

PANACHE NEWSLETTER

ISSUE
#9



editorial

Dear Reader,

Welcome to the ninth 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 and hepatic diseases*”. 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 and liver diseases. The project is now in a crucial stage, the *in vivo* evaluation stage.

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

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

The PANACHE consortium.

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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 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.



5 years

1 March 2020 - 28 February 2025



3.5 millions €

3.503.628,75€ budget



4 partners

1 industrial and 3 academic partners



3 countries

Belgium, Spain, Switzerland

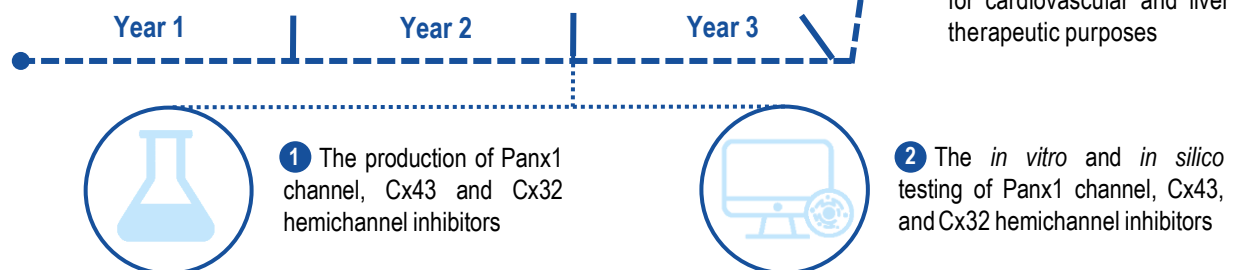
our VISION

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, the focus is put on inflammatory disorders in the cardiovascular system and liver.

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 and liver. PANACHE envisages 3 specific objectives:

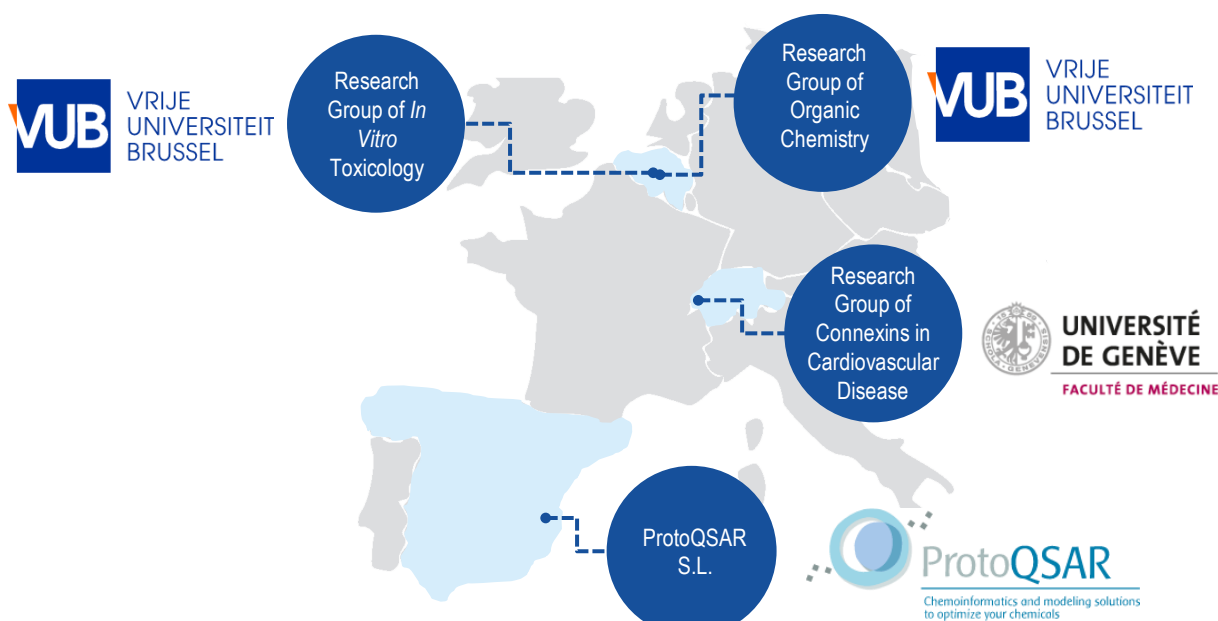


the CONSORTIUM

The PANACHE consortium consists of 3 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, including 2 biomedical subdisciplines, in particular cardiovascular (UNIGE Research Group of Connexins in Cardiovascular Disease) and liver (VUB Research Group of *In Vitro* Toxicology).

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. Steven Ballet.

Steven Ballet – VUB

‘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?

