PANACHE NEWSLETTER

ISSUE #3

editorial

Dear Reader,

Welcome to the third issue of the PANACHE newsletter!

It has been a very long year with some unique challenges, particularly in the scientific community. Work-from-home orders, travel bans, COVID exposure quarantines, PCR reagent shortages, dealing with public denialism, and more have all impacted us and our work to varying degrees. Despite this, we continue on with the production and testing of our connexin and pannexin (hemi)channel inhibitors, and have even added additional compounds to be examined by the project consortium.

In this issue we will be covering the UNIGE cardiovascular team, the ongoing gap junction webinars, and giving you the first information on this year's 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.

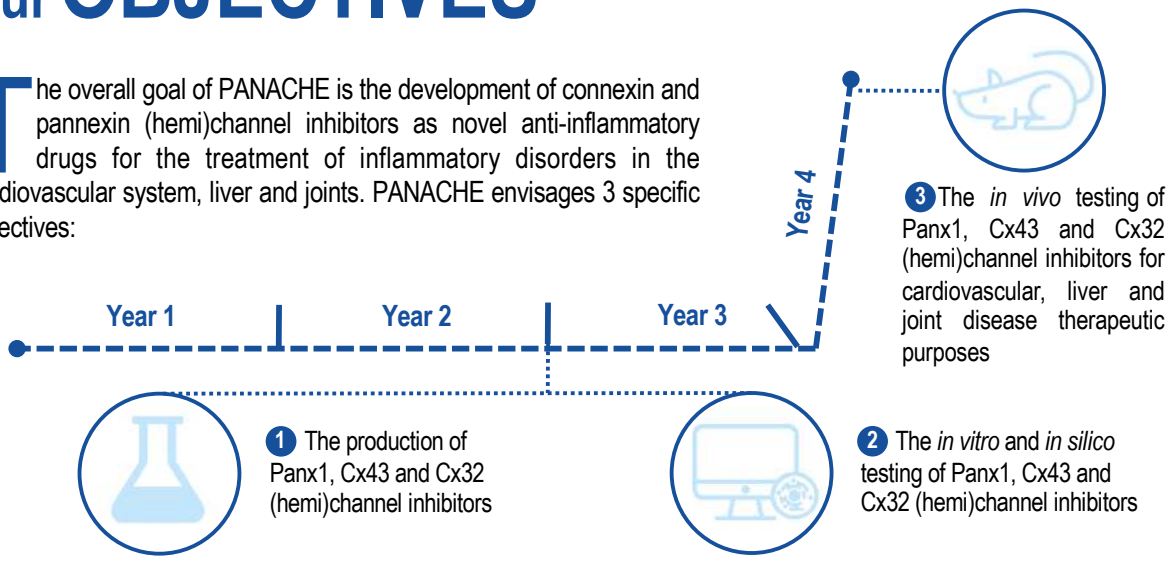
our VISION

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

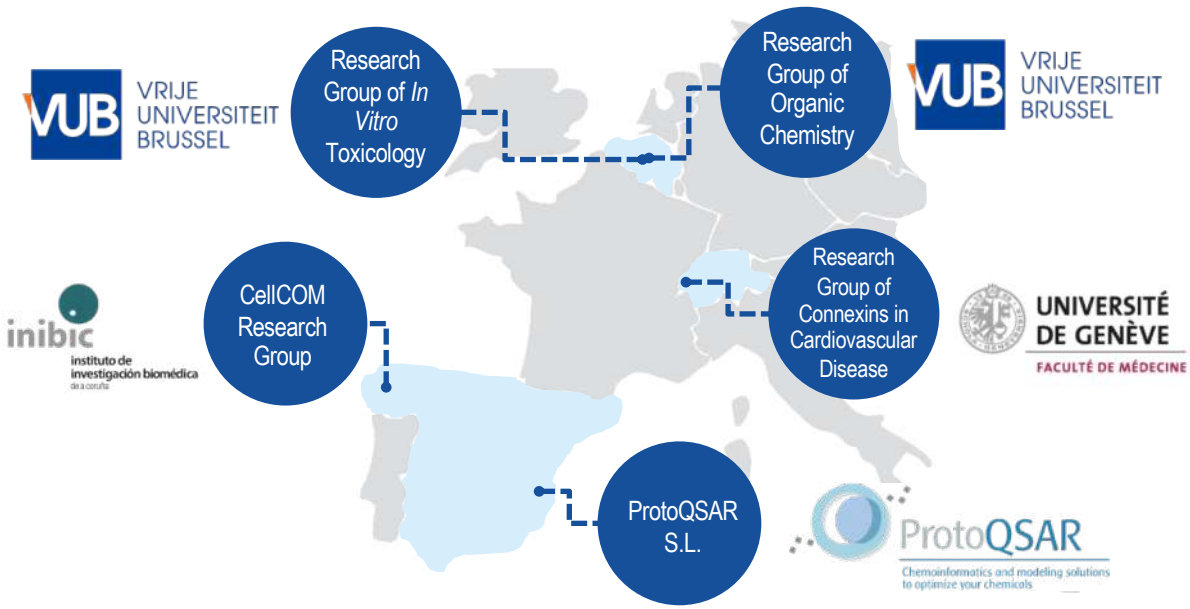
The overall goal of PANACHE is the development of connexin and pannexin (hemi)channel inhibitors as novel anti-inflammatory drugs for the treatment of inflammatory disorders in the cardiovascular system, liver and joints. PANACHE envisages 3 specific objectives:



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.) and biomedical research, as well as 3 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 *Connexins in Cardiovascular Disease*

The Research Group of Connexins in Cardiovascular Disease is centrally embedded in the Department of Pathology and Immunology at the Faculty of Medicine of the University of Geneva (UNIGE) in Switzerland.

The research team led by Prof. Brenda Kwak was established in 2002 with help of the Swiss National Science Foundation and has performed pioneering work on the role of connexins and pannexins in cardiovascular diseases with a strong immuno-inflammatory component, such as atherosclerosis, restenosis, cardiac ischemia-reperfusion and thrombosis. More recently, the group has added pannexin-related projects and translational research focusing on biomechanical forces in the pathogenesis of vascular disease. With the PANACHE project, the group has added another translational component to their research portfolio.

