



# NEWSLETTER

N°02 NOVEMBER 2022



## Welcome to the i-GPCRnet network!

**Dear colleagues, dear friends, dear GPCR-ists,**

It is our great pleasure to congratulate and thank the ECS Committee for their commitment, not only to assemble this 2<sup>nd</sup> NEWSLETTER of the i-GPCRnet but also for the excellent organization of our meeting in Würzburg. It was not easy to assemble and manage a 1-evening + 1-day meeting and to find a balance between « to get the most out of it without being constantly in a rush » . Congratulations, well-done! Without you the meeting would not have been possible.

The last action of the i-GPCRnet for this year will be the 3<sup>rd</sup> i-GPCRnet workshop in November in collaboration with our long-term partner PerkinElmer-Cisbio. Great event!

The coming year is already casting its shadow with the new edition of our virtual « Educational Workshop » in spring with GPCR expert lectures and our next Annual meeting in autumn in Strasbourg (France). Thanks to our colleagues in Strasbourg for having accepted the challenge!

Thanks to the i-GPCRnet community, including the industrial partners, for your continuous support and enthusiasm!

Enjoy the reading of the i-GPCRnet-NEWSLETTER

**Martin Lohse**

**Steve Hill**

**Ralf Jockers**



## Editorial

**This is the second issue of the i-GPCRnet Newsletter.**

This newsletter will provide you a brief summary of our 2<sup>nd</sup> Annual Meeting (and 1<sup>st</sup> in person meeting!) that just took place in Würzburg (Germany) last month, as well as all the information you need to be up-to-date on GPCR world (next important meetings, our upcoming Workshop, latest VIP (Very Important Publications) on GPCRs, and news from our members and Industrial partners.

We would like to remind you that we are willing to take into account any comments or suggestions regarding the newsletter sections, to accept contributions from everybody and to hear any criticisms you might have to improve the quality of the newsletter. Furthermore, anyone from each of the participating teams of the i-GPCRnet is more than welcome to contribute by using the address

[i-gpcrnet@services.cnrs.fr](mailto:i-gpcrnet@services.cnrs.fr)

**by ECS Committee**



# NEWSLETTER

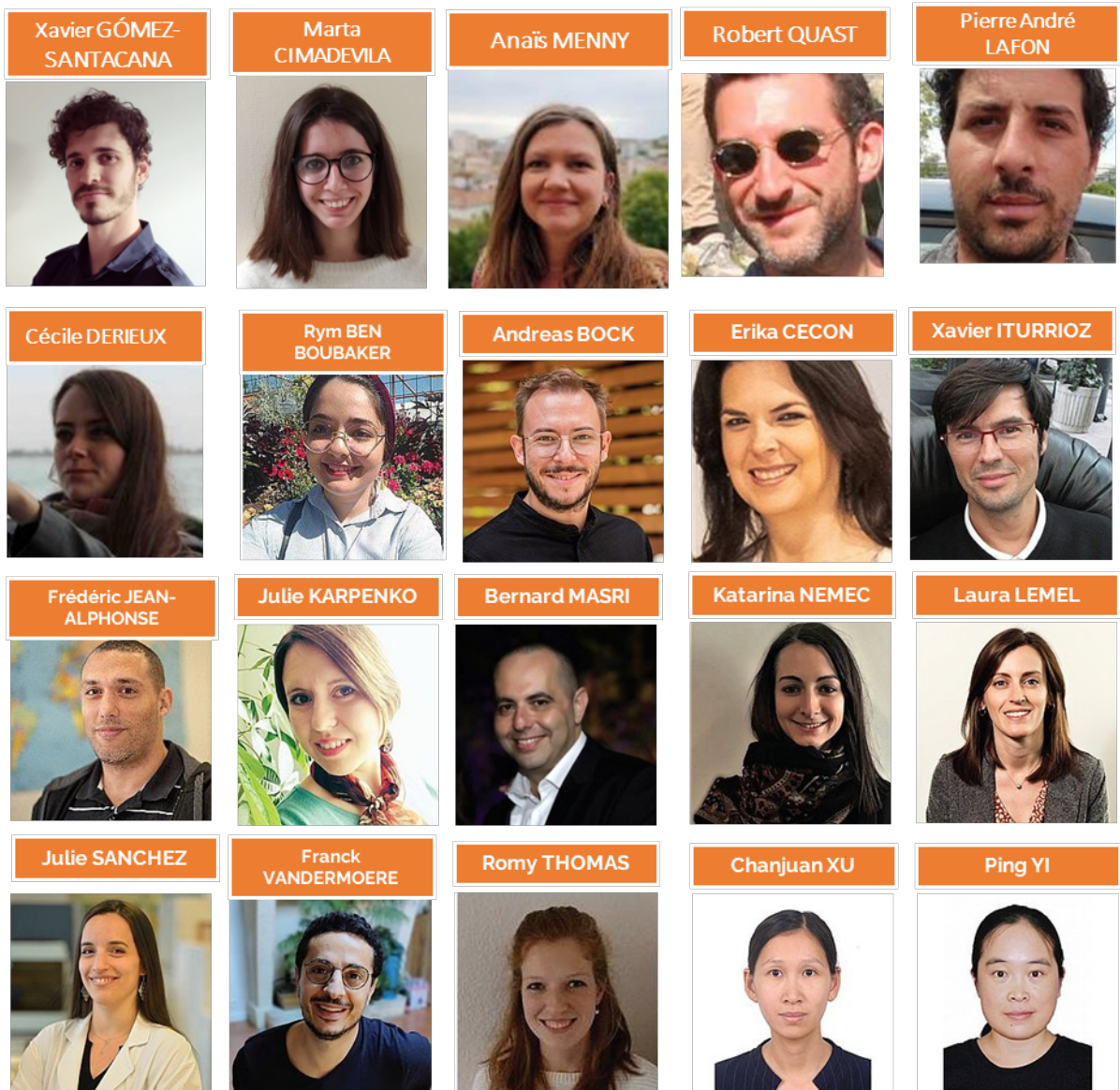
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## The Early Career Scientist Committee

