PANACHE NEWSLETTER

ISSUE #2

editorial

Dear Reader,

Welcome to the second issue of the PANACHE newsletter!

Despite the worldwide COVID-19 situation, the PANACHE project is now in full progress and the first sets of connexin and pannexin (hemi)channel inhibitors have been produced, and are currently being tested.

Through this newsletter, we invite you to learn more about the project, including its research teams, activities and events. You will also find a report of the first PANACHE workshop.

Stay tuned to PANACHE by subscribing to our newsletter, by visiting our webpage and by following us on Twitter, Instagram, Facebook and LinkedIn.

The PANACHE consortium.

in this issue

about PANACHE

PANACHE is a 4-years 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 generate a novel generation of connexin and pannexin (hemi)channel inhibitors as potential drugs. This will be 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 will allow 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.

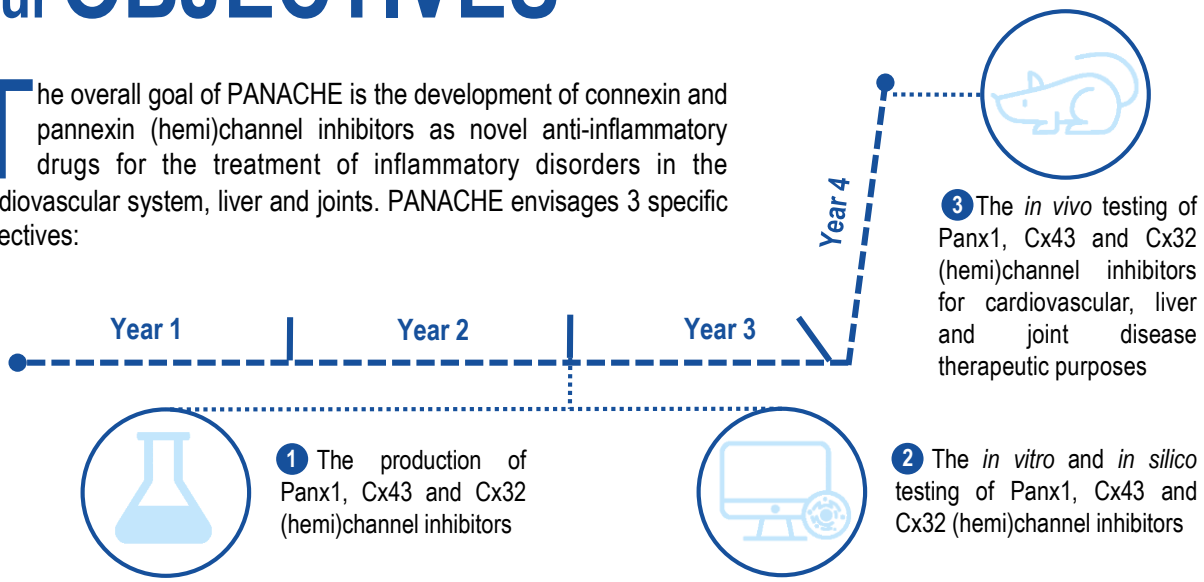
our VISION

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 will be 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 are known to be involved. Such applications will be tested in follow-up initiatives of PANACHE, thereby realizing its long-term vision.

our OBJECTIVES

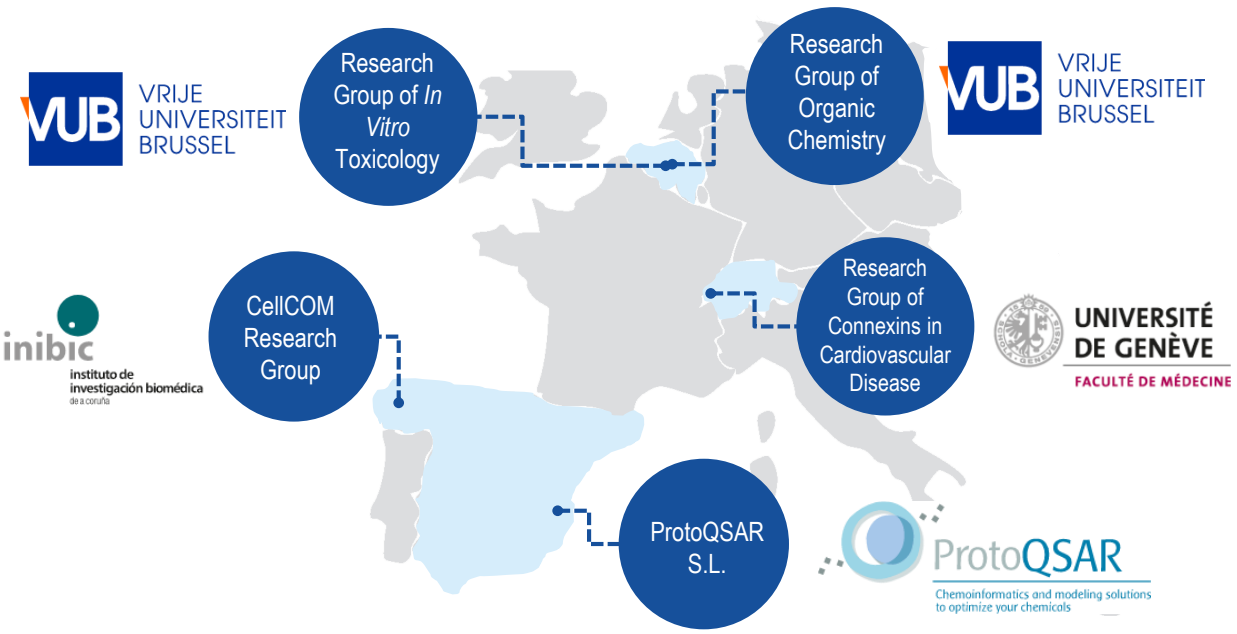
The overall goal of PANACHE is the development of connexin and pannexin (hemi)channel inhibitors as novel anti-inflammatory drugs for the treatment of inflammatory disorders in the cardiovascular system, liver and joints. PANACHE envisages 3 specific objectives:



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.) as well as 3 biomedical biomedical subdisciplines, in particular cardiovascular (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



PARTNER in the spotlight

The Research Group of Organic Chemistry

Located at the Vrije Universiteit Brussel (VUB) in Belgium, the Research Group of Organic Chemistry (ORGC) mainly focuses its research activities on the synthesis of modified peptides together with low molecular weight molecules ('small molecules') for various applications in medicinal chemistry.
The research team led by Prof. Steven Ballet has developed a long-standing expertise in the fields of peptide medicinal chemistry and peptide materials by means of ingenious methods to assemble uncommon amino acids and customized peptide sequences.

Thanks to a national and international multidisciplinary collaboration network, ORGC aims at a high-end approach to investigate and develop peptide-based molecules for biological and biomedical applications.

Prof. Steven Ballet, Ph.D. (Belgium)

Team leader of ORGC-VUB.
After an academic trajectory in the field of peptide-like compounds, Prof. Steven Ballet was appointed as a VUB faculty member at his *Alma Mater* in 2010. His main research themes include synthetic organic methodology intended for medicinal chemistry purposes, peptide and protein epitope mimicry, and soft materials for regenerative medicine and controlled-drug release applications.

Prof. Charlotte Martin, Ph.D. (France)

Part-time professor at ORGC-VUB.
Prof. Charlotte Martin has a Ph.D. degree in chemical sciences specialized in molecular engineering from the University of Montpellier-France. Since 2019, she is a part-time professor at the VUB within the ORGC group with a focused interest on the development of peptide-based hydrogels for controlled drug delivery.

Arthur Lamouroux, Ph.D. (France)

Postdoctoral researcher at ORGC-VUB.
Dr. Arthur Lamouroux has a Ph.D. in organic chemistry from the University of Bordeaux-France. He joined the team of Prof. Steven Ballet in 2019 as a postdoctoral fellow, working on the development of Panx1, Cx43 and Cx32 (hemi)channel inhibitors in the context of PANACHE.

Debora Iaculli, M.Sc. (Italy)

Predoctoral researcher at ORGC-VUB.
Debora Iaculli has a bachelor degree in chemistry and a master degree in organic chemistry from the University of Bologna-Italy. After joining the ORGC team medio 2020, she is currently involved in the development of Cx43 and Cx32 hemichannel inhibitors in PANACHE.

To learn more about the group and its members please visit www.orgc.research.vub.be

ROLE in PANACHE

The ORGC-VUB team is responsible for the design, the development and the synthesis of Panx1, Cx43 and Cx32 (hemi)channel inhibitors.
In collaboration with all PANACHE partners, the rational approach is to efficiently identify relationships between structure and activity of the potential anti-inflammatory drugs. Based on a sound know-how in organic chemistry and on specific design, the ORGC-VUB group will improve their intrinsic properties to generate the next generation of inhibitors of Panx1, Cx32 and Cx43 (hemi)channels.

LATEST event

First PANACHE-Science Xpression workshop

The first PANACHE-Science Xpression workshop was organized by María Mayán on 6 and 7 October 2020 as an online event. This inter-disciplinary and international workshop offered an excellent opportunity for 98 participants to interact and discuss about advanced research on the role of connexins and pannexins in health and disease.