My name is Steven and I have been the head of the Research Group of Organic Chemistry at the VUB since 2010. I did my PhD research there, graduating in 2007 and afterwards, I undertook two postdoctoral research stays: the first in Australia with Andrew Abell and the second in Canada under Peter Schiller. After I came back, I was appointed as associate professor in Bioorganic Chemistry and have devoted my research interest into peptides: their behaviour, their manipulation and their interactions with biological targets.

► What is your expertise and role in PANACHE?

Our group, even from before I came to lead it, has been involved in the design and synthesis of bioactive peptides and my own doctoral and postdoctoral research was devoted to the topic, albeit towards peptides for the treatment of pain. Now our research has broadened, and we devote our research efforts to multiple pathophysiological conditions such as a cancer and liver diseases, as here, and even beyond: we also look at functional peptide-based materials for drug delivery and tissue regeneration. So it is a privilege to be able to apply this knowledge and expertise to an exciting and far-reaching project like PANACHE.

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

Since the overall goal of the PANACHE project is to generate new agents that can be used in various inflammatory cardiovascular and hepatic diseases, a logical achievement from our side, being involved in the design and synthesis of peptide-based inhibitors, would be to have developed a peptide that is active in models of these diseases, knowing that we contributed to its function, through the strategic rational



Prof. Steven Ballet in a nutshell

Nationality: Belgian

Academic degrees: PhD in Sciences

Current position: Full professor (since 2021) and Head of the Research Group of Organic Chemistry at the Vrije Universiteit Brussel (since 2010)

Role in PANACHE: Design and synthesis of Panx1 channel, Cx43, and Cx32 hemichannel inhibitors

Contact: steven.ballet@vub.be



design steps that we have taken throughout the project. Of course, that development is not possible without our talented partners, but for us we would enjoy watching our peptides do what they are supposed to in these inflammatory disorders. Once validated pre-clinically, we hope to push these compounds as far as possible through the development track.

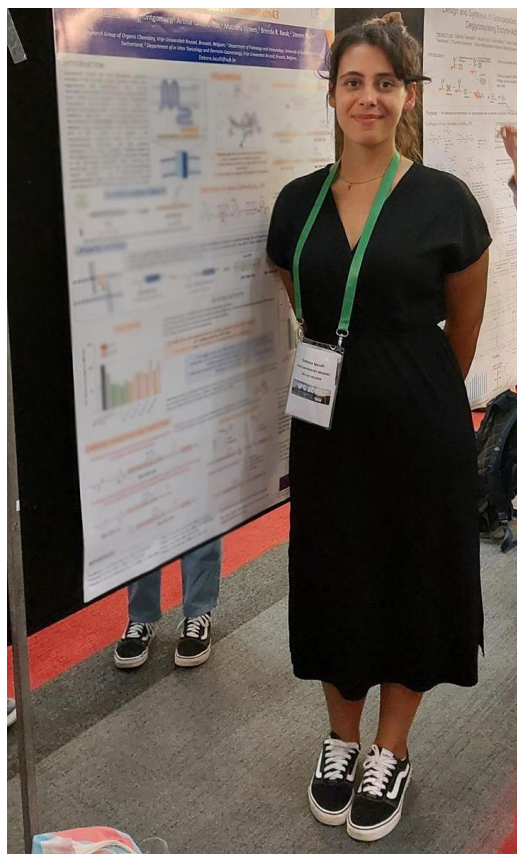
LATEST event

15th Australian Peptide Conference and 13th International Peptide Symposium

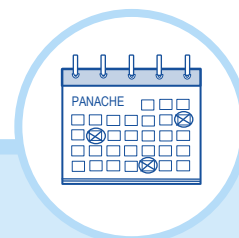
The 15th Australian Peptide Conference and 13th International Peptide Symposium took place in Brisbane, Australia from the 15th to the 20th of October 2023. The congress reunited junior and senior researchers involved in different fields of peptide research, including peptide design and optimization. Attendees were treated to a plethora of captivating lectures, notably featuring talks from two Nobel Laureates: Prof. Morten Meldal and Prof. Sir Gregory Winter.

Noteworthy, Debora Iaculli (a member of the VUB-ORGC group) presented a poster regarding the targeting of the cardiac endothelium with peptides based on the C-terminal end of Cx43, resulting from Debora's work conducted in the framework of the PANACHE research program. Moreover, Debora was honoured with a Poster Award supported by Mimotopes, recognising her outstanding PhD research within our consortium.

On the picture: Debora Iaculli (from the VUB-ORGC team) presenting her insights on the targeting of the cardiac epithelium with peptides based on the C-terminal end of Cx43.