is composed by young scientists from all levels, including PhD students, post-doctoral fellows and permanent researchers, from lab members of the i-GPCRnet IRN. The ECS committee aims to promote and support activities directed to young scientists of the i-GPCRnet IRN. Some of our actions include: active participation in the organisation of the i-GPCRnet IRN annual meeting; selection of

oral short talks and poster prizes at the annual meeting; organisation and promotion of the annual i-GPCRnet WORKSHOP dedicated to ECS of the i-GPCRnet IRN; editing of the i-GPCRnet NEWSLETTER dedicated to all i-GPCRnet IRN members highlighting the latest news of the GPCR field and our industrial partners.





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## News from i-GPCRnet members

**Floriane ESHASK**, PhD student supervised by Francine Acher (Laboratoire de Chimie et Biochimie, Pharmacologiques et Toxicologiques (LCBPT), CNRS UMR 8601, Université Paris Cité, Paris, France), in collaboration with Philippe Rondard and Jean-Philippe Pin (Institut de Génétique Fonctionnelle, CNRS UMR 5203, Inserm U1191, Université de Montpellier, France), has been twice awarded for **Best Communication**:

<https://www.sppin.fr/2022/09/22/floriane-eshak-is-twice-awarded-for-best-communication/>



**Philippe RONDARD**, Research Director from INSERM (Institut de Génétique Fonctionnelle, CNRS UMR 5203, Inserm U1191, Université de Montpellier, France) received the **Léon Velluz prize 2022**.

<https://www.academie-sciences.fr/fr/Laureats/laureat-2022-du-prix-leon-velluz-philippe-rondard.html>



**Jean-Philippe PIN**, Research Director from CNRS (Institut de Génétique Fonctionnelle, CNRS UMR 5203, Inserm U1191, Université de Montpellier, France) received the **Lamonica de neurologie/ Fondation pour la recherche biomédicale PCL 2022** prize.

<https://www.academie-sciences.fr/fr/Laureats/laureat-2022-du-prix-lamonica-de-neurologie-jean-philippe-pin.html>



**Lucie PELLISSIER** (Physiologie de la reproduction et des comportements, PRC - CNRS, INRAE, Université de Tours, France) was awarded the **CNRS Bronze Medal 2022**.

<https://www.cnrs.fr/fr/personne/medailles-de-bronze-2022>

*"Congratulations"*





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## i-GPCRnet ACTIONS

### Summary of the 2<sup>nd</sup> IRN i-GPCRnet meeting

The 2nd annual IRN i-GPCRnet (and first in person) meeting took place on 30th of September and 1st of October at the University of Würzburg (Germany). The meeting was organized by the i-GPCRnet ECS committee together with Ralf Jockers and Martin Lohse. We were happy to welcome 103 participants, including 36 non-IRN members, from a total of 13 different countries encompassing not only Europe but also Australia, Canada, Brazil and USA.



**The 2nd annual IRN « i-GPCRnet » meeting**



International Research Network (IRN) on GPCRs

**Challenges and future directions in the GPCR field**

Sep 30th - Oct 1st, 2022 *registration open!*  
Würzburg (Germany)

Keynote speaker : **Brian Kobilka**  
Confirmed speakers :  
**Michel Bouvier, Jean-Philippe Pin, Steve Briddon**

Great opportunity for Early-Career Scientists  
(Talk slots available - selection on abstracts)

3 Sessions on GPCR function - "Where, When and How?!"  
2 Round-tables on current and future challenges in the field  
2 Poster sessions



Registration at: [www.i-gpcrnet.com](http://www.i-gpcrnet.com)

It has been 2 great days with 2 keynote lectures by Brian Kobilka and Jean-Pierre Vilardaga, 3 invited speakers (Michel Bouvier, Jean-Philippe Pin, Steve Briddon), 13 selected talks by ECIs and 45 posters – covering the main topics of GPCR signaling, spatial organization, functional dynamics and novel investigation techniques.





