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Effective combinational treatment of chronic pain in individual patients by an innovative quantitative systems pharmacology (QSP) pain relief approach

Newsletter 3 - December 2021

[Major steps forward & 3rd GA Meeting](#)

[New SEAB members](#)

[New team members](#)

[Masterclasses & E-Learning](#)

[Seminars, Presentations & Project brochure translations](#)

[Bachelor students working on QSPainRelief](#)

[Save the dates](#)

together **10 partner institutions** from 5 European countries and the USA. The 5-year-long project started in January 2020 and uses an innovative quantitative systems pharmacology (QSP) pain relief approach in developing effective combinational treatment of chronic pain in individual patients. In our half-yearly newsletter, we inform you of scientific advances in the project, new team members, events, and other relevant news. Watch the project video below to gain an overview of what QSPainRelief is all about. **Sign up here to receive our newsletter.** We wish everyone Happy Holidays & a healthy and successful New Year!

Chronic pain: The role of the Brain

The problem occurs when the brain starts to interpret normal nerve signals as danger.

When this happens people can feel pain when there is no danger present and this can lead to chronic pain.

Normal **Chronic Pain**

Body signal Body signal

Source: <https://davidpapo.wordpress.com/2014/05/11/reconstructing-functional-brain-networks-have-we-got-the-basics-right/>

This project has received funding from the EU Horizon 2020 research and innovation programme under grant agreement No 848068. 3

Project Video: Liesbeth de Lange's keynote lecture at Pain Alliance Europe's General Assembly Meeting in June 2020.

Major steps forward & 3rd GA Meeting

The 3rd QSPainRelief General Assembly (GA) Meeting took place this month as a virtual Zoom meeting from 13-15 December 2021. Highlights were the two Masterclasses held by **Prof. Dr. Jesús Giraldo** (UAB, Barcelona, Spain) and **Robert Carr** together with **Dr. Athan Spiros** (ISB, Boston, USA), a productive Impact and Innovation Board (IIB) meeting, as well as the early-career scientists' (ECS) presentations.

We also learned about the progress made in the different work packages (WPs), such as developing the QSPainRelief models (**WP2**), set-up and optimisation of the database and platform (**WP3**), *in silico* computation & risk/benefit analysis (**WP4**), untangling cellular signaling pathways via computational approaches (**WP5**), new results of the preclinical studies (**WP6**), planning of the healthy volunteers' study (**WP7**), and discussed how to increase recruitment in the pain patient study (**WP8**)!

Fun treats during the virtual coffee breaks were a quiz of what everybody would bring to a desert island if they could only choose a single item (anything from water, sunscreen, a desalination unit, a luxurious yacht, a "Calvin & Hobbes" comic book, or a solar-powered laptop to continue working was listed) and the quiz "Who done it?" (one of our scientists had gotten caught in an avalanche while skiing, while another one had read the entire "Count of Monte Cristo" in candlelight during a 3-day power-blackout).



New SEAB members

We cordially welcome two new members to the project's scientific and ethical advisory board (SEAB), namely **Deirdre Ryan**, the new president of Pain Alliance Europe (PAE), and **Dr. Petra Bloms-Funke**, managing director at **BlomsFunkeResearch** - a professional research consulting agency. While Deirdre provided very valuable feedback and also ideas for dissemination and workshops from the perspective of chronic pain patients in Europe, Petra's comments and input will help the consortium streamline and improve our scientific work and the QSPainRelief model platform.

We are also very grateful for constructive criticism and feedback from our continued SEAB members, Dr. Jan Freijer, Prof. Dr. Erwin Kompanje, who had also freed their schedules to participate in the 3rd QSPainRelief GA Meeting.

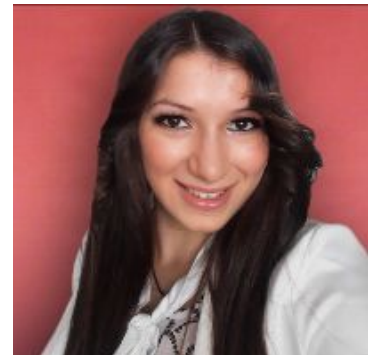
**Deirdre Ryan***President of Pain Alliance Europe***Dr. Petra Bloms-Funke***Managing Director at BlomsFunkeResearch*

Welcome,
**Deirdre and
Petra!**

New team members

A cordial welcome to one new early-career scientist (ECS) at **UNIBO** and to the **NeuroPhar Laboratory** project manager (**UPF**, Barcelona). We are very happy to have you both within the QSPainRelief team!