Prof. Brenda Kwak, PhD (Netherlands)

Team leader of the Research Group of Connexins in Cardiovascular Disease, Brenda Kwak is a full professor and director of the Department of Pathology and Immunology in the Faculty of Medicine at UNIGE. She holds a doctoral degree (University of Amsterdam) and a registration (S.M.B.W.O.) in physiology. She joined the connexin research field in 1988 immediately after her medical studies and has not left it since. Author of over 120 publications in peer-reviewed journals, Brenda Kwak leads her multinational research team in various research projects involving connexins and pannexins in cardiovascular disease.

Filippo Molica, PhD (Italy)

Research & teaching fellow at UNIGE, with a Master's in biochemistry and a PhD in biology. Dr. Molica joined the laboratory of Prof. Brenda Kwak as a postdoctoral fellow in 2013. He currently leads projects in the cardiovascular field with a particular focus on the role of Panx1 in atherothrombosis and lipid metabolism.

Jade Montgomery, PhD (Australia)

Postdoctoral researcher at UNIGE, with a PhD in biomedical engineering and a background in Cx43 peptide therapeutic treatment analysis. Her PANACHE work currently focuses on *in vitro* testing of Cx43 inhibitors.

Olga Rusiecka, MSc (Poland)

PhD student at UNIGE, with a Master's in molecular biotechnology. She is working with cardiac I/R injury models and developing Panx1 channel inhibitors in collaboration with the VUB team.

Malaury Tournier, MSc (France)

PhD student at UNIGE, with Bachelor's and Master's degrees in integrative biology and physiology. She is currently testing PANACHE Panx1 channel inhibitors *in vitro* in cardiac and endothelial cells.

Viviane Bes, BSc (France)

Laboratory technician at UNIGE, with a professional Bachelor's degree in technology of physiology and physiopathology. She assists in cardiovascular *in vitro* and future *in vivo* testing for the PANACHE project.