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## Summary of the 2<sup>nd</sup> IRN i-GPCRnet meeting



The two round table sessions were dedicated exclusively to the young scientists (mainly PhD students and postdoctoral researchers). In the first one the attendees had the opportunity to freely ask questions to two experienced and renowned scientists Prof. Brian Kobilka, USA (Nobel prize winner) and Dr. Jean Philippe Pin, France), exchanging opinions on the challenges and future directions in the GPCR field.



In the second round table on “Career challenges and opportunities in the GPCR field” the young scientists had the opportunity to discuss with early stage career as well as experienced scientists working in academic (Dr. Robert Quast, France; Prof. Michel Bouvier, Canada; Isabella Maiellaro, UK) or industrial sectors (Dr. Laura Lemel, UK; Dr. Xavier Leroy, France).



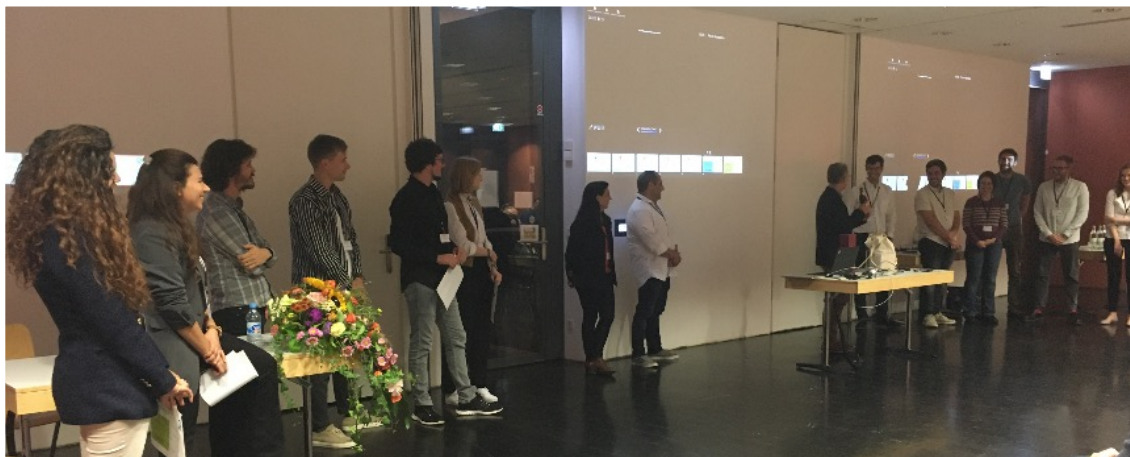


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## Summary of the 2<sup>nd</sup> IRN i-GPCRnet meeting



We are pleased to congratulate once more our 6 poster prize winners: Charlotte Kayser (Berlin), Xavier Gomez-Santacana (Barcelona), Floriane Eshak (Paris), Philipp Gmach (Berlin), Lauri Urvas (Strasbourg) and Ghazi Al Hamwi (Bonn).

We would like to warmly thank the speakers, poster presenters and attendees for having a great meeting full of insightful discussions.

A special thanks to our sponsors CNRS, ISAR Bioscience, Calixar, Berthold and Université Paris Cité for their support and the University of Würzburg and Martin Lohse for hosting the meeting.



## Announcement of upcoming meeting



**Keep in mind:  
Next (3rd) i-GPCRnet Annual meeting:  
Autumn 2023 - Strasbourg, France.**



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## Announcement of the upcoming 3<sup>rd</sup> i-GPCRnet workshop (Nov 17<sup>th</sup>-18<sup>th</sup>, 2022)



### i-GPCRnet WORKSHOP 2022



**Objective:** Intensive and interactive theoretical & practical training on HTRF and AlphaLISA assays, focused on GPCR applications

- New classroom training at PerkinElmer/Cisbio location in Codolet (South of France)
- Facilities to host theoretical and hands-on training in small groups, provided by our experienced trainers
- Dedicated lab environment equipped to run cell-based assays



#### HTRF cAMP

Monitoring cAMP accumulation as read out of GPCR activation



#### HTRF Taglite

GPCR ligand binding assay



#### Alpha SureFire phospho-ERK

Monitoring the cell signalling pathway activation via the phosphorylation of ERK1/2



