PANACHE NEWSLETTER

ISSUE #6

editorial

Dear Reader,

Welcome to the sixth 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 currently almost halfway.

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 (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.

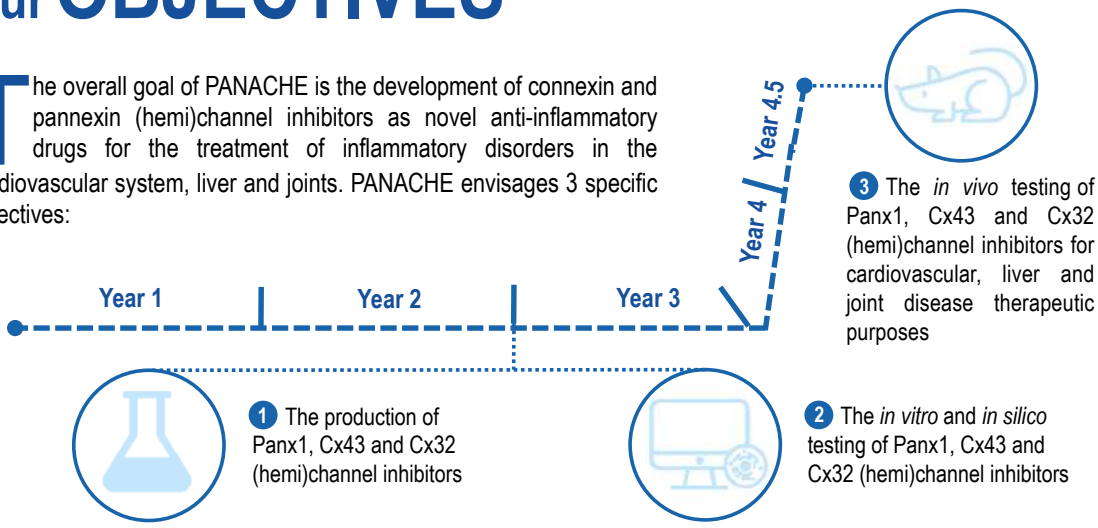
our VISION

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

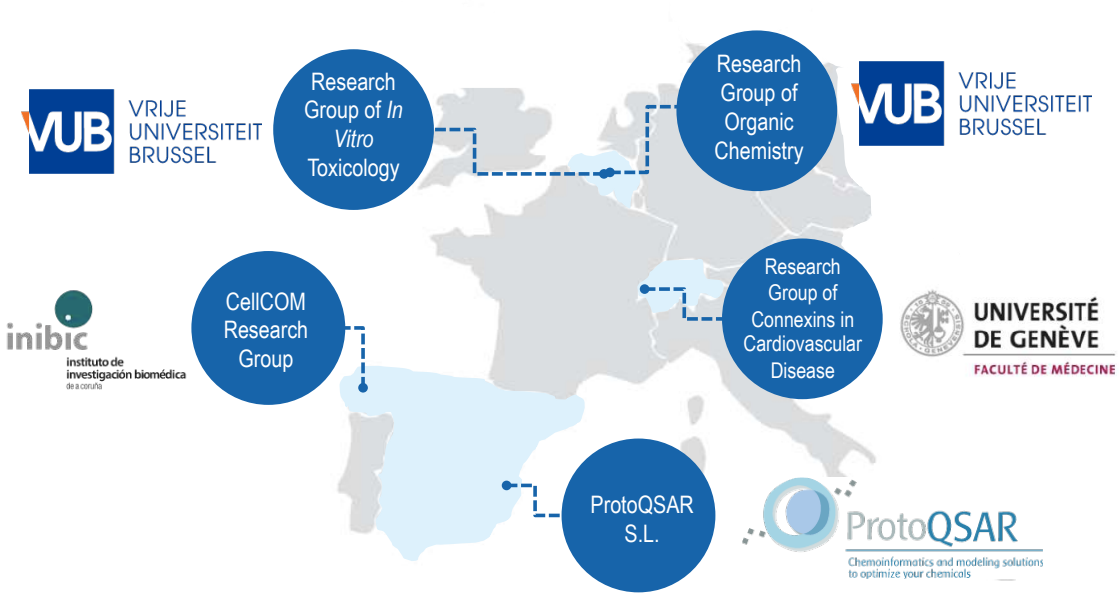
The overall goal of PANACHE is the development of connexin and pannexin (hemi)channel inhibitors as novel anti-inflammatory drugs for the treatment of inflammatory disorders in the cardiovascular system, liver and joints. PANACHE envisages 3 specific objectives:



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 (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 your place! In this section, a series of interviews with the principal investigators of the consortium will be published, starting with Rafael Gozalbes in this newsletter.

