefore, there is a high unmet need for newer and safer treatments for pain.

In previous work, our research team has identified TRPM3, a member of the transient receptor potential family of cation channels as a key player in the pain pathway and a potential novel target for pain treatment. With the support of the Queen Elisabeth Medical Foundation for Neurosciences, we have established the role of TRPM3 in sensing acute heat, and obtained novel insights into the altered expression and regulation of TRPM3 in various models of inflammatory and neuropathic pain. Moreover, we and others have found that TRPM3 antagonists show analgesic efficacy in disease-relevant animal assays of ongoing pain and hypersensitivity, without obvious unwanted side-effects. Therefore, this research may form the scientific basis for the development of novel analgesic therapies based on inhibition of TRPM3 function.

→ Prix CBC Banque prijs – € 15.000

- **Lauréate/Laureate: Prof. dr. Veerle Baekelandt, PhD (KU Leuven)**

The role of α-synuclein aggregation, spreading and neuroinflammation in Parkinson's disease and related disorders

Misfolded protein aggregates are a common feature of several neurodegenerative diseases, although the major protein component and the affected brain regions differ for each neurodegenerative disorder. Synucleinopathies, including Parkinson's disease (PD), Dementia with Lewy bodies (DLB) and Multiple System Atrophy (MSA), are determined by the formation of αSYN-rich deposits but segregate in distinct pathological phenotypes and diagnostic criteria. However, why αSYN inclusions are found in diseases that present with different phenotypic traits remains unresolved. Recent findings propose that alpha-synuclein aggregates exist in structurally different conformations or 'strains', which might explain the clinical heterogeneity. Moreover, these diseases are accompanied by different neuroinflammation profiles in humans and in animal models.

In this project, we are studying the pathological and inflammatory effects of distinct alpha-synuclein aggregates, derived from the brains of PD, DLB and MSA patients, in advanced experimental rodent models. These new insights will contribute to early diagnosis, prevention and the development of novel therapeutic strategies for alpha-synuclein related disorders.

→ Prix Janine & Jacques Delruelle prijs – € 12.500

- **Lauréat/Laureaat: Prof. dr. Luc Leybaert, MD. PhD (UGent)**

Exploring the role of astroglial Cx43 hemichannels as therapeutic targets in stroke

Stroke is, like cancer and cardiovascular disease, associated with significant mortality. When not lethal, the disease significantly impacts the quality of life as a result of motor paralysis, speech defects and other neuronal defects. Ischemic stroke, caused by the obstruction of blood flow due to a thrombus, accounts for

the majority of cases. Current therapy is based on administration, within 3-4h after the first symptoms, of tissue plasminogen activator (tPA) to dissolve the clot or within the first 6h by endovascular mechanical clot retrieval. Only a limited fraction of patients are eligible to receive such treatments and there is a strong need for novel therapeutic options. In the core of the brain infarct, cells die off by necrosis; by contrast, in the penumbra zone around the infarct, the brain tissue is at risk for delayed cell death and infarct expansion. The cornerstone of therapy is to prevent infarct expansion into the penumbra zone, but extensive research work has demonstrated that therapeutic strategies based on targeting single neuronal or vascular-based mechanisms have failed in human studies. Here, we targeted astrocytes, which are star-shaped glial cells characterized by a high expression of connexin proteins. Connexins form gap junctions that connect astrocytes with each other, but also form hemichannels that open under ischemic conditions, forming non-selective leakage pores that disturb astrocyte function and enhance inflammation. In collaborative work involving researchers at the Fred Hutchinson Cancer Research Centre, Seattle, USA and the University of British Columbia, Vancouver, Canada, we tested the effect of hemichannel block in a mouse model by genetic and peptide-based approaches, and found that this significantly reduced infarct size and glial scar, and improved functional recovery. Our work demonstrates that targeting connexin hemichannels has astrocyte-linked neuroprotective effects, opening up new research lines directed to investigating combined neuro-glio-vascular approaches aiming to maximize treatment benefits.

Conférence/Conferentie

- **Par/Door prof. Richard Frackowiak**
  “Advances in Human Brain Studies with Neuroimaging”

The human brain is massively redundant in its organisation. When brain systems are damaged, or when reinforced by learning mechanisms, they reorganise by a variety of methods including strengthening or renewing synaptic connections, or by engaging new pathways or constituent brain regions in the learning and recovery processes. Clinical scientists have deployed novel, quantitative MR imaging protocols to track such differential changes by using new, non-linear, multi-variate analytical and statistical methods to explore whether human imaging patterns improve complex brain image classification and hence diagnostic or prognostic precision. The results are encouraging.

The eventual ambition is to link genetic, proteomic, electro-physiological, biochemical and clinical features of many patients within a standardised anatomical framework. In the end, the aim is a rewriting of diagnostic manuals that seeks to classify diseases in clinical-biological terms. Implications for personal privacy and other ethical issues resulting from this strategy will be discussed. Recent advances in terms of how diagnostic accuracy, prognosis and personal therapeutics will result from such a strategy and a description of state-of-the-art will be presented with reference to the dementias.

Frackowiak RSJ, Markram H. (2015) The future of human cerebral cartography: a novel approach. Phil. Trans. R. Soc. B 370: 20-32.

Programme/Programma

15:00

→ **Introduction/Inleiding**
- Monsieur/de Heer Hein Deprez
  Président du conseil d'administration/Voorzitter van de raad van bestuur

→ **Présentation et remise des prix scientifiques de la F.M.R.E. 2019/ Voorstelling en uitreiking van de wetenschappelijke prijzen G.S.K.E. 2019**
- Prix Ernest Solvay prize prijs
  - Présentation/Voorstelling
  - Remise du/Overhandiging van de Ernest Solvay prize
  - S.A.R. la Princesse Astrid/H.K.H. Prinses Astrid, Monsieur/de Heer Jean-François Misonne & Monsieur/de Heer Hein Deprez

- Prix Fonds Elisabeth Vreven prijs
  - Présentation/Voorstelling
  - Remise du prix/Overhandiging van de Fonds Elisabeth Vreven prijs
  - S.A.R. la Princesse Astrid/H.K.H. Prinses Astrid, Monsieur/de Heer Fernand de Donnea & Monsieur/de Heer Hein Deprez

- Prix CBC Banque prijs
  - Présentation/Voorstelling
  - Remise du prix/Overhandiging van de CBC Banque prijs
  - S.A.R. la Princesse Astrid/H.K.H. Prinses Astrid, Monsieur/de Heer Clemens Scholzen & Monsieur/de Heer Hein Deprez

- Prix Janine & Jacques Delruelle prijs
  - Présentation/Voorstelling
  - Remise du prix/Overhandiging van de Janine et Jacques Delruelle prijs
  - S.A.R. la Princesse Astrid/H.K.H. Prinses Astrid, le Baron et la Baronne Delruelle & Monsieur/de Heer Hein Deprez

→ **Conférence/Conferentie**
- Prof. Richard Frackowiak
  Advances in Human Brain Studies with Neuroimaging

→ **Receptie/Réception**