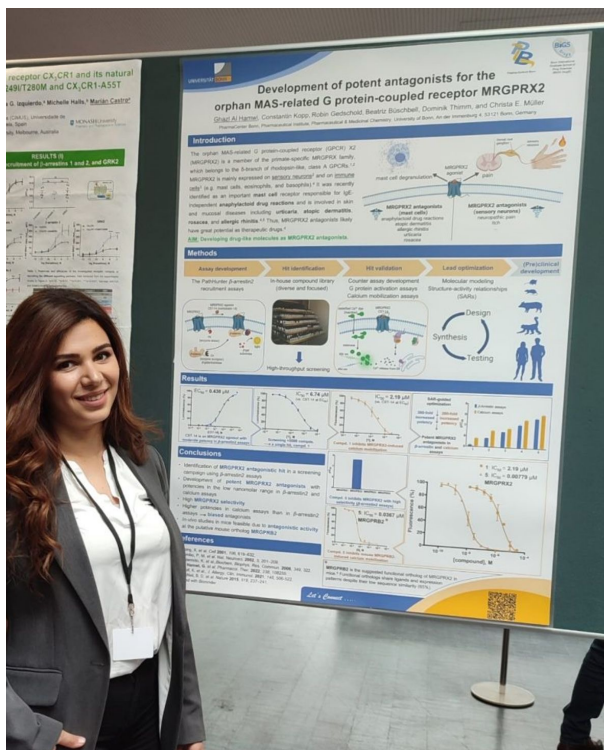


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## Sponsors / Partners corner



### Back to the 2nd IRN I-GPCRnet Annual Meeting in late September at Wurzburg University in Germany

CALIXAR was honored to sponsor for the second time the I-GPCRnet. Once again, congratulations to Ghazl Al Harmar, for her amazing work on the development of potent antagonists for the orphan MAS-related G protein-coupled receptor MRGPRX2 and winning the CALIXAR poster price. Her work focused on MRGX2, an orphan MAS-related G protein-coupled receptor, with the aim of developing several powerful antagonists. Selected antagonists are now undergoing further characterization in preclinical models. CALIXAR is currently working on MRGX2 receptor, and other promising targets, to enrich the pipeline, and respond to current and future therapeutic needs. For collaboration opportunities, please contact us at [contact@calixar.com](mailto:contact@calixar.com).





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## VIP List of recent GPCR-related publications

### Research Articles

We would like to show a brief review of the work that has been done in the last 6 months in the field of GPCRs. For that, we have selected several publications and divided them in 6 categories: molecular structure, dynamics, signal transduction, physiology and disease, drug development and novel tools

#### MOLECULAR STRUCTURE

**Qian, Y. et al.** Structural insights into adhesion GPCR ADGRL3 activation and Gq, Gs, Gi, and G12 coupling. *Mol. Cell* 82, 1-13 (2022). <https://doi.org/10.1016/j.molcel.2022.10.009>

**Zhu, X. et al.** Structural basis of adhesion GPCR GPR110 activation by stalk peptide and G-proteins coupling. *Nat. Commun.* 13, 5513 (2022). <https://doi.org/10.1038/s41467-022-33173-4>

In these sister papers, Qian et al. and Zhu et al. use single-particle cryoEM to solve structures of ADGRL3 and GPR110 bound to Gq, Gs, Gi and G12. GPR110 is also resolved bound to G13. They complement these structures with an array of functional recordings to interrogate their self-activation mechanisms. This colossal work sheds important light on the molecular determinants of aGPCRs coupling specificities

**Haider, R.S. et al.**  $\beta$ -arrestin1 and 2 exhibit distinct phosphorylation-dependent conformations when coupling to the same GPCR in living cells. *Nat. Commun.* 13, 5638 (2022). <https://doi.org/10.1038/s41467-022-33307-8>

**Bous, J. et al.** Structure of the vasopressin hormone-V2 receptor- $\beta$ -arrestin1 ternary complex. *Sci. Adv.* 8, eabo7761 (2022) <https://doi.org/10.1126/sciadv.abo7761>

**Yue, Y. et al.** Structural insight into apelin receptor-G protein stoichiometry. *Nat. Struct. Mol. Biol.* 29, 688–697 (2022). <https://doi.org/10.1038/s41594-022-00797-5>

**Yang, X. et al.** Molecular mechanism of allosteric modulation for the cannabinoid receptor CB1. *Nat. Chem. Biol.* 18, 831–840 (2022). <https://doi.org/10.1038/s41589-022-01038-y>

#### DYNAMICS

**Asher, W. B. et al.** GPCR-mediated  $\beta$ -arrestin activation deconvoluted with single-molecule precision. *Cell* 185, 1661-1675.e16(2022). <https://doi.org/10.1016/j.cell.2022.02.011>

Asher et al. use single molecule FRET to reveal that relieving autoinhibition to activate  $\beta$ -arrestin1, mediated by the C-terminal tails of  $\beta$ 2-adrenergic receptor and arrestin, depends on the degree of receptor tail phosphorylation and concurrent agonist-mediated activation.

**Kleist, A. B. et al.** Conformational selection guides  $\beta$ -arrestin recruitment at a biased G protein-coupled receptor. *Science* 377, 222–228(2022). <https://doi.org/10.1126/science.abj4922>

**Culhane, K. J., Gupte, T. M., Madhugiri, I., Gadgil, C. J. & Sivaramakrishnan, S.** Kinetic model of GPCR-G protein interactions reveals allokaireic modulation of signaling. *Nat. Commun.* 13, 1–9 (2022). <https://doi.org/10.1038/s41467-022-28789-5>



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## SIGNAL TRANSDUCTION

**Kwon, Y. et al.** Non-canonical  $\beta$ -adrenergic activation of ERK at endosomes. *Nat.* 2022 6117934 611, 173–179 (2022).  
<https://doi.org/10.1038/s41586-022-05343-3>

Using subcellularly-targeted biosensors, Kwon et al. reveal a non-canonical mechanism for the spatial regulation of ERK activation through endosome-localized  $\beta$ 2-adrenergic receptors and Gas.

