

PANACHE NEWSLETTER

ISSUE
#7



editorial

Dear Reader,

Welcome to the seventh 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!

in this issue

- 1 Editorial
- 2 About PANACHE
- 2 Our vision
- 3 Our objectives
- 3 The consortium
- 4 PI in the spotlight
- 5 Latest event
- 5 Upcoming event
- 6 Stay tuned

The PANACHE consortium.

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 (hemi)channels at the plasma membrane surface. These connexin and pannexin (hemi)channels mediate cellular communication and have emerged as key players in inflammation. This carries translational relevance, as connexin and pannexin (hemi)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 and pannexin (hemi)channel inhibitors.

PANACHE therefore is a timely project, since it will deliver a novel generation of connexin and pannexin (hemi)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 and pannexin (hemi)channel inhibitors that can be used for the establishment of a generic approach to synergize current therapy of hard-to-treat inflammatory diseases.



4.5 years

1 March 2020 - 31 August 2024



3.5 million €

3.503.628,75€ budget



5 partners

1 industrial and 4 academic partners



3 countries

Belgium, Spain, Switzerland

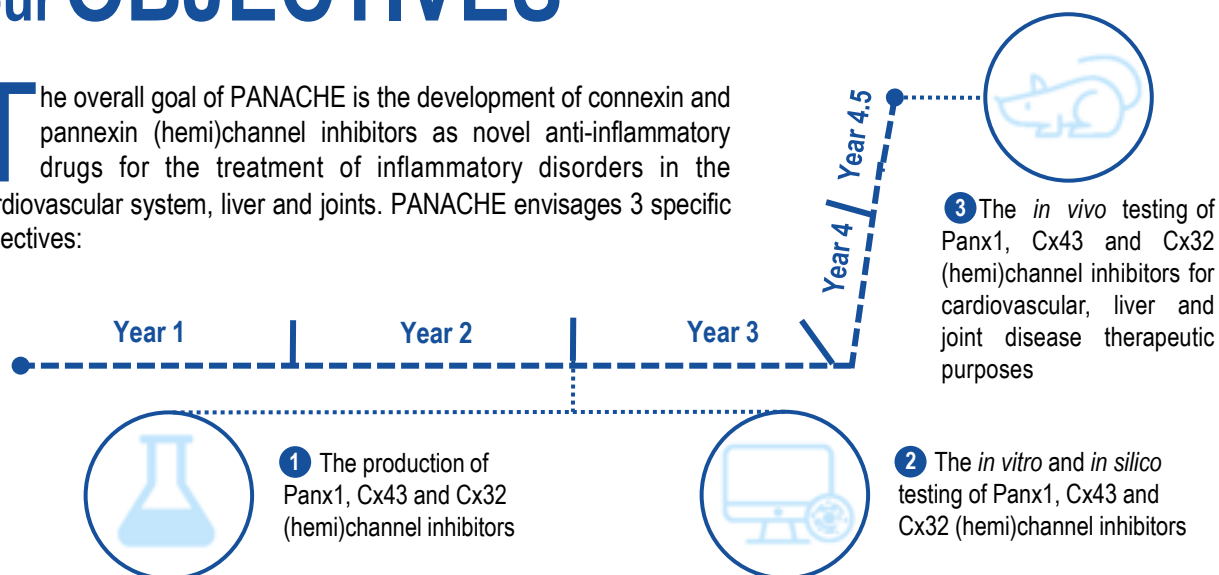
our VISION

The long-term vision of PANACHE is the production of an unprecedented set of connexin and pannexin (hemi)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 and pannexin (hemi)channel inhibitors are anticipated to be equally applicable for the therapy of a number of other inflammatory disorders in which Panx1, Cx43 and Cx32 (hemi)channels 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 and pannexin (hemi)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:

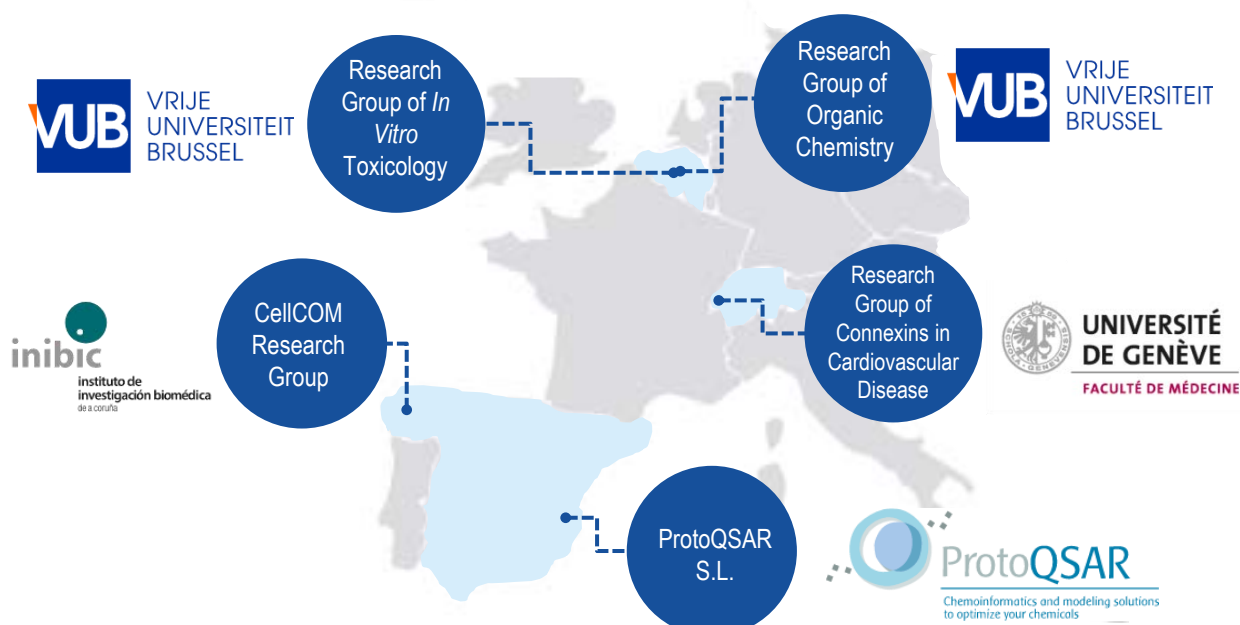


the CONSORTIUM

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. Brenda R. Kwak.

Brenda R. Kwak - UNIGE

'Specific and stable connexin and pannexin (hemi)channel inhibitors are an urgent need in our research field to further the knowledge on these fascinating channels.'

► Can you shortly introduce yourself?

I am a full professor and director of the Department of Pathology and Immunology at the Faculty of Medicine of the University of Geneva in Switzerland. I was born in the Netherlands. After my medical studies at the University of Amsterdam, I joined the gap junction research field as a PhD student in 1988 and have not left it since. In 2003, I established my research group in Switzerland supported by a Swiss National Science Foundation professorship. My research principally focuses on the role of connexins/pannexins in cardiovascular diseases with a strong immunoinflammatory component. More recently, I have extended my research interests towards translational research investigating the role of biomechanical forces in the initiation, growth and rupture of intracranial aneurysms, an important neurovascular disease.

► What is your expertise and role in PANACHE?

I have always been interested in "how the body functions". Research in cardiovascular pathophysiology was thus a logical career choice and I have worked throughout my career on different aspects in this field, ranging from cellular electrophysiology, to organ physiology as well as pathophysiology in sophisticated animal models. This diverse expertise is important for the PANACHE project as a whole, even though our laboratory mainly focuses on cardiovascular inflammation in the context of this project.

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

The PANACHE project aims to generate a novel set of



Prof. Brenda R. Kwak in a nutshell

- Nationality:** Dutch and Swiss
- Academic degrees:** PhD in medical physiology
- Current position:** Full professor at the University of Geneva
- Role in PANACHE:** cardiovascular pathophysiology
- Contact:** brenda.kwakchanson@unige.ch



connexin and pannexin (hemi)channel inhibitors to treat cardiovascular, liver and joint inflammatory diseases. It would be a main achievement of this consortium if we have produced at least one compound able to ameliorate the course of a maladaptive inflammatory response in an animal model by the end of the project (August 2024). The development of specific and stable connexin and pannexin (hemi)channel inhibitors represents an urgent need in our research field to further the knowledge on these fascinating channels.

