opnMe by Boehringer Ingelheim

# GPR149 in psychiatric symptoms and obesity

## Using suitable model systems, how would you propose to elucidate and validate the molecular role of GPR149 in symptoms related to mental health and obesity?

Answers to this question including a proposal for collaboration can only be considered if they arrive no later than October 9, 2025, 11:59 pm PST.

Boehringer Ingelheim

# Table of contents

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

GPR149, an orphan G-protein coupled receptor, could be a therapeutical target of particular interest as its expression is phylogenetically conserved across mammalian species. However, little is known about its physiology and function.

GPR149 expression is restricted to the brain and is highly expressed in areas such as the basal ganglia[1]. Basal ganglia are key regulators of motivation, emotion, and impulsivity[2]; deficits in the basal ganglia circuitry are core symptoms in many psychiatric illnesses and are still quite overlooked in patients' treatment. Understanding the role of GPR149 in regulating action selection and reward behavior may help in developing treatment strategies.

Other brain areas of interest expressing GPR149 are the feeding regulating centers, located in the hypothalamus and the dorsal vagal complex[3]. Given that these areas are key to current treatment strategies against obesity, the understanding of the function and role of GPR149 in regulating food intake and body weight is of utmost importance.

The lack of a selective pharmacological compound and knowledge about the endogenous ligand has hampered progress in our understanding at the systems level. While the behavior of constitutive knockout mice has not been fully explored[4], a lot remains to be learned about the wider role of GPR149 in both psychiatric- and obesity-related behaviors.

So, to summarize, as part of this call, we are looking for solutions which are likely to increase our understanding of GPR149's impact on these behaviors.

# What potential solutions could be in scope?

Suitable model systems that allow the identification and validation of one or more of the following aspects:

- Intracellular signaling cascade / mode of action / dimerization partners
- Functional characterization of GPR149 in distinct brain areas (arcuate nucleus, ventro-medial hypothalamus, nucleus tractus solitarius, area postrema, basal ganglia…)
- Protein expression regulation
- Identifying endogenous ligand
- *In vivo* modulation of GPR149 expression in brain areas of interest in behavioral studies relevant for feeding behaviors and motivation/emotion/impulsivity related behaviors

# What potential solutions would be out of scope?

- Proposals focusing on non-mammalian systems
- Proposals elucidating a role of GPR149 in peripheral tissues
- Proposals that are based solely on *in silico* data

- Proposals that include the use of non-validated pharmacological tools
- Proposals that are purely based on technologies that require upfront substantial establishment and validation (no previous hands-on experience)

## 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 directly collaborate with the CardioRenalMetabolic Diseases and Neuroscience & Mental Health Research Teams 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 milestone and does not exceed 250,000 euros per year for a maximum period of two years per submitted project in total.

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).

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

The proposal needs to be highly feasible, should be based on established and existing methods, assays and involve tools / reagents that are either available or which can be easily produced. We expect that the project will be executed in your laboratory and takes advantage of existing technologies and assays.

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. 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 250,000 euros per year for a maximum period of two years.
- 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 including access to a wet laboratory and/or suitable animal facility.
- Proposals with a realistic chance to generate tangible results within 2 years will be prioritized.

## 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 9, 2025, 11:59 pm PST** at the very latest. |
| Phase 2 | Our review of all proposals will be completed by end of November 2025 and scientists will be informed after that. |
| Phase 3 | Start of discussions for the collaboration agreement beginning of Q1/2026. |

## Submitting a collaboration proposal

- Check the outline of the opn2EXPERTS "GPR149 in psychiatric symptoms and obesity" 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.

## References


1. Zhang M., Pan X., Jung W., Halpern A., Eichhorn S. W., Lei Z., Cohen L., Smith K. A., Tasic B., Yao Z., Zeng H., Zhuang X. A molecularly defined and spatially resolved cell atlas of the whole mouse brain *bioRxiv* **2023**, 624(7991):343-354. DOI: 10.1038/s41586-023-06808-9, PubMed.

2. Nicola S.M. The nucleus accumbens as part of a basal ganglia action selection circuit *Psychopharmacology (Berl)* **2007**, 191(3):521-50. DOI: 10.1007/s00213-006-0510-4, PubMed.
3. Affinati A. H., Sabatini P. V., True C., Tomlinson A. J., Kirigiti M., Lindsley S. R., Li C., Olson D. P., Kievit P., Myers M. G., Rupp A. C. Cross-species analysis defines the conservation of anatomically segregated VMH neuron populations *Elife* **2021**, 10:e69065. DOI: 10.7554/eLife.69065, PubMed.
4. Wyler S., Surbhi S., Cao N., Merchant W., Bookout A., Gautron L. Gpr149 is involved in energy homeostasis in the male mouse *PeerJ*. **2024**, 12:e16739. DOI: 10.7717/peerj.16739, PubMed.