**Moreno, E. et al.** Pharmacological targeting of G protein-coupled receptor heteromers. *Pharmacol. Res.* 185, 106476 (2022).  
<https://doi.org/10.1016/j.phrs.2022.106476>

**Shin, H. R. et al.** Lysosomal GPCR-like protein LYCHOS signals cholesterol sufficiency to mTORC1. *Science* 377, 1290–1298 (2022).  
<https://doi.org/10.1126/science.abg6621>

**Chen, S. et al.** Capturing a rhodopsin receptor signalling cascade across a native membrane. *Nature*, 6047905 604, 384–390 (2022).  
<https://doi.org/10.1038/s41586-022-04547-x>

**Liu, J. et al.** Biased signaling due to oligomerization of the G protein-coupled platelet-activating factor receptor. *Nat. Commun.* 2022 131 13, 1–16 (2022).  
<https://doi.org/10.1038/s41467-022-34056-4>

**Anton, S. E. et al.** Receptor-associated independent cAMP nanodomains mediate spatiotemporal specificity of GPCR signaling. *Cell* 185, 1130–1142.e11 (2022).  
<https://doi.org/10.1016/j.cell.2022.02.011>

## PHYSIOLOGY AND DISEASE

**Meng, J. et al.** Nanobody-based sensors reveal a high proportion of mGlu heterodimers in the brain. *Nat. Chem. Biol.* 18, 894 (2022).  
<https://doi.org/10.1038/s41589-022-01050-2>

Using nanobody-based sensors specific for both mGlu2 and mGlu4 subunits, authors were able to reveal the existence of endogenous mGlu2-mGlu4 heterodimers, in addition to mGlu2 and mGlu4 homodimers, in various brain regions, by FRET. Surprisingly, mGlu4 subunits appeared to be mainly involved in heterodimers than in homodimers in the brain

**Schulze A.S. et al.** Evolutionary analyses reveal immune cell receptor GPR84 as a conserved receptor for bacteria-derived molecules. *iScience* 25 (10), 105087 (2022).  
<https://doi.org/10.1016/j.isci.2022.105087>

**Si M. et al.** CXCL12/CXCR7/ $\beta$ -arrestin1 biased signal promotes epithelial-to-mesenchymal transition of colorectal cancer by repressing miRNAs through YAP1 nuclear translocation. *Cell & Bioscience* 12, 171 (2022).  
<https://doi.org/10.1186/s13578-022-00908-1>

**Huang Y. et al.** G protein-biased GPR3 signaling ameliorates amyloid pathology in a preclinical Alzheimer's disease mouse model. *PNAS* 119, e2204828119 (2022).  
<https://doi.org/10.1073/pnas.2204828119>

## DRUG DEVELOPMENT

**Fink, E. A. et al.**, Structure-based discovery of nonopioid analgesics acting through the  $\alpha$ 2A-adrenergic receptor. *Science*, 377, 6614 (2022).  
<https://doi.org/science.abn7065>

The authors aimed to seek for new non-opioid analgesics targeting  $\alpha$ 2A, but with no sedative side-effects and orally bioavailable. After a virtual screening of +300 million molecules, they identified new  $\alpha$ 2A agonists. Experimental structures and subsequent hit optimisation led to new promising leads effective in a neuropathic pain model without causing sedation.



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**Kaplan, A.L., et al.**, Bespoke library docking for 5-HT<sub>2A</sub> receptor agonists with antidepressant activity. *Nature*, 610, 582–591 (2022).  
<https://doi.org/10.1038/s41586-022-05258-z>.

**Huang, Y., et al.**, G protein-biased GPR3 signaling ameliorates amyloid pathology in a preclinical Alzheimer's disease mouse model. *PNAS* 119 (40) e2204828119 (2022)  
<https://doi.org/10.1073/pnas.2204828119>

**García-Cárceles, J.,** 2-(Fluoromethoxy)-4'-(S-methanesulfonimidoyl)-1,1'-biphenyl (UCM-1306), an Orally Bioavailable Positive Allosteric Modulator of the Human Dopamine D1 Receptor for Parkinson's Disease. *J. Med. Chem.*, 65, 18, 12256–12272, (2022)  
<https://doi.org/10.1021/acs.jmedchem.2c00949>

**Baidya, M., et al.** Allosteric modulation of GPCR-induced  $\beta$ -arrestin trafficking and signaling by a synthetic intrabody. *Nat. Commun.* 13, 4634 (2022).  
<https://doi.org/10.1038/s41467-022-32386-x>

