



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

Newsletter 2 - July 2021

[Major steps forward & 4th SC Meeting](#)

[Masterclass videos & E-Learning](#)

[Save the dates](#)

[New team members](#)

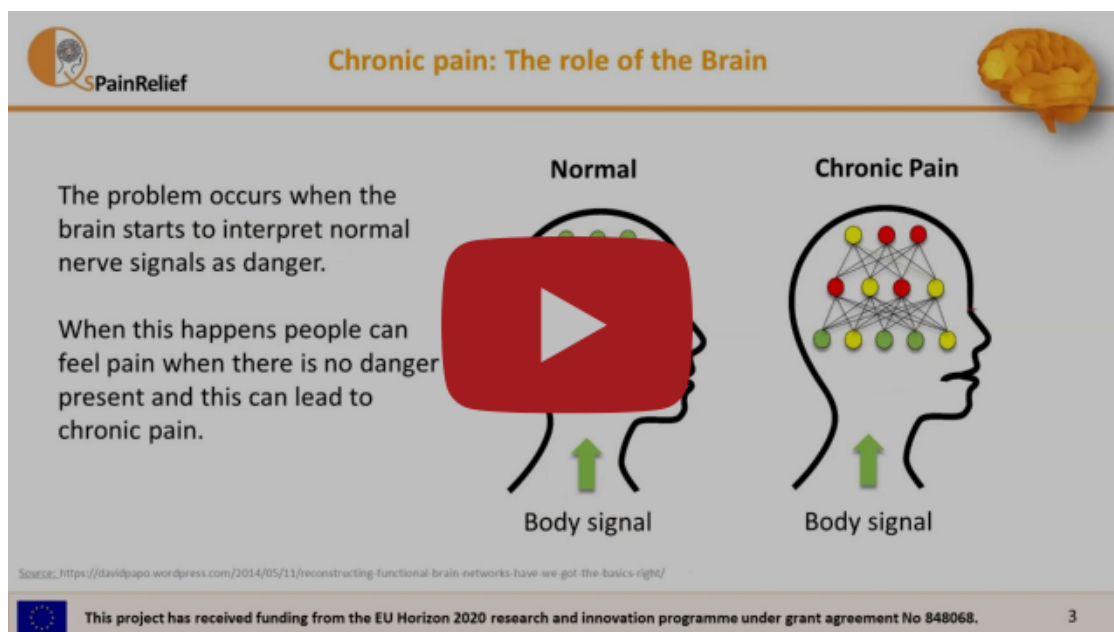
[Bachelor students working on QSPainRelief](#)

[Announcements & Achievements](#)

[Publications & Presentations](#)

Welcome to our 2nd newsletter! **QSPainRelief** is an international, collaborative **Horizon 2020** research project, funded by the European Commission,

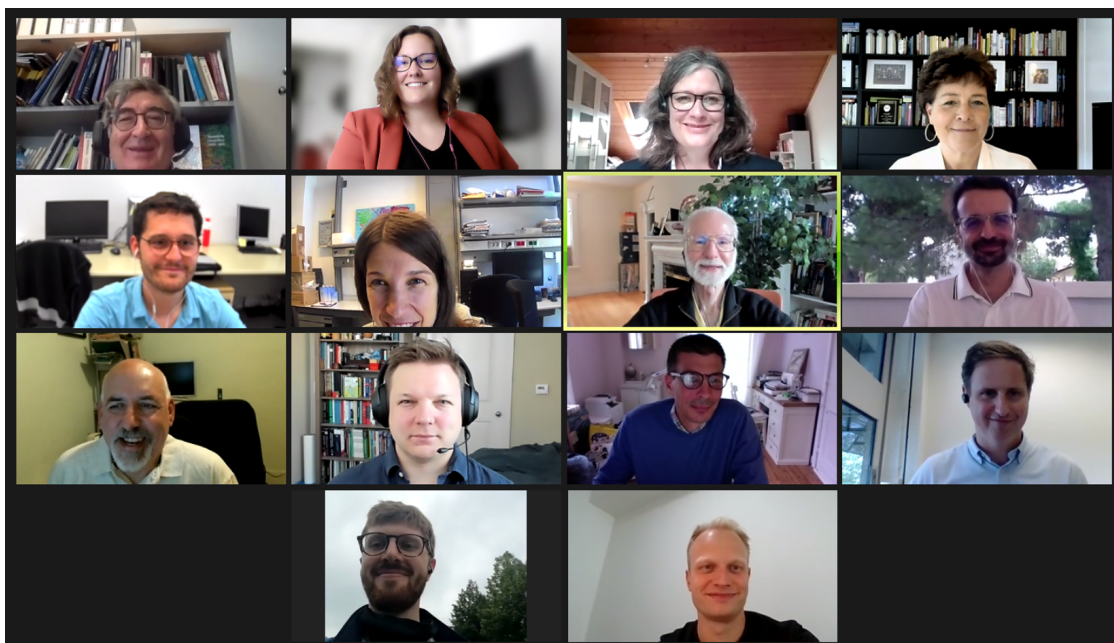
that brings together **10 partner institutions** from 5 European countries and the USA. The 5-year-long project started in January 2020 and uses an innovative quantitative systems pharmacology (QSP) pain relief approach in developing effective combinational treatment of chronic pain in individual patients. In this 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!**