Rafael Gozalbes - ProtoQSAR S.L.

'I expect to achieve specific computational goals, such as the development of dedicated models and tools that can be useful to evaluate various pharmacokinetic parameters of new connexin and pannexin (hemi)channel inhibitors.'

▸ Can you shortly introduce yourself?

I was born in Játiva-Spain and I got my degree in pharmacy in 1991 from the University of Valencia-Spain. I earned my doctoral degree in pharmacy from University of Valencia-Spain in 1998. I worked as a postdoctoral researcher and as a senior scientist in different (inter)national institutions. Between 1997 and 2007, I worked as a postdoctoral researcher at the research group 'Chimie Informatique et Modélisation' from the Université Paris VII-France and as a senior scientist at the molecular modelling group of the biotechnology company Eurofins Cerep Paris-France. Between 2007 and 2010, I worked as a research scientist at the Laboratory of Structural Biochemistry from the Príncipe Felipe Research Center Foundation in Valencia-Spain, where I was responsible for the computational management of the internal datasets of chemicals, the development of structure-activity relationships and the modelling aspects of several drug design projects. Since 2010, I act as an independent consultant in the area of chemo-informatics and molecular modelling for different companies and chemical/pharmaceutical academic groups. Currently, I am the founder and director of 2 companies, namely ProtoQSAR S.L. and MolDrug AI Systems S.L., related to computer simulations in toxicology and drug discovery, respectively.

▸ What is your expertise and role in PANACHE?

I have always been interested in the use of computational approaches to predict (physico-chemical, biological and toxicological) properties of chemical substances, as a complement to standard experimental bioassays. In the PANACHE project, I am responsible for the ProtoQSAR team, which is in charge of developing computational models to predict different pharmacokinetic and pharmacological properties of the newly produced connexin and pannexin (hemi)channel inhibitors.

Dr. Rafael Gozalbes in a nutshell

- **Nationality:** Spanish
- **Academic degrees:** * B.Sc. in pharmacy
  * PhD in pharmacy
- **Current position:** director of * ProtoQSAR S.L.
  * MolDrug AI Systems S.L.
- **Role in PANACHE:** *in silico* modelling
- **Contact:**

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

The main result of the PANACHE project will be the generation of novel connexin and pannexin (hemi)channel inhibitors to treat liver, cardiovascular and inflammatory joint diseases. I also expect to achieve specific computational goals, such as the development of dedicated models and tools that can be useful to evaluate various pharmacokinetic parameters of new connexin and pannexin (hemi)channel inhibitors.

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LATEST event

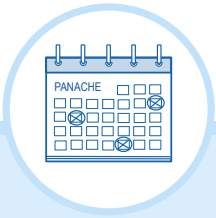
International Gap Junction Conference

The International Gap Junction Conference (IGJC) was held in A Coruña-Spain from 16 to 20 July 2022. The conference was hosted by María D. Mayán and organized by the Executive Committee consisting of María D. Mayán, Trond Aasen, Arantxa Tabernero, Henrique Girao and Luis Barrio. Several PANACHE consortium members presented their latest results during the conference. Paula Carpintero and Filippo Molica received the Emerging Star Awards.

Overall, it was a successful conference that reunited, for the first time in Spain, the connexin and pannexin research community. Besides the scientific events, there was plenty of time for social interaction and opportunities to explore the city and the surroundings with different organized activities, including a visit to Santiago de Compostela and a cycling trip. The next IGJC will be organized by in 2024 by Silvia Penuela and Jamie Smyth in Washington DC-US.