To learn more about the group and its members please visit unige.ch/medecine/pati/en/groupes/665kwak/

ROLE in PANACHE

The UNIGE Research Group is leader of the cardiovascular therapeutic testing work package. The team is responsible for testing the efficacy and selectivity of the Panx1 channel and Cx43 hemichannel inhibitors in endothelial and cardiac cells. In later stages of the project, the team will employ selected (hemi)channel inhibitors in *ex vivo* and *in vivo* cardiac disease testing schemes in order to examine their effectiveness in cardioprotection and prevention of atherosclerosis.

LATEST event

Gap Junction Webinar Series

This past half year has been a hard time to be a scientist! With the ongoing global health crisis, many conferences and meetings have had to be cancelled, postponed, or moved into an online format. Unfortunately the International Gap Junction Conference also succumbed to this fate, being delayed to 2022. In order to keep the community together and informed in the absence of in-person meetings, the IGJC committee has elected to run a series of webinars occurring approximately every two weeks. In this time of restricted travel and cancelled conferences, it's nice that our scientific community can still stay connected online while waiting for next year's meeting in A Coruña.

Selected previous webinars

January 19th 2021

Dr. Henrique Girao
University of Coimbra, Portugal
Chair

Connexin43 hemichannels and intracellular calcium: An axis of dysfunction in sudden cardiac death

Prof. Mario Delmar
NYU Langone Health, USA

EHD proteins mediate remodeling of Connexin 43 channels during myocardial ischemia

Dr. Tanya Marques
University of Coimbra, Portugal

Viral subversion of intercellular coupling: bridging the gap from mouse to human heart disease

Rachel Padget
Virginia Tech, USA

February 23rd 2021

Dr. Trond Aasen
VHIR, Barcelona, Spain
Chair

Endothelial pannexin 1 contributes to impaired cardiac function following myocardial infarction

Dr. Miranda Good
Tufts Medical Center, USA

Regulation of venous barrier function by Pannexin1

Prof. Michael Koval
Emory University, USA

For more information on previous and upcoming webinars, please visit
https://sites.google.com/view/gapjunctionwebinars/

UPCOMING event

Second PANACHE Workshop 2021

When: Open conference day: Monday 22 November 2021
PANACHE network day: Monday 29 November 2021

Organizer: Brenda Kwak

Join us online for the second PANACHE meeting! The PANACHE network day, for PANACHE consortium members only, will be held on Monday the 29th of November. Save the date for the open conference day of the workshop! To be held on the 22nd of November 2021, keynote talks will be given by researchers outside the PANACHE consortium including Prof. Brant Isakson from University of Virginia, interspersed with flash talks by young researchers. Applications for flash talks will be announced shortly.

For more information about the event please stay tuned to PANACHE announcements

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

PROTEINS STRUCTURE · FUNCTION · BIOINFORMATICS

Barigye SJ *et al.* **(pQSAR)**

PeptiDesCalculator: Software for computation of peptide descriptors. Definition, implementation and case studies for 9 bioactivity endpoints

Click here to read more

International Journal of Molecular Sciences

Cooreman A *et al.* **(IVTD)**

Cholestasis Differentially Affects Liver Connexins

Click here to read more

SCIENTIFIC REPORTS

Aljkna Khan A *et al.* **(UNIGE)**

Detecting early myocardial ischemia in rat heart by MALDI imaging mass spectrometry

Click here to read more

International Journal of Molecular Sciences

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

Mechanisms Underlying Connexin Hemichannel Activation in Disease

Click here to read more

RELEVANT publications selected from PubMed

Basic Research in Cardiology

Hirschhäuser C *et al.*

Connexin 43 phosphorylation by casein kinase 1 is essential for the cardioprotection by ischemic preconditioning

Click here to read more

Bone Research

Riquelme MA *et al.*

Mechanotransduction via the coordinated actions of integrins, PI3K signaling and Connexin hemichannels

Click here to read more

Circulation Research

Good ME *et al.*

Endothelial Pannexin 1 Regulates Cardiac Response to Myocardial Infarction

Click here to read more

International Journal of Molecular Sciences

Flores-Muñoz C *et al.*

Restraint of Human Skin Fibroblast Motility, Migration, and Cell Surface Actin Dynamics, by Pannexin 1 and P2X7 Receptor Signaling

Click here to read more

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