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

Major steps forward & 4th SC Meeting

The 4th QSPainRelief Steering Committee (SC) Meeting took place this month as a virtual Zoom-meeting from 13-14 July 2021. We learned about the progress made in developing the QSPainRelief model platform (**WP2**, Petri Takkala), set-up and optimisation of the database (**WP3**, Liesbeth De Lange), *in silico* computation & risk / benefit analysis (**WP4**, Jeroen Elassaiss-Schaap), untangling cellular signalling pathways via computational approaches (**WP5**, Jesus Giraldo), first procedural results of the preclinical studies (**WP6**, Rafael Maldonado), planning of the healthy volunteers study (**WP7**, Geert Jan Groeneveld), and the fantastic news that the pain patient study recruitment can start now (**WP8**, André Mouraux)! **WP9** (Nina Donner) has completed the first dissemination performance evaluation, and thanks to Andrea Bedini (**WP10**), all ethics requirements are in place or on track as well. A special treat was the physical work-out session during a break & a quiz of baby photos from consortium members.



Masterclass Videos & E-Learning

On the QSPainRelief website, we now feature an **E-Learning Area** that is targeted towards the project-internal early-career scientists (ECS) as well as patients, relatives, pharmacology students, or anyone interested in learning more about pain perception, pain treatment, animal models, quantitative systems pharmacology, or *in silico* modelling. In addition to the introductory project video, our first two Masterclasses have been recorded, cut, and produced as videos for the **E-Learning Area**. They can also be found in the **QSPainRelief playlist** on YouTube. Feel free to support us by leaving a few "likes" on the videos.

QSPainRelief

Operant self-administration models: how may we evaluate reward, reinforcement, abuse liability and addiction

10-12-2020

Laboratory of Neuropharmacology
Barcelona, Spain
Pompeu Fabra University

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 848068.

*This Masterclass, held by consortium member and **WP6** leader **Prof. Dr. Rafael Maldonado** from University Pompeu Fabra (**UPF**, Barcelona), elucidates the value and necessity of animal models in researching addictive behaviors and related brain regions, in particular the use of the operant self-administration model to investigate the concepts of reward, reinforcement, abuse liability, and addiction in rodent models.*

An example

- 45 yr old patient tumor of the jaw
- 1 yr ago surgery: tumor removed (y)
- Neuropathic symptoms, phain?
- Step 2 and 3 planned
- Step 4: Diagnosis
- Step 5 Treatment
- Step 6 Review



The other Masterclass by our scientific and ethical advisory board (**SEAB**) member **Prof. Dr. Albert Dahan** from Leiden University Medical Center (LUMC), an expert on chronic pain treatment, provides first-hand insight on the current clinical approaches used to treat chronic pain patients.

Save the dates

XXV World Congress of Neurology (WCN 2021)

3 - 7 October 2021, Rome, Italy

PharmSci 360's Hybrid Meeting

17 - 20 October 2021, Philadelphia, USA

European Congress of Pharmacology (EPHAR)

6 - 8 December 2021, Prague, Czech Republic

Quantitative Systems Pharmacology Conference (QSPC)

19 - 22 April 2022, Leiden, The Netherlands

The QSPC 2021 meeting has been postponed to 2022 due to COVID-19.

