opn2EXPERTS – Skeletal muscle molecular mechanisms to combat obesity

Using novel targeted approaches, how would you identify and validate molecular mechanisms that regulate skeletal muscle mass and function to increase weight loss and improve cardiometabolic outcomes in patients with obesity?

Answers to this question including a proposal for collaboration can only be considered if they arrive no later than November 8, 2023, 11:59 pm PST.

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

The global obesity pandemic currently impacts more than 39% of adults and is linked to a multitude of health risks, including cardiovascular diseases, type 2 diabetes, and certain types of cancer[1]. Of particular importance, aged patients with obesity can experience significant reductions in lean muscle mass, a condition known as sarcopenic obesity. This predisposes them to frailty, disability, increased comorbidities, and death[2,3]. Sarcopenic obesity exacerbates the negative effects of both sarcopenia and obesity, leading to a higher risk of functional decline, impaired mobility, and a reduced quality of life[4]. Furthermore, the loss of muscle mass and strength in older adults can result in a vicious cycle of decreased physical activity, which in turn contributes to further muscle wasting and increased fat accumulation[5].

Existing therapies to treat generalized obesity primarily focus on reducing food intake and total body mass. Unfortunately, this body mass loss does not spare skeletal muscle mass[3,6,7]. This may have long-term consequences for patient health given this tissue's pivotal role in whole body energy expenditure, thermogenesis, glucose control, mobility (increased risk for sarcopenia), and autonomic functions. Given the limitations of current obesity treatments, there is a pressing need for the development of targeted interventions that can specifically address sarcopenic obesity. Such interventions should aim to preserve or increase muscle mass and function while simultaneously reducing excess adiposity, ultimately improving overall health outcomes for aged patients with obesity.

Through this opnMe call, we aim to identify primary anti-obesity mechanisms, as well as concepts that enhance existing therapies for obesity or address the lean muscle mass loss that accompanies sarcopenic obesity. We are also interested in ideas and mechanisms that enhance skeletal muscle function and could counteract sarcopenia. Specifically, we are looking for new therapeutic avenues derived from human disease models to treat patients with generalized obesity, sarcopenic obesity, or sarcopenia and improve their cardiometabolic health and quality of life.

What potential solutions could be in scope?

We are seeking research proposals that harness molecular mechanisms of the regulation skeletal muscle mass and function to identify new therapeutic approaches against obesity. The following solutions are in scope:

- Studies that characterize human-derived skeletal muscle tissue, biopsies or primary skeletal myotubes from patients with obesity, sarcopenic obesity, or after weight loss, and identify new genes, proteins, or pathways relevant to energy metabolism and/or the maintenance of lean muscle mass during weight loss.
  - Next generation sequencing, single cell sequencing or advanced proteomic approaches in this context would be of high interest.

- Computational approaches are highly welcome (e.g., that may provide evidence for decreased adiposity with enhanced lean muscle) if they include wet lab methodologies for mechanistic validation.
- Any identified pathway / gene with preliminary validation as a skeletal muscle mechanism with a clear human disease link in obesity or sarcopenia.
- The ideal solution should generate new therapeutic avenues to treat patients with generalized obesity, sarcopenic obesity, or sarcopenia and improve their cardiometabolic health and quality of life.

What potential solutions would be out of scope?

- Proposals focusing on models from non-human species that lack a clear link to the human disease condition.
- Proposals for cell systems lacking applications to the disease setting of obesity/sarcopenic obesity.
- Proposals that aim only to repurpose existing muscle-centric molecules.
- Purely lifestyle or behavioral-based approaches or any experimental human study (e.g. human exercise programs).
- Solutions only based on computational outputs by using publicly available data sources, without the possibility of wet lab validation.

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 Cardiometabolic Diseases Research 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 and does not exceed 200,000 euros per submitted project in total (including direct, indirect, and overhead costs).

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.

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

We are seeking research collaboration proposals that contain:

- A well-structured proposal outlining a new and compelling scientific approach including an experimental plan that will be used to test your hypothesis
- A novel, testable working hypothesis distinct from those previously published
- A thorough validation that includes an in-depth analysis package consisting of biochemical, and biophysical analyses
- 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
- Potentially includes (non-confidential) existing data and results
- 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 200,000 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 including access to a laboratory
- Proposed project hypotheses should have a time horizon of 24 months and should deliver tangible results within this period. Projects that may require more than 24 months will unfortunately not be considered.

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 **November 8, 2023, 11:59 pm PST at** the very latest
Phase 2	Our review of all proposals will be completed through end of January 2024 and scientists will be informed after that.
Phase 3	Potential collaboration starting date in Q2/2024.

Submitting a collaboration proposal

- Check the outline of the opn2EXPERTS "Skeletal muscle molecular mechanisms to combat 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

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