**Duran-Corbera, A. et al.**, A Photoswitchable Ligand Targeting the  $\beta$ 1-Adrenoceptor Enables Light-Control of the Cardiac Rhythm,(2022). *Angew. Chem. Int. Ed.*, 61, 30, e202203449 (2022) <https://doi.org/10.1002/anie.202203449>

## NOVEL TOOLS

**Wang, L. et al.** A high-performance genetically encoded fluorescent indicator for in vivo cAMP imaging. *Nat. Commun.* 13, 5363 (2022).  
<https://doi.org/10.1038/s41467-022-32994-7>

The authors engineered a fluorescent cAMP sensor that can be used to selectively monitor cAMP changes in vitro and in vivo. This sensor emerges as a novel tool to detect the modulation of intracellular pathways in living animals in real time.

**Beerkens, B.L.H. et al.** A Chemical Biological Approach to Study G Protein-Coupled Receptors: Labeling the Adenosine A1 Receptor Using an Electrophilic Covalent Probe. *ACS Chem. Biol.* (2022).  
<https://doi.org/10.1021/acscchembio.2c00589>

**Chen, S. et al.** Capturing a rhodopsin receptor signalling cascade across a native membrane. *Nature*. 604, 384–390 (2022)  
<https://doi.org/10.1038/s41586-022-04547-x>

**Garrido-Charles, A. et al.** Photoswitchable Molecular Prosthetics Control Neuronal Activity in the Cochlea. *J. Am. Chem. Soc.* 144 (21), 9229-9239 (2022)  
<https://doi.org/10.1021/jacs.1c12314>

**White, A.M. et al.** Late-Stage Functionalization with Cysteine Staples Generates Potent and Selective Melanocortin Receptor-1 Agonists. *J. Med. Chem.* 65 (19), 12956-12969 (2022)  
<https://doi.org/10.1021/acs.jmedchem.2c00793>

**Zhang, K. et al.** Fusion protein strategies for cryo-EM study of G protein-coupled receptors. *Nat. Commun.* 13, 4366 (2022)  
<https://doi.org/10.1038/s41467-022-32125-2>

On top of that, we would like to share the Community guidelines for GPCR ligand bias, the last guideline published by the IUPHAR on GPCRs:

**Kolb, P. et al.** Community guidelines for GPCR ligand bias: IUPHAR review 32. *Br. J. Pharmacol.* 179(14):3651-3674 (2022)  
<https://doi.org/10.1111/bph.15811>



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## JOB OFFERS



**University of  
Nottingham**  
UK | CHINA | MALAYSIA

RESEARCH ASSOCIATE/FELLOW (FIXED TERM)

<https://jobs.nottingham.ac.uk/vacancy.aspx?ref=MED478222>

<b>Location:</b>	UK Other
<b>Salary:</b>	£28,762 to £36,386 per annum, (pro rata if applicable) depending on skills and experience (minimum £32348 with relevant PhD). Salary progression beyond this scale is subject to performance
<b>Closing Date:</b>	Wednesday 23 November 2022

The role will provide support to a new MRC project grant that aims to design and synthesise an armoury of high-affinity fluorescently-labelled antagonists and agonists for the P2Y2R receptor. These will be used to develop novel P2Y2R fluorescence and luminescence based assays and state-of-the-art imaging to unravel the interaction of P2Y2R with other cell surface receptors using 3D cell culture models involving multiple cell types, such as endothelial, fibroblasts and cancers cells (for cancer models) and epithelial, smooth muscle cells and fibroblasts for airway fibrosis models. The role holder will work closely with a postdoctoral medicinal chemist and undertake resonance energy transfer measurements (both BRET and TR-FRET), confocal and super-resolution imaging, fluorescence correlation spectroscopy, CRISPR/Cas9 genome editing and complex molecular and cellular biology assays.

Candidates should have a PhD (or close to completion) or equivalent in pharmacology or a related discipline, along with a proven track record of molecular pharmacology research and experience with using imaging based approaches to study G protein-coupled receptors in cell systems.

The successful candidate will join a vibrant cell signalling research group within the Centre of Membrane Proteins and Receptors in Nottingham.

The post is offered on a full time (36.25 hours per week), fixed term contract available from 01 January 2023 to 30 June 2026. Job share arrangements may be considered.

Informal enquiries may be addressed to Professor S J Hill tel: 0115 8230082 Or email [steve.hill@nottingham.ac.uk](mailto:steve.hill@nottingham.ac.uk). Please note that applications sent directly to this email address will not be accepted.



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## JOB OFFERS

### POSTDOCTORAL FELLOWS ON CELLULAR COMMUNICATION IN CANCER, DEVELOPMENT AND NEUROTRANSMISSION AT BOSTON UNIVERSITY (BOSTON, MA, US)

We are seeking to fill two postdoctoral positions broadly related to the topic of signal transduction via G protein-coupled receptors (GPCRs). Our laboratory is in a phase of expansion with multiple active NIH-funded grants to provide stable support for personnel. You would join a dynamic team of international researchers (PhD students and other postdocs) with an interest in collaborating and helping each other. Dr. Garcia-Marcos seeks to mentor the next generation of scientists by providing abundant one-on-one time and the support required to transition into subsequent career stages, including establishing their independent research programs. The laboratory has an excellent track record of facilitating the transition of former postdoctoral fellows to competitive positions.

