# PANACHE NEWSLETTER

ISSUE #8

## editorial

Dear Reader,

Welcome to the eighth issue of the PANACHE newsletter!

PANACHE stands for "*Production of next generation modulators of pannexins and connexins as novel therapeutics in the treatment of inflammatory cardiovascular, hepatic and joint disease*". PANACHE is a multidisciplinary collaborative project funded by the European Commission's Horizon 2020 Future and Emerging Technologies (FET) programme and aims at the development of new anti-inflammatory drugs for the treatment of cardiovascular, liver and joints diseases. The project is now entering the crucial stage, the *in vivo* evaluation stage.

Through this newsletter, we invite you to learn more about the project, including its researchers, activities and events. Stay tuned to PANACHE by subscribing to our newsletter, by visiting our webpage and by following us on Twitter, Instagram, Facebook and LinkedIn.

We hope you will enjoy the new edition of the PANACHE newsletter!

The PANACHE consortium.

## in this issue

# about PANACHE

## PANACHE is a multidisciplinary international project that aims at the development of new anti-inflammatory drugs

The modulation of membrane-bound proteins by drugs is receiving increasing attention from both academia and industry. Among such proteins are pannexin1 (Panx1), connexin (Cx) 43 and Cx32 that form channels at the plasma membrane surface. These connexin hemichannels and pannexin channels mediate cellular communication and have emerged as key players in inflammation. This carries translational relevance, as connexin hemichannel and pannexin channel inhibition could represent an innovative strategy for the treatment of a plethora of diseases. However, a hurdle in clinical exploration is the lack of appropriate connexin hemichannel and pannexin channel inhibitors.

PANACHE therefore is a timely project, since it will deliver a novel generation of connexin hemichannel and pannexin channel inhibitors as potential drugs. This is accomplished by joining academic and industrial scientists from the chemical, chemo-informatics and biomedical fields, as well as by relying on *in vitro* and *in silico* studies, animal experimentation and testing human material.

PANACHE allows taking a leap forward to the realization of its long-term vision, namely the production of metabolically robust and selective connexin hemichannel and pannexin channel inhibitors that can be used for the establishment of a generic approach to synergize current therapy of hard-to-treat inflammatory diseases.