Elisabetta Cuna: I am 26 years old and I come from Puglia, a region in the south of Italy. I received my bachelor's degree in Biotechnology at the University of Lecce and then graduated in Pharmaceutical Biotechnology at the University of Bologna (**UNIBO**). Since this fall, I joined **Prof. Dr. Andrea Bedini's** group at **UNIBO** to work on the QSPainRelief project towards my Ph.D. degree.



Jolita Jancyte: At this point, we'd also like to introduce Jolita who is the **NeuroPhar Laboratory** project manager at the Universitat Pompeu Fabra (**UPF**) in the team around **Prof. Dr. Raffael Maldonado**.

Masterclasses & E-Learning

targeted towards the project-internal early-career scientists (ECS) as well as patients, relatives, medical and pharmacology students, and anyone interested in learning more about pain perception, pain treatment, animal models, quantitative systems pharmacology, or *in silico* modeling. The two new Masterclasses from the 3rd GA Meeting are by WP5 leader **Prof. Dr. Jesús Giraldo (UAB)** on "Molecular modeling and dynamic simulations of G protein-coupled receptors (GPCRs)" and by **Robert Carr** and **Dr. Athan Spiros (ISB, leading WP2)** on "CNS quantitative systems biology in the research of new drugs". Keep an eye on the **QSPainRelief YouTube Playlist** when we will add the edited and subtitled videos of these Masterclasses next year.



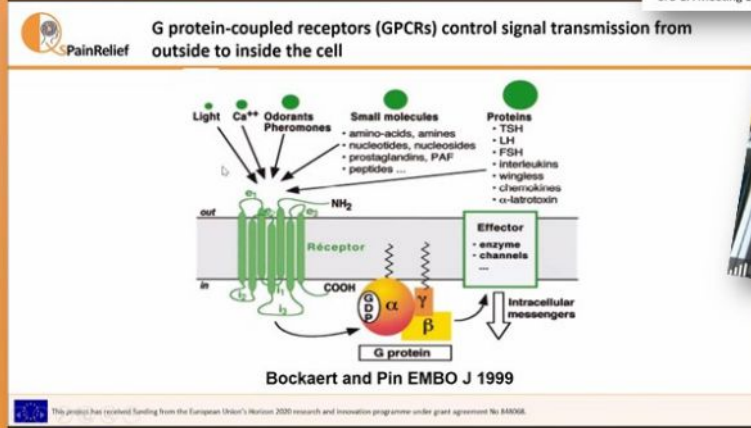

PainRelief Masterclass

Molecular modelling and dynamic simulations of G protein-coupled receptors (GPCRs)

Discover effective novel combination treatments, using existing drugs, in chronic pain treatment

Jesús Giraldo
QSPainRelief Consortium - Universitat Autònoma de Barcelona

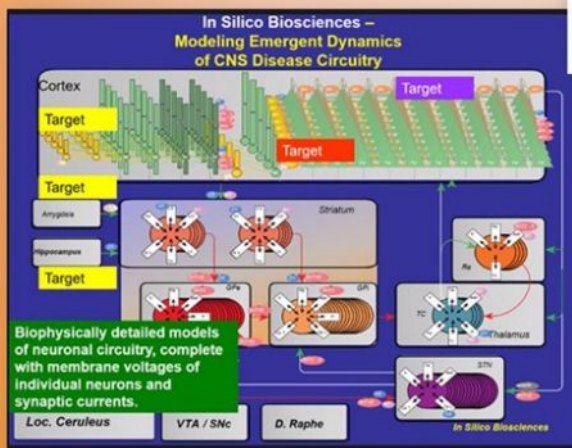
3rd GA Meeting 13th – 15th December 2021

