opnMe by Boehringer Ingelheim

opn2EXPERTS – Ligands for studying GPR151's function

Could you be the first to identify a validated GPR151 specific ligand?

Answers to this question including a proposal for collaboration can only be considered if they arrive no later than October 11, 2022 11:59 pm PST.

Boehringer Ingelheim

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What is the context of the problem that we would like to solve?

The G-protein-coupled receptor 151 (GPR151; also known as GALR4, GALRL, PGR7) is an orphan GPCR that signals through the G-alpha inhibitory subunit to inhibit adenylyl cyclase activity and decrease intracellular cAMP concentration. GPR151 is highly enriched in the habenula brain region of humans and rodents. The protein is expressed at presynaptic membranes and associates with synaptic components controlling vesicle release and ion transport[1]. GPR151 may therefore have a role in CNS-related disorders. Recent human genetic evidence has also linked GPR151 variants with metabolic diseases, including obesity[2] and inflammatory bowel disease (IBD)[3]. However, the underlying biological mechanisms connecting GPR151 to any of these human diseases is lacking in the absence of a selective ligand.

Identification and validation of selective ligand(s) for GPR151 would facilitate more specific studies testing the biological role of GPR151 in the context of human disease and therefore provide valuable insights into the full therapeutic potential of this poorly understood receptor. We invite you to share your selective GPR151 ligand with us to be tested in relevant biological systems. These can be binders, fragments, tool compounds, and/or endogenous ligands which you have identified and where you have generated evidence that they specifically bind to GPR151. The validation step may comprise of any form of test system, i.e., either based on biochemistry or *in vitro* or *in vivo* models. Besides, we also invite scientists to submit any unconventional, but feasible methodology that allows identifying and verifying GPR151 ligands. We expect that the project will be executed in your laboratory and takes advantage of existing technologies and assays. To respect your full intellectual property rights on your proposal, we kindly ask you to submit only non-confidential data which do not include structures and/or primary sequences.

Research funding will be provided to proposals endorsed by the review committee. Depending on the level of validation of your proposed GPR151 ligand (please refer to “in scope section”), we are flexible to establish a simple material transfer agreement (MTA) or a full collaboration with a funding up to 500,000 euros.

Please share only non-confidential data with your proposal to preserve intellectual property. In particular, do not share any chemical structures or any information which could lead to its discovery even if the chemical structure is publicly known. As a safety precaution on our end, all incoming proposals will at first be evaluated as part of a sanity check by an independent, neutral representative. Only projects which meet the requirements above will be passed on for further internal review. Should there be any doubt, you would be contacted to provide you with the chance to resubmit your proposal without confidential data. Later, during the evaluation process, for the purpose of a fair collaboration, Boehringer Ingelheim may propose a third-party due diligence on your chemical matter to evaluate independently from Boehringer Ingelheim its level of quality.

In summary, we invite chemists and biologists to share with us selective GPR151 ligands which have undergone some form of biologic validation, either *in vitro* or *in vivo.*

What potential solutions could be in scope?

Any modality that directly binds to GPR151 or modulates GPR151 allosterically or orthosterically, independent on publication status

- Any binders, fragments, tool compounds, and/or endogenous ligands of GPR151 are in scope.
- Also, non-selective ligands with poor drug-like properties can be considered if they are suitable as assay controls.
- New molecular entities with validation in an *in vivo* model would be highly prioritized independently from the disease background.

Besides, we are open to accept any unconventional but feasible methodology that allows identifying and verifying GPR151 ligands.

What potential solutions would be out of scope?

- Please note that any proposals referring to already known tools or pan-GPCR screens that included GPR151 are out of scope (cf. references 4 – 6 as examples).
- Proposals for ligand screens for the galanin receptor (a receptor closely related to GPR151) will not be considered.
- Proposals identifying downstream signaling pathways of GPR151 are not of interest as they will not identify the primary ligand(s) for GPR151.
- Proposals that represent merely work that could be considered as a fee for service will not be considered.
- Virtual screening approaches based on any computational chemistry approaches.

What benefits do we offer to you in exchange for having submitted a solution?

If your project is selected, you will have the opportunity to collaborate with the Medicinal Chemistry team of Boehringer Ingelheim. You can expect appropriate funding for the prospective collaboration period. Your exact funding request should be outlined in your proposal. As a framework, we suggest that your initial funding request is structured in milestones. Depending on the level of validation of your proposed GPR151 ligand (please refer to “in scope section”), we are flexible to establish a simple material transfer agreement (MTA) or a full collaboration with a funding up to 500,000 euros.

The opportunity for a funded stay at Boehringer Ingelheim for technology exchange / training is potentially available, as is the availability of custom biological tools and reagents.

Our collaboration agreement will provide full transparency about each partner's rights & obligations (including intellectual property rights). As part of the agreement, you will be encouraged to publish following the collaboration agreement (to be negotiated in good faith).

To maintain the highest degree possible in an open innovation environment, we plan to announce the winner(s) publicly and feature them on opnMe.com and our social media channels. We would guide you through this process and as part of it we would kindly ask for your upfront consent, in case our scientific jury had selected your answer.

What are the key success criteria on which we base our selection for the best answer?

- The primary key success criterion of this call is the provision of compelling evidence for a GPR151 ligand based on non-confidential information (confirmation based on biochemical and ideally functional activity read-out)
- A secondary key success criterion represents the provision of an unconventional, but feasible methodology that allows identifying and verifying GPR151 ligands.

In addition, we are seeking research collaboration proposals that contain:

- A well-structured proposal outlining a new and compelling scientific approach.
- Outlining of the technical feasibility, and potentially existing data or previous publications that support feasibility / experience with outlined technology, based on existing techniques and established assays.
- Your exact funding request should be outlined in your proposal based on a well thought-through project plan. The project should be structured in milestones and planned with key decision points (clear Go/No-Go criteria). The funding request for the initial milestones resulting in a Go/No-Go decision should not exceed 500,000 euros per submitted project in total.
- Proven track record in the required field of expertise.
- Ability to implement the outlined solution as part of a scientific collaboration project with Boehringer Ingelheim.
- We expect that the project will be executed in your laboratory and takes advantage of existing technologies and assays.

What information should be included in your answer submission?

Please use our answer submission template to provide a 2-3 page non-confidential proposal (available for download on the following site).

If confidential data exists that would strengthen the proposal, please indicate that information is available to share under a Confidential Disclosure Agreement (CDA). If we find the non-confidential concept proposal sufficiently interesting, we will execute a CDA for confidential discussions.

Anticipated Project Phases or Project Plan

Phase 1	Please complete your submission by **October 11, 2022, 11:59 pm PST** at the very latest
Phase 2	Right after your submission, we will conduct an independent sanity check of your submission by a neutral third party to validate that only non-confidential data have been submitted. In case they are unsure, you will be notified to provide you with an option to resubmit your proposal with only "non confidential" data.
Phase 3	Our review of all proposals will be completed by end of November 2022 and scientists will be informed beginning of December 2022.
Phase 4	Potential collaboration starting date in Q1/2023

Submitting a collaboration proposal

- Check the outline of the opn2EXPERTS "Ligands for studying GPR151´s function" on opnMe.
- Alternatively, you may click the "Get Submission Template" banner to access the material transfer template.
- Follow the instructions to upload your submission document (requires login or registration).
- The upload allows you to attach additional application files if desired.
- You will be able to access your final submitted collaboration proposal in your personal dashboard and follow its review status.
- Please also visit the FAQ section on opnMe.com to learn more about our opn2EXPERTS program.

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