We are located at the heart of Boston, a scientifically and culturally vibrant location. The minimum salary is \$58,000/ year plus a sign-on bonus for relocation expenses. Health plan and other benefits included.

Our laboratory is interested in the following general lines of investigation:

- Defining new mechanisms of signal transduction via GPCRs and heterotrimeric G proteins across scales, from molecules to whole organisms
- Non-canonical heterotrimeric G protein signaling in epithelial planar cell polarity, cilia and development
- Development of optical biosensors and chemogenetic tools to detect and manipulate the signaling activity of heterotrimeric G proteins
- Characterization and pharmacological targeting of non-canonical heterotrimeric G protein signaling in cancer metastasis
- Biochemical, functional and structural characterization of atypical G protein signaling complexes.

The candidate should have at least one of the following technical skillsets:

- Extensive experience with fluorescence microscopy and image analysis. Live-cell microscopy desirable.
- Xenopus and/or zebrafish experience. Egg microinjections and other general aquatic model procedures.
- High proficiency in cell culture. Viral gene delivery, generation of stable cell lines, different types of cells (e.g., transformed and non-transformed, primary cell cultures), signaling assays. Basic knowledge of mouse colony maintenance desirable.

Fast paced in molecular biology (cloning by Gibson assembly, Golden Gate, etc), and knowledge of protein purification (batch, FPLC) and protein binding assays (pulldowns, immunoprecipitations). Structural biology background desirable.

See "Representative publications" by scrolling down in:

<https://www.bumc.bu.edu/biochemistry/profiles/mikel-garcia-marcos/>

Complete list of publications in:

<https://www.ncbi.nlm.nih.gov/myncbi/1ZIXmzi80H8Q6/bibliography/public/>

Please submit a cover letter with details on what project you want to pursue, a CV and names/contact for 3 reference letters. Mikel Garcia-Marcos, PhD. Professor. [mikel.garcia.marcos@gmail.com](mailto:mikel.garcia.marcos@gmail.com)



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**i-GPCRnet**

International Research Network (IRN) on GPCRs

## JOB OFFERS



### BACKGROUND

G-Protein Coupled Receptors (GPCRs) form a large family of membrane proteins that constitute key privileged targets for the design of new drugs. Despite a large set of available structures, their regulation mechanism at the molecular scale still requires to be characterized. This is principally due to the fact that this mechanism involves the modulation by different partners (ligands, lipids, ions, intra-cellular effectors, etc...) of the equilibria between different intrinsic conformations, some features that are hard to be captured by structural methods. Things are even more complicated if we consider homo- or hetero-dimers of GPCRs. Only a few structures in the PDB describe the possible orientation of GPCR protomers in such assemblies. Some years ago, we proposed a model of the Ghrelin:Dopamin hetero-dimer in which each receptor was bound to its favorite G-protein partner at the same time. This model was experimentally validated by the measurement of crossed distances between the two receptors and the two G-proteins. Thanks to the "Grand Challenge" phase on the Jean-Zay machine provided by GENCI, we already performed extensive simulations of this dimeric model and its isolated entities. The objective of these simulations is to understand the cross-talk that operates in such large molecular assemblies and help to the design of new potent ligands.

We propose here an **18 months** contract, funded by FRM (foundation pour la recherche médicale) for a highly motivated post-doctoral fellow, ideally beginning in **January 2023**. The objective of the recruited post-doc will be to analyze the already obtained data and run complementary molecular dynamics simulations to provide a global mechanical view of how these complex systems behave at the membrane surface. The work will be performed in close collaboration with experimentalists in the laboratory, including biochemists and chemists for validation purposes. This collaboration could include the production of protein variants and the synthesis/testing of new ligands.

### CANDIDATE PROFILE

The sought candidate would ideally have a good experience in running / analyzing molecular dynamics simulations of peptides and proteins, and a validated PhD in a related field. She/He will have good knowledge of classical force-fields and MD codes and especially Gromacs; a plus would be to already have practiced coarse-grained force-fields (MARTINI FF). The candidate must be autonomous under the linux environment, and know at least one scripting language to analyze all produced data (python, R, etc ...). The candidate must be fluent in English and able to present her/his results either to specialists or non-specialists.

Contact us @ [nicolas.floquet@umontpellier.fr](mailto:nicolas.floquet@umontpellier.fr) for further detail and planification of an interview.

Institut des Biomolécules Max Mousseron (IBMM CNRS UMR5247)

Pôle Chimie BALARD, campus CNRS 1919 route de Mende, MONTPELLIER, France.