EFIC 2022 Congress "Pain in Europe XII"

27 - 30 April 2022, Dublin, Ireland

IASP 2022 World Congress on Pain

19 - 23 September 2022, Toronto, Canada



New team members

A cordial welcome to two new early-career scientists (ECS). We are very happy to have you within the QSPainRelief research team. We asked each of them to write a few sentences to introduce themselves.

Solenn Gousset: After completing two different Master's theses at the Université Catholique de Louvain (**UCL**), one on "Experimental induction of secondary hyperalgesia in healthy volunteers" and the other one on "How negative expectations about pain influence the development of secondary hyperalgesia in healthy volunteers", I worked on the *IMI PAINCARE Biopain* project. In the beginning of this year, I started working on the **QSPainRelief** project, where I will be involved in the clinical study of **WP8**. Using non-invasive biomarkers of CNS activity, such as electroencephalogram (EEG) data, measurable CNS effects within pain-relevant neuronal networks will be compared with the clinical therapeutic effects in patients suffering from persistent post-surgical pain (PPSP).



Wouter Bakker: Currently, I am a Clinical Scientist and PhD candidate within the department of Neurology and Pain led by Prof. Geert Jan Groeneveld at the Centre for Human Drug Research (**CHDR**). Being involved in the



set-up, execution and reporting of clinical trials (especially human experimental pain studies) are part of my work activities. Additionally, I am in training for becoming a clinical pharmacologist. In 2018, I obtained a Master's degree in Drug Innovation at the faculty of chemistry with a special interest in clinical drug development. My role within the **QSPainRelief** consortium is to perform the experimental human pain studies as described in work package 7 (**WP7**) together with Hemme Hijma.

Bachelor students working on QSPainRelief

From April to June 2021, six *Pharmaceutical Sciences* Bachelor students conducted their research project on QSPainRelief-related topics. Three students focused on the central nervous system (CNS) target site pharmacokinetics of a wide variety of drugs under normal versus pain-related conditions. They performed an extensive literature search and have shown that changes may occur in blood brain barrier permeability and cerebral blood flow during various pain conditions that can affect the CNS target site profiles. The other three students focused on identifying changes in mu-opioid receptor expression in different brain regions among various age groups (young and old), genders (male and female), and physiological conditions (chronic morphine use vs. healthy subjects). Their research has identified interesting changes (up- or down-regulations) in receptor expression, which holds great significance for the objectives of QSPainRelief. We thank them for their important contribution to our research!

Announcements & Achievements

A big thank you to Joop van Griensven for his excellent service on QSPainRelief's Scientific and Ethical Advisory Board (**SEAB**) and congratulations to receiving the well-deserved "Lifetime Achievement Award" from the EFNA Advocacy Awards. We are quite sad to see him leave as president of Pain Alliance Europe (**PAE**), but wish him all the best, and are looking forward to collaborate with his successor!

Thank you, Joop!



The QSPainRelief consortium submitted the session "Towards the improvement of treatment of chronic pain by mechanism-based modeling approaches" for the **19th World Congress of Basic and Clinical Pharmacology (WCP)**, and we are happy to announce that it has been provisionally accepted into the programme! The next WCP congress will take place from **02 - 07 July 2023** in **Glasgow, Scotland (UK)**.



Publications & Presentations

We congratulate the team around **Prof. Dr. Jesús Giraldo** at Universitat Autònoma de Barcelona (**UAB**) on two newly published manuscripts since the start of the year. Keep them coming!

- Renault P, and Giraldo J (2021) **Dynamical Correlations Reveal Allosteric Sites in G-Protein-Coupled Receptors**. *Int J Mol Sci*. 22: 187. [PDF](#)
- Ricarte A, Dalton JAR, Giraldo J (2021) **Structural Assessment of Agonist Efficacy in the μ -Opioid Receptor: Morphine and Fentanyl Elicit Different Activation Patterns**. *J Chem Inf Model*. ePub ahead of print. [PDF](#)

