Inserm
Délégation régionale
Midi-Pyrénées, Limousin

UMR 1048 (I2MC)
Equipe 14

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Rôle des Peptides Bioactifs dans le Remodelage Cardiaque lié à l'Obésité

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Objectif scientifique

Obesity-related cardiac remodeling is associated with dysregulation of several peptide-secreting systems. The main focus of our work is to understand how cardiac cells respond to bioactive factors to contribute to remodeling processes, and thereby to heart adaptation or disease. Our most recent research has centered on the role of two biologically active peptides, apelin and galanin.
Apelin is produced by the adipose tissue and plays an important and beneficial role in regulating cardiovascular and metabolic homeostasis. Previously, we have shown that apelin prevents oxidative stress and hypertrophic responses in cardiac cells. We have recently demonstrated that the transition from compensated hypertrophy to heart failure is characterized by defective myocardial energy metabolism and mitochondrial defects. Furthermore, apelin is able to prevent such myocardial metabolic abnormalities and mitochondrial dysfunction.
Our interest for galanin is more recent but gave already very promising results. Galanin is a bioactive peptide hormone that regulates the numerous physiological processes such as food intake, memory, the neuroendocrine function, gut secretion, and motility. In the cardiovascular system, galanin has important vasoactive effects and galanin expression is elevated significantly in cardiac sympathetic neurons after myocardial infarction. More recent study has reported that galanin may directly affect glucose metabolism in cardiac and skeletal muscles suggesting that the galaninergic system may play an important role in metabolic and cardiovascular homeostasis. Unlike apelin, for which the role in prevention of ROS-dependent oxidative damage has been reported by our group, the potential role of galanin in the regulation of ROS production in obesity-related heart disease remains to be defined.

Retombées attendues en santé

The direction of our research is driven by three specific objectives: 1) to determine the role of bioactive peptides in the regulation of cardiac remodeling processes during the transition from hypertrophy to heart failure in obesity; 2) to delineate the cellular and molecular mechanisms governing cardiac cell responses to bioactive peptides in obesity-related myocardial remodeling; 3) to develop new preventive and therapeutic strategies for obesity-related cardiometabolic complications.

Mots clés

Cardiac remodeling, obesity, bioactive peptides, myocardial infarction, cardiac hypertrophy, heart failure

Formation à la recherche

Master in Research Physiopathology, Innovation in Pharmacology from the Doctoral School Biologie Santé Biotechnologies of Toulouse; PhD Students, MD students, BTS.

Coopérations / Partenariats

- Dmitry Pchejetski: Norwich Medical School, University of East Anglia, UK

- Vadim Sumbayev: Medway School of Pharmacy, University of Kent, UK

- Elizaveta Fasler-Kan: Department of Pediatric Surgery and Department of Clinical research, Universität Bern , Bern, Switzerland ·
- Assia Shisheva: Wayne State University's School of Medicine, Detroit, USA

- Christophe Dejugnat: IRMCP, Université Paul Sabatier, Toulouse, France

- Oleg Pisarenko: Russian Cardiology Research-and-Production Complex, Moscow, Russia

- Minodora Mazur: Université d'Etat de Médecine et Pharmacie Nicolae Testemitanu, Chisinau, Moldavie

Principales publications du laboratoire

1. Timotin, A. et al. Myocardial protection from ischemia/reperfusion injury by exogenous galanin fragment. Oncotarget 8, 21241?21252 (2017).
2. Tronchere, H. et al. Inhibition of PIKfyve prevents myocardial apoptosis and hypertrophy through activation of SIRT3 in obese mice. EMBO Mol Med 9, 770?785 (2017).
3. Boal, F. et al. Apelin-13 administration protects against ischaemia/reperfusion-mediated apoptosis through the FoxO1 pathway in high-fat diet-induced obesity. Br. J. Pharmacol. 173, 1850?1863 (2016).
4. Boal, F. et al. Apelin regulates FoxO3 translocation to mediate cardioprotective responses to myocardial injury and obesity. Sci Rep 5, 16104 (2015).
5. Pisarenko, O. et al. Structural apelin analogues: mitochondrial ROS inhibition and cardiometabolic protection in myocardial ischemia-reperfusion injury. Br J Pharmacol (2014). doi:10.1111/bph.13038
6. Alfarano, C. et al. Transition from metabolic adaptation to maladaptation of the heart in obesity: role of apelin. Int J Obes 39, 312?320 (2014).
7. Pchejetski, D. et al. Apelin prevents cardiac fibroblast activation and collagen production through inhibition of sphingosine kinase 1. Eur Hear. J 33, 2360?2369 (2012).

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Role of Bioactive Peptides in Cardiac Remodeling related to Obesity

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Scientific objective

Obesity-related cardiac remodeling is associated with dysregulation of several peptide-secreting systems. The main focus of our work is to understand how cardiac cells respond to bioactive factors to contribute to remodeling processes, and thereby to heart adaptation or disease. Our most recent research has centered on the role of two biologically active peptides, apelin and galanin.
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Expected health effects

The direction of our research is driven by three specific objectives: 1) to determine the role of bioactive peptides in the regulation of cardiac remodeling processes during the transition from hypertrophy to heart failure in obesity; 2) to delineate the cellular and molecular mechanisms governing cardiac cell responses to bioactive peptides in obesity-related myocardial remodeling; 3) to develop new preventive and therapeutic strategies for obesity-related cardiometabolic complications.

Key words

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Research training

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