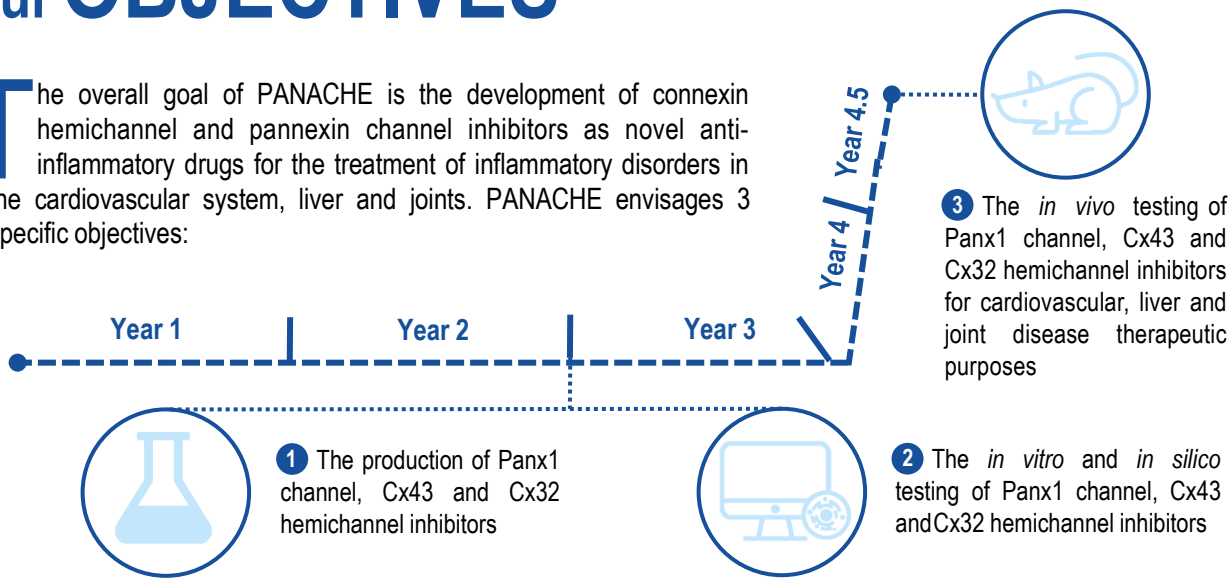

# our VISION

The long-term vision of PANACHE is the production of an unprecedented set of connexin hemichannel and pannexin channel inhibitors that can be used for the establishment of a mechanistically-anchored and generic approach to synergize current therapy of hard-to-treat inflammatory diseases. For proof-of-concept purposes, focus is put on inflammatory disorders in the cardiovascular system, liver and joints.

The scope of PANACHE is, however, much broader, as these innovative connexin hemichannel and pannexin channel inhibitors are anticipated to be equally applicable for the therapy of a number of other inflammatory disorders in which Panx1 channels, Cx43 and Cx32 hemichannels are known to be involved. Such applications will be tested in follow-up initiatives of PANACHE, thereby realizing its long-term vision.

# our OBJECTIVES

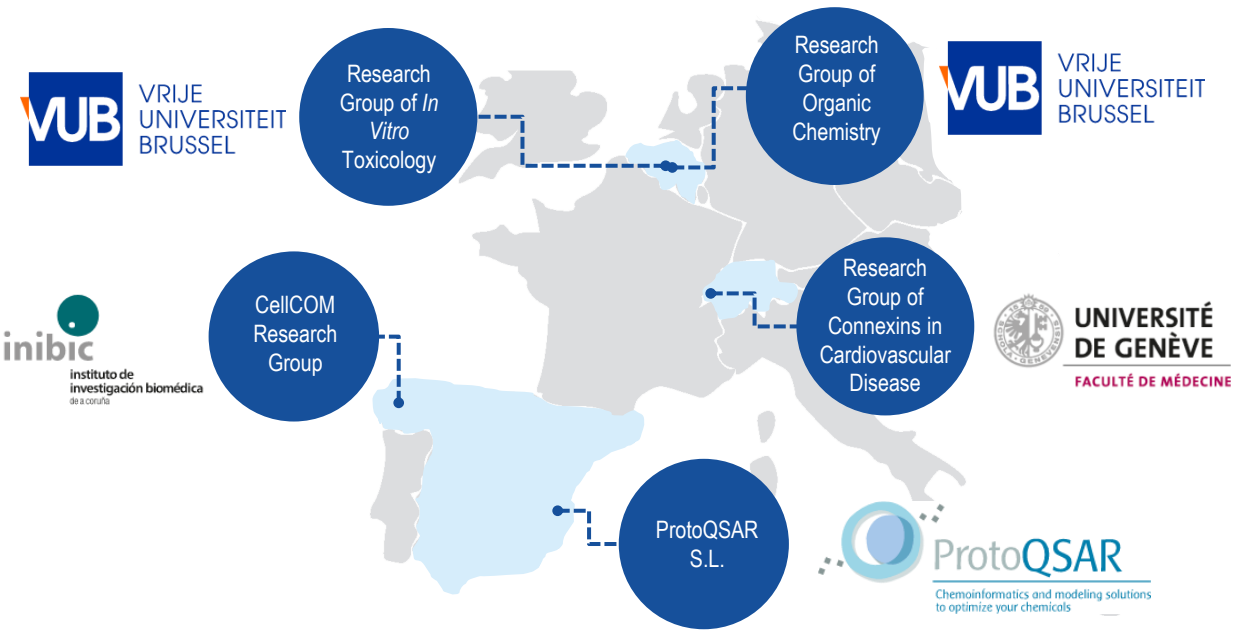
The overall goal of PANACHE is the development of connexin hemichannel and pannexin channel inhibitors as novel anti-inflammatory drugs for the treatment of inflammatory disorders in the cardiovascular system, liver and joints. PANACHE envisages 3 specific objectives:




# the CONSORTIUM

The PANACHE consortium consists of 4 academic partners and 1 industrial partner from 3 European countries (Belgium, Spain and Switzerland). The consortium is coordinated by the Research Group of *In Vitro* Toxicology of the Vrije Universiteit Brussel (VUB)-Belgium. The consortium joints experts in 3 different disciplines, namely bio-organic chemistry (VUB Research Group of Organic Chemistry), chemo-informatics (ProtoQSAR S.L.) and biomedical research, as well as 3 biomedical subdisciplines, in particular cardiovascular (UNIGE Research Group of Connexins in Cardiovascular Disease), liver (VUB Research Group of *In Vitro* Toxicology) and joint research (CellCOM Research Group).

**To learn more about the consortium members please visit www.panache-project.eu**



# PI in the spotlight

For all of you who want to know more about the principal investigators (PI) of the PANACHE consortium, this is the right place! In this section, a series of interviews with the principal investigators of the consortium will be published. This newsletter features Prof. Mathieu Vinken.

## Mathieu Vinken – VUB

"PANACHE will deliver the next generation of young researchers that have been trained in a 3I context, which will highly benefit their future employability and career perspectives."

### ▸ Can you shortly introduce yourself?

I am Mathieu Vinken (Belgian; born 1 February 1978), professor affiliated with the Vrije Universiteit Brussel-Belgium. I have a background in pharmaceutical sciences, hold a doctoral degree in the field of toxicology and I am a European registered toxicologist. My research focus is situated in the fields of experimental hepatology (connexin hemichannels and pannexin channels as drug targets and biomarkers for the therapy and diagnosis of liver disease), *in vitro* toxicology (mechanistic modelling of liver toxicity as the basis for the development of liver-based *in vitro* systems) and space toxicology (adverse effects of pharmaceutical drugs in astronauts).

### ▸ What is your expertise and role in PANACHE?

I act as coordinator of the PANACHE project, which implies that I am responsible for the overall management of the consortium, follow-up of the scientific work, communication, dissemination, exploitation, monitoring of financial and administrative aspects as well as for the interaction with the scientific advisory board and the European Commission. Furthermore, my team at the Vrije Universiteit Brussel-Belgium is responsible for all the practical work that relates to liver pathology in PANACHE, including both *in vitro* (cell culture testing) and *in vivo* (animal experimentation) studies.

### ▸ What would be the main achievement or impact of PANACHE in your opinion?

First and foremost, the scientific breakthrough of PANACHE will be the production of a novel generation of inhibitors of connexin hemichannels and pannexin channels that act in a target-specific way and that are applicable for clinical purposes. These compounds will also be of use in fundamental research. In addition, PANACHE will deliver the next generation of young researchers that have been trained in a 3I (international, interdisciplinary and intersectoral) context, which will highly benefit their future employability and career perspectives.