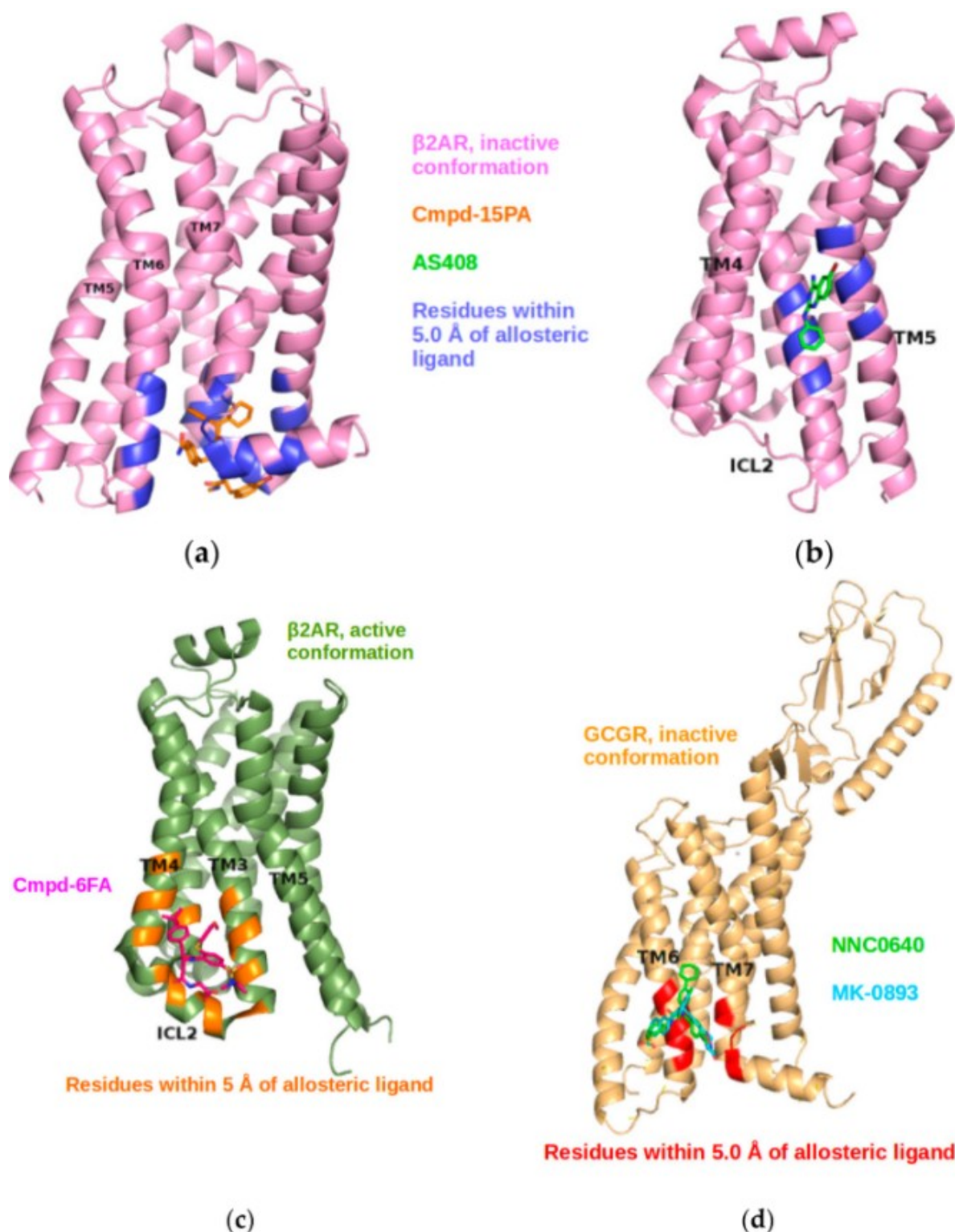


Figure 1 in Renault and Giraldo (2021). Experimental structures of β 2AR and glucagon receptor (GCGR) in the presence of allosteric modulators. β 2AR in the inactive conformation (pink) bound to (a) Cmpd-15PA (PDB: 5X7D); (b) AS408 (PDB: 6OBA); (c) β 2AR in the active conformation (green), bound to Cmpd-6FA (PDB: 6N48); (d) GCGR in the inactive conformation, in the presence of the allosteric ligands NNC0640 and MK-0893 (green and cyan; PDB codes 5XEZ and

5EE7, respectively). Ligands are shown as sticks and residues within 5.0 Å of a ligand are highlighted in different colors.



Dr. Pedro Renault from Universitat Autònoma de Barcelona (**UAB**) gave a flash presentation about "Dynamical correlations reveal allosteric sites in the β_2 adrenergic receptor" during the session on computational approaches during the 9th Annual Meeting of GDR 3545 in 2020 (*G-Protein Coupled receptors - From Physiology to Drugs*, virtual meeting). Congrats!



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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