<https://www.ibmmpharmaco.com/>

### Some of our last publications in the field :

- (1) Louet, M.; Casiraghi, M.; Damian, M.; Costa, M. G.; Renault, P.; Gomes, A. A.; Batista, P. R.; M'Kadmi, C.; Mary, S.; Cantel, S.; Denoyelle, S.; Ben Haj Salah, K.; Perahia, D.; Bisch, P. M.; Fehrentz, J.-A.; Catoire, L. J.; Floquet, N.; Banères, J.-L. Concerted Conformational Dynamics and Water Movements in the Ghrelin G Protein-Coupled Receptor. *Elife* **2021**, *10*, e63201. <https://doi.org/10.7554/eLife.63201>.
- (2) Damian, M.; Louet, M.; Augusto Severo Gomes, A.; M'Kadmi, C.; Denoyelle, S.; Cantel, S.; Mary, S.; Bisch, P.





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## Upcoming GPCR meetings

### **Dr. GPCR Summit 2022**

(Still available talks online!)

Virtual

October 10-14, 2022

### **2022 Chemistry and Biology of Peptides (GRC)**

*Rising Tide of Peptides as Research Tools,  
Therapeutics, and Biomaterials*

October 29 - 30, 2022

### **2022 Chemistry and Biology of Peptides**

*Exploring the Natural and Unnatural of Peptide  
Sc*

October 30 - November 4, 2022

### **2023 GPCR WORKSHOP**

Kona, Hawaii

January 3 -6, 2023

### **2nd GPCR-Targeted Drug Discovery Summit**

Hyatt Regency Boston, MA, United States

February 21-23, 2023

### **8th German Pharm-Tox Summit**

Ulm, Germany

March 6-9, 2023

### **GEMXXII CONGRESS - Structure, dynamics, and function of membranes**

Autrans, France

March 14-17, 2023

### **Genomics in Drug Discovery and Development (Training Workshop)**

online

March 23, 2023

### **Binding Kinetics and Mechanistic PK/PD modeling in early Drug Discovery**

online and in-person: Cambridge, UK

March 27 - 28, 2023

### **ICEBA 2023: 17. International Conference on Experimental Biology and Applications**

Athens, Greece

April 3-4, 2023

### **Cell and Experimental Biology**

Houston, TX

April 24-26, 2023

### **8th and final ERNEST Meeting & Celebration**

Crete, Greece

May 3th -7, 2023

### **The ASPET Annual Meeting**

St.Louis, USA

May 18-21, 2023

### **2023 Molecular Pharmacology (GRC)**

*Insights Into GPCR Action: From Molecules to  
Mechanisms*

June 10 - 11, 2023

### **19th World Congress of Basic & Clinical Pharmacology 2023**

Glasgow, Scotland

July 2 - 7, 2023

### **3rd Transatlantic ECI GPCR Symposium**

online

Summer 2023

### **iGPCRnet conference**

Strasbourg, France

Autumn 2023

### **GPCR Retreat**

Quebec, Canada

November 2023



# NEWSLETTER

N°02 NOVEMBER 2022



## ONLINE GPCRs RESOURCES

<http://www.i-gpcrnet.com/>

<https://ernest-gpcr.eu/>

- Past conference recordings, Member list with topic and methods assignment,

<https://www.drgpcr.com/>

- Career, Connect, Consulting, Member Form, Newsletter, Podcast, Store, Summit, Virtual Cafe, ...

<https://druggablegenome.net/IDG-Events> -

NIH Common Fund-sponsored consortium, series of 1-hour sessions to learn about new experimental resources and digital tools illuminating the understudied targets in three main druggable protein families: GPCR, kinase, and ion channels...

<https://biasdb.drug-design.de/>

- A manually curated database of biased GPCR ligands

<https://submission.gpcrmd.org/home/>

- molecular dynamics database for GPCRs

<https://gpcrdb.org/>

- Reference data, Analysis tools, Visualization, Experiment design, Data deposition for GPCRs for GPCRdb, GproteinDb, ArrestinDb and Biased Signaling Atlas

<https://gpcrladies.com/>

<https://gpcrm.biomodellab.eu/> - Structure Modeling Server

<http://www.ssfa-7tmr.de/ssfe2/>

- GPCR-Sequence-Structure-Feature-Extractor

<https://gomodo.grs.kfajuelich.de/php/begin.php>

- GPCR Online Modeling and Docking server

<https://mmcg.grs.kfa-juelich.de/>

- Hybrid Molecular Mechanics/Coarse-Grained (MM/CG) simulations

<http://gpcr-modsim.org/>

- A pipeline for computational modeling and simulation of GPCRs

<https://gpcrsignal.biomodellab.eu/>

- Service for the GPCR-effector protein complexes (molecular dynamics in implicit environments, making mutations, analysis/comparison of dynamic interfaces)

<https://www.guidetopharmacology.org/>

<https://bisejdiu.github.io/GPCR-lipid-interactions/>

<https://www.gpcr-hetnet.com/>

<https://gproteindb.org/>

<https://arrestindb.org/>

<https://biasedsignalingatlas.org/>