Left: attendants and organizers of IGJC2022 together with the Royal Bagpipe Band of the County Council of Ourense. *Right:* winners of the Emerging Star Awards *(left to right:* Joseph Palatinus, Kirk Taylor, Francisca Acosta, Tania Martinez, Natisha Genet, Teresa Ribeiro, Rocio Talavero, Paula Carpintero and Filippo Molica).

UPCOMING event



International Colloquium on Gap Junctions and Cancer

When: 16-20 July 2023
Where: São Paulo-Brazil
Organizers: Maria Lucia Zaidan Dagli-Laboratory of Experimental and Comparative Oncology, School of Veterinary Medicine and Animal Science, University of São Paulo-Brazil, Mark Mesnil-STIM laboratory, University of Poitiers-France and Christian Naus-Department of Cellular and Physiological Sciences, The Life Sciences Institute, University of British Columbia-Canada.

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 PANACHE consortium members.

CONSORTIUM publications

International Journal of Molecular Sciences

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

Effects of drugs formerly proposed for COVID-19 treatment on connexin43 hemichannels

Click here to read more

International Journal of Molecular Sciences

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

Effects of drugs formerly suggested for COVID-19 repurposing on Pannexin1 channels

Click here to read more

Cell Death & Disease

Varela-Eirín *et al.* **(FPNS)**

Extracellular vesicles enriched in connexin 43 promote a senescent phenotype in bone and synovial cells contributing to osteoarthritis progression

Click here to read more

Bioelectricity

Carpintero-Fernandez *et al.* **(FPNS)**

Osteoarthritis: mechanistic insights, senescence, and novel therapeutic opportunities

Click here to read more

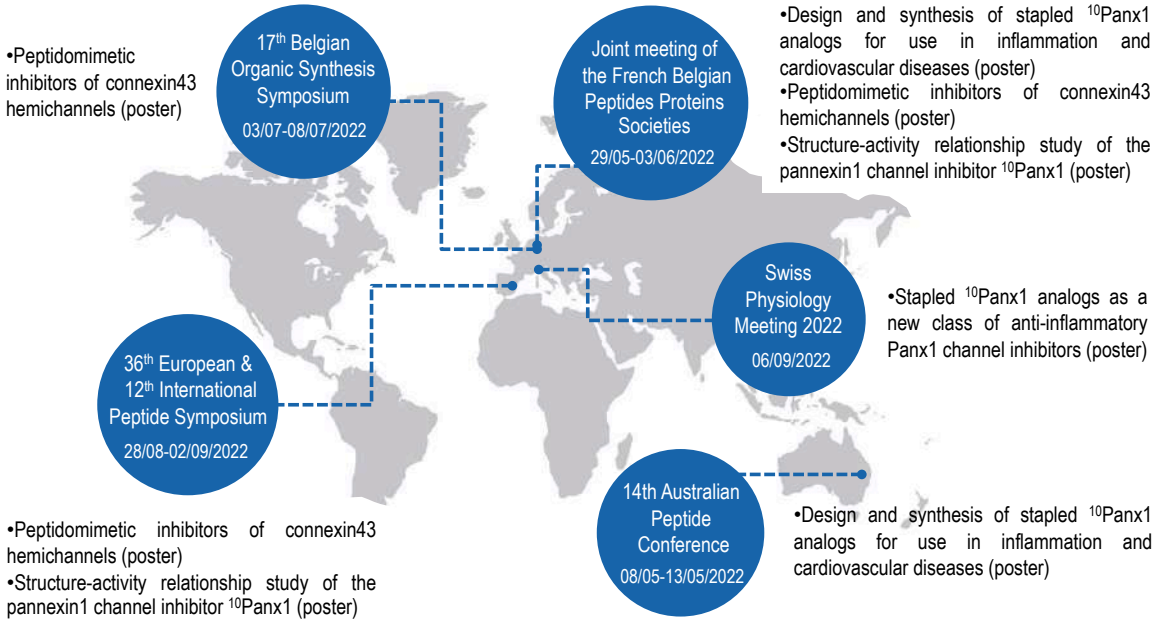
Cardiovascular Research

Diagbouga *et al.* **(UNIGE)**

Primary cilia control endothelial permeability by regulating expression and location of junction proteins

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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ProtoQSAR
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