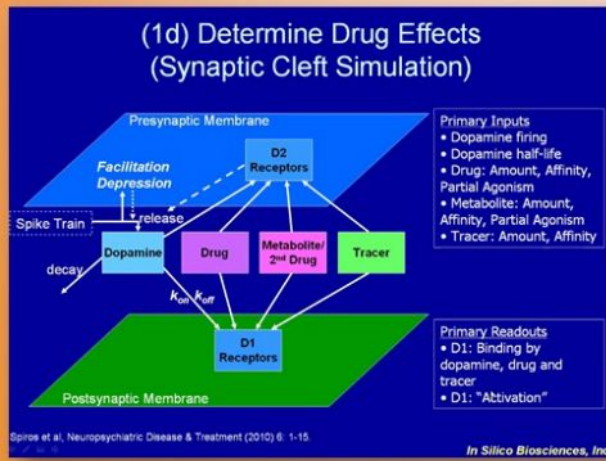
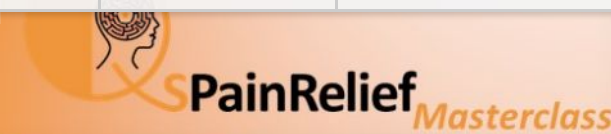
PainRelief Masterclass

CNS quantitative systems biology in the research of new drugs

- Platform Architecture - Robert
- Reaction of Pharma towards QSP and Opportunities - Robert
- Case Study to Elaborate Technology - Athan



"In the land of the blind, the one-eyed man is king."
- Erasmus of Rotterdam



- ❑ Platform Architecture - Robert
- ❑ Reaction of Pharma towards QSP and Opportunities - Robert
- ❑ Case Study to Elaborate Technology - Athan



Quantitative systems biology in the research of new drugs in CNS

1. Example: Cortical Model of Working Memory
2. Example: Addition of New Receptor
3. New Drug Development

Seminars, Presentations & Project brochure translations

On 1st December 2021, **Carlo Matej Rinaudo** and **Solenn Gousset** from **André Mouraux's** group at the Université Catholique de Louvain (UCL) gave a detailed seminar presentation about the **QSPainRelief** project in front of students in the Bio-Engineering Master's programme at the Louvain-La-Neuve campus in an effort to establish and explain the link between pharmacological engineering and health.



Conclusion



QSPainRelief merges novel pharmacological and in silico technologies to tailor chronic pain treatment to the specific needs of individuals and stratified patients groups.

From idea to application



Direct benefits for chronic pain patients:

- Novel and improved combinational treatment strategies in clinical practice
- Higher treatment efficacy due to personalised medicine and effective patient stratification
- Improved acceptance of combinational therapies in the clinical setting
- Reduced stigmatisation of chronic pain as a health condition



This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 633058.

Berfin Gülave, another PhD student in **Prof. Dr. Liesbeth de Lange's** group at the Division of Systems Biomedicine and Pharmacology at

on "Opioid distribution in human CNS is moderately altered due to pain-related changes in BBB functionality". Well done!



Divakar Buddha from **Prof. Dr. Liesbeth de Lange**'s group at the Division of Systems Biomedicine and Pharmacology at Leiden University (**ULEI**) gave a presentation at the **PAGE 2021** conference with the title "Age, gender, chronic morphine altered mu-opioid receptor occupancy in rat brain". Congrats!

The **QSPainRelief** project info brochure is now also available in Dutch (NL) and French (FR) on the **Downloads page** of the website. You can access and download a web version or a print version, whatever suits the intended purpose best. We hope the brochure will be well-received by French-speaking patients participating in the **clinical study** of **WP8** and by Dutch-speaking individuals participating in the **healthy-volunteer trial** of **WP7**.



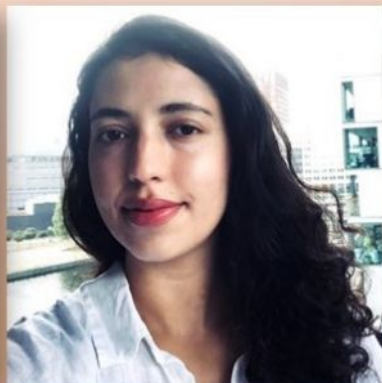
Bachelor students working on QSPainRelief

From April to June 2021, six bachelor's students from the Pharmaceutical Sciences programme at **ULEI** conducted their research project on **QSPainRelief**-related projects. Three of them completed an extensive literature search and have shown that various pain conditions led to changes in mu-opioid receptor expression in different brain regions. **Fleur** has helped with the identification of receptor level changes in mu-opioid receptor between young and old rats, **Dalia** with identification of data showing differences among genders (male and female), and **Lotte** by showing the contribution of physiological conditions (chronic morphine use vs.

helped in predicting CNS distribution of anti-epileptics in neuropathic/chronic pain and **Marloes** helped in predicting anti-epileptic and antidepressant distribution in inflammatory pain conditions in the CNS. Finally, **Robbin** examined the opioid distribution in changing physiological conditions, including paracellular transport. The students' work has provided very useful insights and added interesting observations for the research objectives of the **QSPainRelief** consortium.