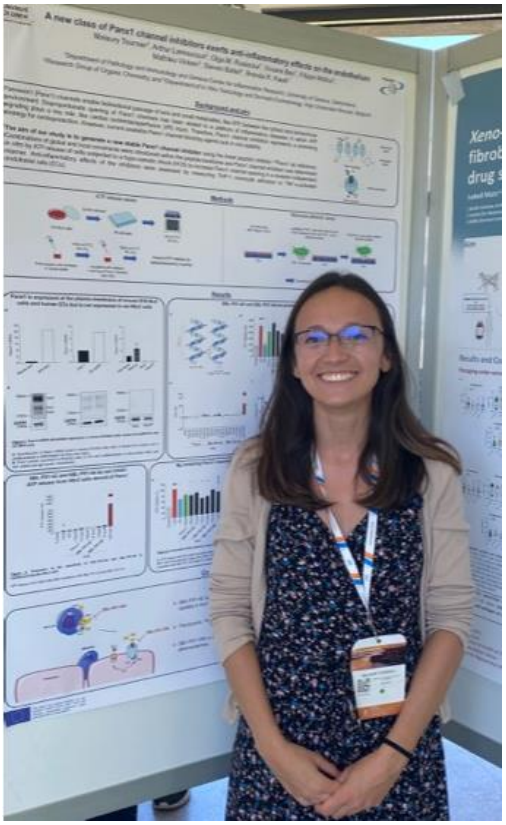
**Prof. Mathieu Vinken in a nutshell**

- **Nationality:** Belgian
- **Academic degrees:** Pharmacist and doctoral degree in pharmaceutical sciences
- **Current position:** Professor at the Vrije Universiteit Brussel
- **Role in PANACHE:** Coordinator and leader of the liver pathology work package
- **Contact:** Mathieu.Vinken@vub.be

# LATEST event

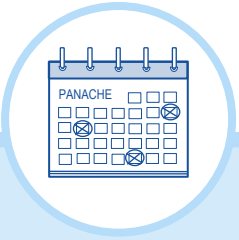
## 37th Annual Meeting of the International Society for Heart Research European Section

The 37th Annual Meeting of the International Society for Heart Research European Section (ISHR-ES) took place in Porto, Portugal from the 10th to the 13th of July 2023. The congress was chaired by Prof. Mauro Giacca, Prof. Paula da Costa Martins and Prof. Inês Falcão Pires and reunited junior and senior researchers involved in research on the cardiovascular system and metabolism as well as on cardioprotection. Of particular interest, one session was dedicated to cellular communication and cardiac diseases during which Prof. Brenda R Kwak (group leader of the research group "Connexins and pannexins in cardiovascular diseases" at UNIGE) presented a new role of mitochondrial Panx1 channels in cardiac ischemia/reperfusión injury. Noteworthy, Malaury Tournier (a member of the same research group) presented a poster titled "A new class of Panx1 channel inhibitors exerts anti-inflammatory effects on the endothelium" resulting from a collaborative study of ORGC-UNIGE fully conducted in the framework of the PANACHE research program.



On the picture: Malaury Tournier (from the UNIGE team) presenting the poster titled "A new class of Panx1 channel inhibitors exerts anti-inflammatory effects on the endothelium" at the 37th Annual Meeting of ISHR-ES 2023.

# UPCOMING event




## International Gap Junction Conference

**When**: 27/07-31/07/2024
**Where**: Arlington, Virginia, United States
**Organizers**: **Prof. Silvia Penuela** – University of Western Ontario, London Ontario, Canada; **Prof. Jamie Smyth** – Fralin Biomedical Research Institute at VTC, Virginia, United States

**Stay tuned to our social media to keep track of the latest details of the event**

# STAY tuned

For all of you who want to know more about connexin hemichannels and pannexin channels, this is your section! You will find a selection of relevant publications and conference communications published and presented by, but not limited to, PANACHE consortium members.

## (NON-)CONSORTIUM publications

frontiers

Van Campenhout *et al.* **(IVTD)**

**Pannexin1 channels in the liver: an open enemy**

Click here to read more

BIO-ORGANIC CHEMISTRY

Caufriez *et al.* **(IVTD-ORGC)**

**Determination of structural features that underpin the pannexin1 channel inhibitory activity of the peptide $^{10}$Panx1**

Click here to read more

Journal of Medicinal Chemistry

Lamouroux, Tournier *et al.* **(ORGC-UNIGE)**

**Structure-Based Design and Synthesis of Stapled $^{10}$Panx1 analogues for Use in Cardiovascular Inflammatory Diseases**