LATEST event

21st conference of the European Society for Toxicology *In Vitro*

The 21st International Congress of the European Society of Toxicology *In Vitro* (ESTIV 2022) was held in Sitges, Spain, from November 21 to 25 2022, after being postponed in 2020. The conference, chaired by Helena Kandárová, brought together junior and senior researchers and toxicologists involved in the development and use of *in vitro* and *in silico* approaches. Noteworthy, Axelle Cooreman (part of the Research Group of *In Vitro* Toxicology) received the best oral

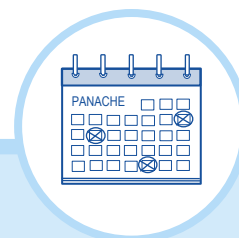
presentation award, granted by the Japanese Society for Alternatives to Animal Experiments (JSAAE) for her presentation titled “Effects of drugs formerly repurposed for COVID-19 treatment on connexin43 hemichannels and pannexin1 channels”. Another member of IVTD, Kaat Leroy, received the best poster presentation award granted by the JSAAE for her poster titled “Connexin-based channel activity is not specifically altered by hepatocarcinogenic chemicals”.



Left: Awards winners of the 21st International Congress ESTIV, flanked by Helena Kandárová.

Right: Axelle Cooreman and Kaat Leroy with Yasunari Kanda (Japanese Society for Alternatives to Animal Experiments) and Helena Kandárová.

UPCOMING event



23rd GFPP Meeting on Peptides and Proteins

When: 17-21 September 2023

Where: Fournols, France

Organizers: **Sophie Faure** - Institut de Chimie de Clermont-Ferrand, Université Clermont Auvergne, France; **Grégory Chaume** - Laboratoire Biomolécules, CY Cergy Paris Université, France; **Simon Gonzalez** - Laboratoire BioCIS, CY Cergy Paris Université, France; **Oliver Roy** - Institut de Chimie de Clermont-Ferrand, Université Clermont Auvergne, France; **Cassandra Guerinot**, Institut de Chimie de Clermont-Ferrand, Université Clermont Auvergne, France; **Nathan Picois** - Laboratoire Biomolécules, CY Cergy Paris Université, France.

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 and pannexin (hemi)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

nature communications *Lee et al.*

Conformational changes in the human Cx43/GJA1 gap junction channel visualized using cryo-EM

[Click here to read more](#)

nature communications *Zhang et al.*

Cryo-EM structure of human heptameric pannexin 2 channel

[Click here to read more](#)

TOXICOLOGY *Yang et al.*

Connexin hemichannels and pannexin channels in toxicity: Recent advances and mechanistic insights

[Click here to read more](#)

frontiers *Rusiecka et al. (UNIGE)*

Pannexin1 channels—a potential therapeutic target in inflammation

[Click here to read more](#)

antioxidants *Gomes Espírito Santo et al. (IVTD)*

The Implications of Connexin 43 Deficiency during the Early Stages of Chemically Induced Mouse Colon Carcinogenesis

[Click here to read more](#)

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

Effects of acute and chronic disease on cell junctions in mouse liver

[Click here to read more](#)

CONSORTIUM conference communications

•Peptidomimetic inhibitors of connexin43 hemichannels (poster)

24th Merck Organic Synthesis Symposium
01/12-02/12/2022

- Effects of drugs formerly repurposed for COVID-19 treatment on connexin43 hemichannels and pannexin1 channels (oral communication)
- Connexin-based channel activity is not specifically altered by hepatocarcinogenic chemicals (poster)

21st Conference of the European Society for Toxicology *in Vitro*
21/11-25/11/2022

Unionstagung der Schweizerischen Gesellschaften für Gefäßkrankheiten
02/11-04/11/2022

- Stapled ¹⁰Panx1 analogs as a new class of anti-inflammatory Panx1 channel inhibitors (Flash presentation + poster)
- Panx1 as a new target for prevention of cardiac ischemia-reperfusion injury (Flash presentation + poster)



KEEPING UP WITH PANACHE!

Stay tuned to our latest news, results and activities



www.panache-project.eu



@FET_PANACHE



PANACHE



@fet_panache



FET project PANACHE



Funded by the Horizon 2020 Framework Programme of the European Union

This project has received funding from the European Commission's Horizon 2020 Future and Emerging Technologies programme under grant agreement number 858014