Lotte



Dalia



Fleur

Save the dates

Quantitative Systems Pharmacology Conference (QSPC)

20 - 22 April 2022, Leiden, The Netherlands

Registrations for the postponed QSPC2020 meeting are valid for QSPC2022, registered participants have received an e-mail about their registration, for queries contact us at info@qspc.eu.

Quantitative Systems Pharmacology Conference 2022



April 20-22, 2022 Leiden, The Netherlands



Universiteit
Leiden
The Netherlands

EFIC 2022 Congress "Pain in Europe XII"

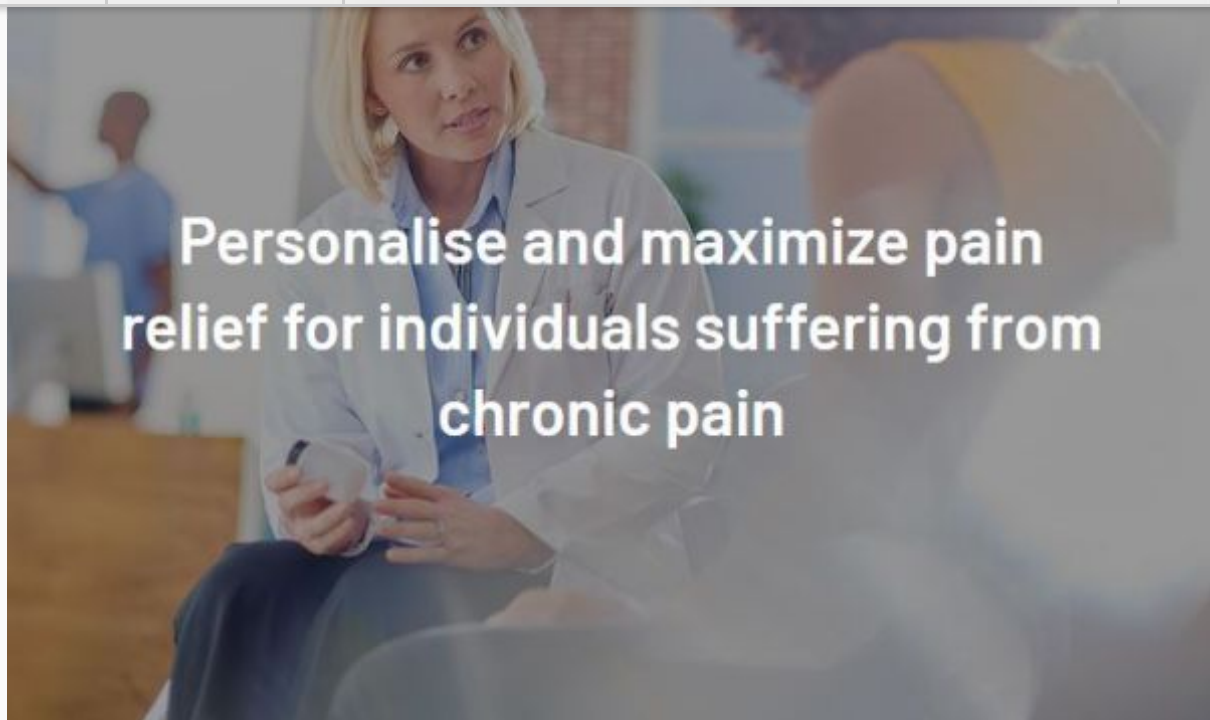
27 - 30 April 2022, Dublin, Ireland



QSPainRelief partners in Europe and in the USA.

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Personalise and maximize pain relief for individuals suffering from chronic pain



This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 848068. This newsletter reflects only the authors' view and the European Commission is not responsible for any use that may be made of the information it contains. You are receiving this half-yearly project newsletter because you are either a member of the research consortium, a member of the scientific and ethical advisory board (**SEAB**), a public-records contact point or press representative, a member of Pain Alliance Europe (**PAE**), or a subscriber from our sign-up page.

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