Click here to read more

BIOCHEMICAL SOCIETY TRANSACTIONS

Wu, Yang *et al.*

**Recent advances in the structure and activation mechanisms of metabolite-releasing Pannexin 1 channels**

Click here to read more

Cardiovascular Research
Published since 1967

Rusiecka *et al.* **(UNIGE)**

**Mitochondrial pannexin1 controls cardiac sensitivity to ischaemia/reperfusion injury**

Click here to read more

MOLECULAR CANCER THERAPEUTICS

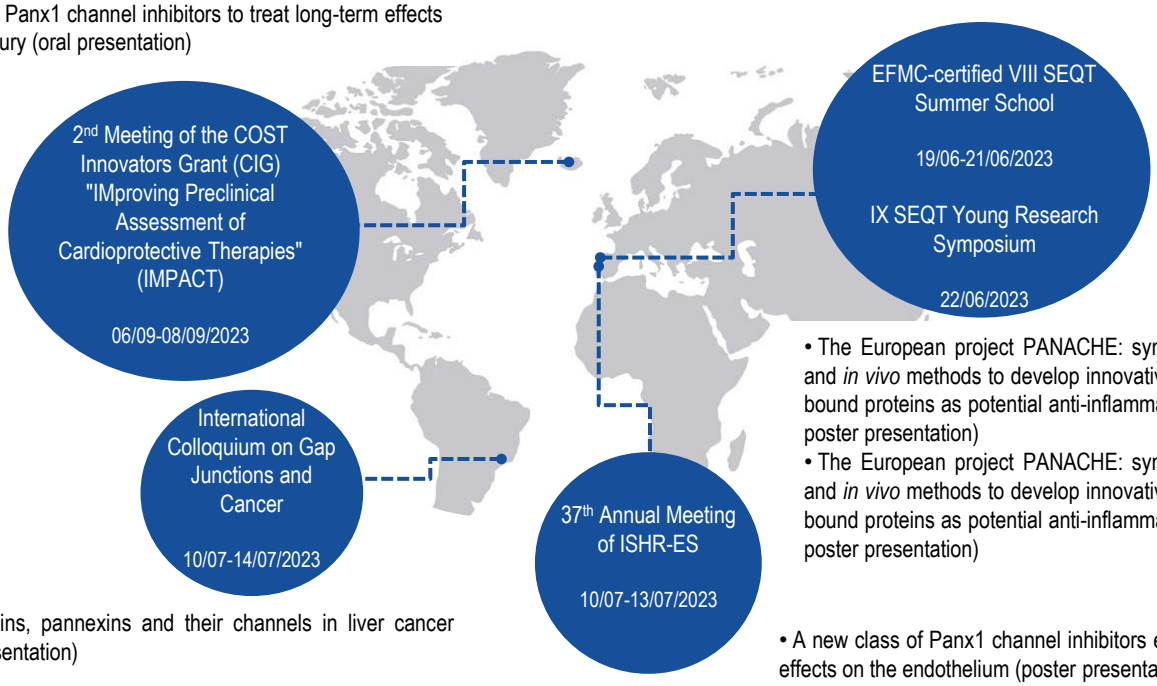
Mulkearns-Hubert *et al.*

**Targeting NANOG and FAK via Cx26-derived cell-penetrating peptides in triple-negative breast cancer**

Click here to read more

## CONSORTIUM conference communications

• A new class of Panx1 channel inhibitors to treat long-term effects of myocardial injury (oral presentation)




• The European project PANACHE: synergizing *in silico*, *in vitro*, and *in vivo* methods to develop innovative inhibitors of membrane-bound proteins as potential anti-inflammatory drugs (short oral and poster presentation)

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• Connexins, pannexins and their channels in liver cancer (oral presentation)

• A new class of Panx1 channel inhibitors exerts anti-inflammatory effects on the endothelium (poster presentation)

# KEEPING UP WITH PANACHE!

Stay tuned to our latest news, results and activities

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