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

Journal of Nanobiotechnology

Van Campenhout *et al.* (IVTD)

Nanobody-based pannexin1 channel inhibitors reduce inflammation in acute liver injury

[Click here to read more](#)



Diagbouga *et al.* (UNIGE)

Impact of disrupted cyclic stretch in intracranial aneurysms: Insights from endothelial cell transcriptomic dataset

[Click here to read more](#)

Science

Wang *et al.*

Fibroblasts in heart scar tissue directly regulate cardiac excitability and arrhythmogenesis

[Click here to read more](#)

SPRINGER LINK

McAllister *et al.*

Targeting Pannexin-1 Channels: Addressing the 'Gap' in Chronic Pain

[Click here to read more](#)



Mezache *et al.*

Vascular Endothelial Barrier Protection Prevents Atrial Fibrillation by Preserving Cardiac Nanostructure

[Click here to read more](#)

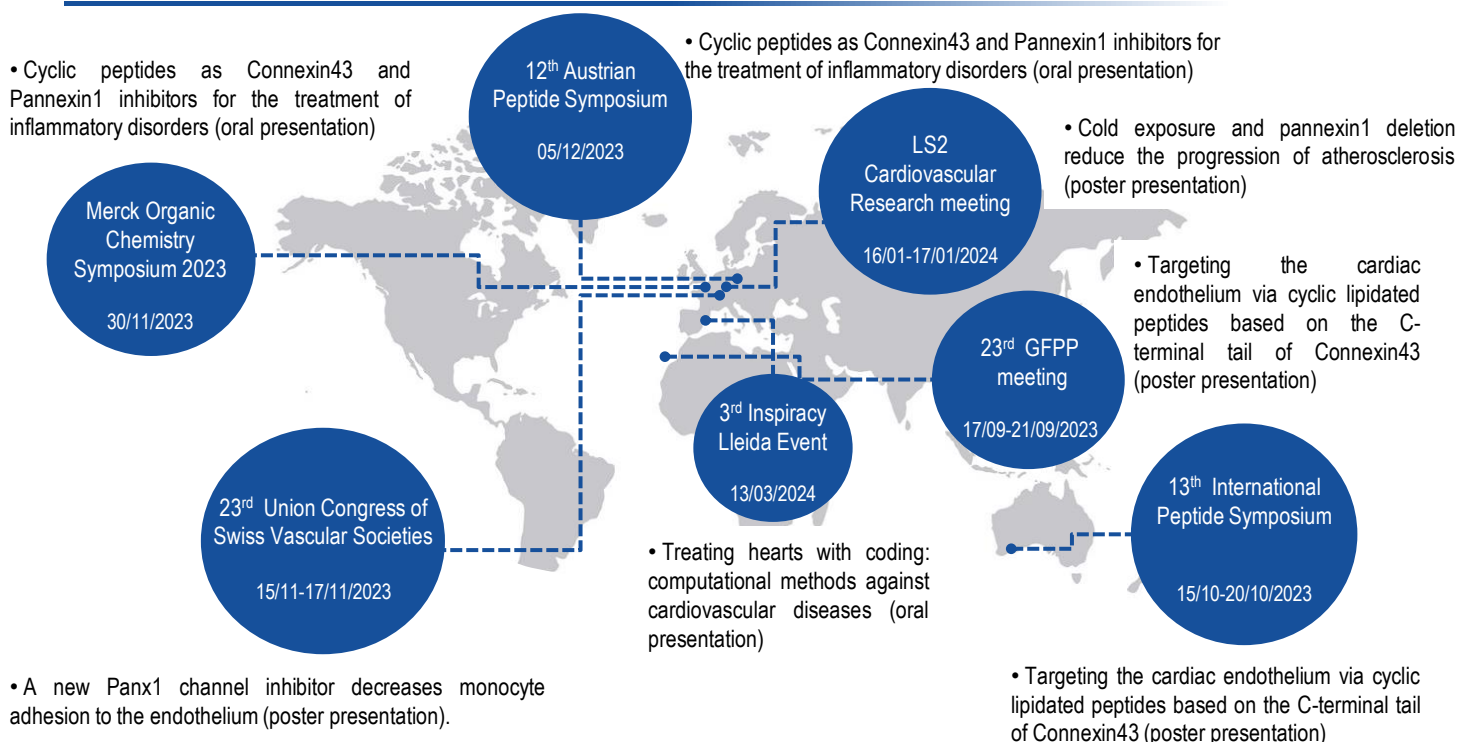
ENVIRONMENTAL TOXICOLOGY

Xu *et al.*

Nano-selenium alleviates cadmium-induced neurotoxicity in cerebrum via inhibiting gap junction protein connexin 43 phosphorylation

[Click here to read more](#)

CONSORTIUM conference communications





KEEPING UP WITH PANACHE!

Stay tuned to our latest news, results and activities



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FET project PANACHE



VRIJE
UNIVERSITEIT
BRUSSEL



ProtoQSAR

Cheminformatics and modeling solutions
to optimize your chemicals



UNIVERSITÉ
DE GENÈVE

FACULTÉ DE MÉDECINE



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