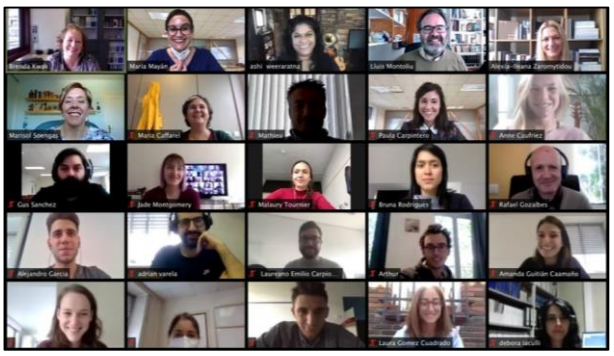
The first part of the workshop was a confidential session between the PANACHE partners and the advisory board to discuss progress of the work and future research plans within the consortium.

On the second day of the workshop, 2 internationally recognized scientists gave inspiring keynote lectures about their research work in the connexin and pannexin research field, namely Dr. Leigh Anne Swayne from the University of Victoria-Canada and Dr. Robert Gourdie from the Fralin Biomedical Research Institute Virginia Tech-USA.

This was followed by a session in which 13 young researchers affiliated to both PANACHE partners and non-PANACHE partners from 8 different countries briefly presented their work in a set of flash communications. This session was an ideal opportunity for the youngsters to broaden their knowledge and to develop their critical thinking and scientific reasoning.

The last part consisted of 3 fascinating keynotes lectures and a final discussion about science communication skills, ethics and the actual situation of women and minorities in science. These were presented by Dr. Alexia-Ileana Zaromytidou (Chief Editor in Nature Cancer, New-York-USA), Dr. Lluís Montoliu (Centro Nacional de Biotecnología and Consejo Superior de Investigaciones Científicas, Madrid-Spain) and Dr. Ashani T. Weeraratna (Johns Hopkins Bloomberg School of Public Health, Baltimore-USA), respectively.

Pictures and social media quotes from the PANACHE-Science Xpression workshop



Dr. Swayne @dr_swayne
Thank you so much Maria and team for an absolutely awesome meeting!!! So much exciting work 🙌! Really looking forward to the talks next year and to @IGJC2022 - can't wait to actually come to Spain! 🇪🇸

Jonathan Bcr @Boucher62424287
Always cool to be back in Cx/Panx world... even at 4 am in 🇨🇦 @ScienceXpress @FET_PANACHE

Maria M Caffarel @MariaCaffarel
Amazing and very inspiring workshop! Congrats Maria and team for the organisation and thanks to all the speakers

Scott Johnstone @ScottRJ_VT
Thank you Maria and the Panache team! It was a great meeting and excellent opportunity for early career researchers to present.

Amanda Guitián-Caamaño @amandagcaamano
Today I just presented our results @adrianvarelavaz on BRAF/MEK inhibitors and Cx43 in melanoma at @ScienceXpress. I hope you enjoyed it 👩‍🔬👩‍🔬💪

Paula Carpintero-Fernandez @PaulaCarpintero · 7 oct.
🗣Science Xpression Session 3 now happening online. @ScienceXpress @FET_PANACHE

Thank you very much to our keynote speakers and good luck to all young researchers that are presenting today.

Hope you enjoy the day! 👏

Trisha Martin @Trisha_CxGCU
Thank you for organising Maria. Great to hear so many excellent talks and exciting data

María D. Mayán @MariaDMayan
Thank you very much to speakers and participants in this workshop within @FET_PANACHE & @ScienceXpress

We were able to keep more between 60-73 researchers connected during 4 hours, including people from USA! 👏🏻

Many young talented people in connexins and Pannexins field🧠🔬

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 recent publications, including those published by the PANACHE consortium.

CONSORTIUM publications

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

Peptide-based targeting of connexins and pannexins for therapeutic purposes

Click here to read more

Varela-Vázquez, A. *et al.* (**INBIC-FPNS**)

Emerging functions and clinical prospects of connexins and pannexins in melanoma

Click here to read more

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

Non-canonical roles of connexins

Click here to read more

Rusiecka, O. M. *et al.* (**UNIGE-IVTD**)

Canonical and non-canonical roles of connexin43 in cardioprotection

Click here to read more

Leroy, K. *et al.* (**IVTD**)

Targeting gap junctional intercellular communication by hepatocarcinogenic compounds

Click here to read more

Molica, F. *et al.* (**UNIGE**)

A genetic polymorphism in the pannexin1 gene predisposes for the development of endothelial dysfunction with increasing BMI

Click here to read more

RELEVANT publications selected from PubMed

Ruan, Z. *et al.*

Structures of human pannexin1 reveal ion pathways and mechanism of gating

Click here to read more

Flores, J. A. *et al.*

Connexin-46/50 in a dynamic lipid environment resolved by cryo-EM at 1.9 Å

Click here to read more

Lee, H.-J. *et al.*

Cryo-EM structure of human Cx31.3/GJC3 connexin hemichannel

Click here to read more

KEEPING UP WITH PANACHE!

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