



opn2EXPERTS - Elucidating mechanisms of equine metabolic syndrome

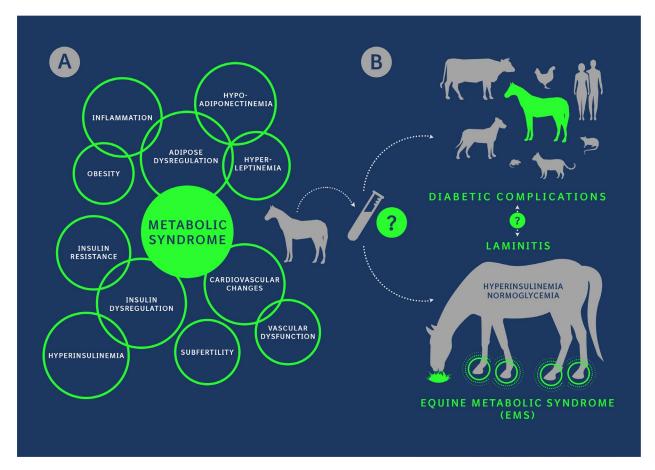
How would you propose to unravel the pathophysiology of the metabolic syndrome based on equine serum and plasma samples obtained during an oral glycemic challenge and supplied by us?

Answers to this <u>question</u> including a proposal for collaboration can only be considered if they arrive no later than January 27, 2022 11:59 pm PST.

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

Similar to the situation in human medicine metabolic pathologies, obesity and related endocrinopathies, also known as metabolic syndrome, play an increasingly significant role in the equine population worldwide. The prevalence of obesity is high in the equine population with rates ranging between 30 to 48 % (Durham *et al.* 2019) and is one common feature of horses and ponies suffering from the Equine Metabolic Syndrome (EMS). Affected horses and ponies develop basal hyperinsulinemia, excessive or prolonged postprandial hyperinsulinemia or tissue insulin resistance all referred to by the term insulin dysregulation (ID). Interestingly, horses – quite different to other species – compensate for a decreased insulin sensitivity with continuous and very high insulin secretion, thus can maintain normoglycemia and rarely develop pancreatic insulin depletion resulting in diabetic conditions. Complications and sequelae of EMS and ID range from cardiovascular changes, adipose tissue dysfunction, impaired fertility and generalized proinflammatory conditions to the most feared consequence: laminitis. Affected laminitic horses suffer from a failure of the laminar tissue of the hooves resulting in structural damage and in pain associated with severe acute or chronic lameness, frequently necessitating euthanasia due

to welfare aspects. Despite successful identification of the link between ID and development of laminitis, the intense research in the last decade failed to unravel the pathophysiological features of EMS and the associated development of endocrinopathic laminitis in affected horses and ponies.



(A) Metabolic syndrome affects all mammals and is in general characterized by a diverse range of pathologic features. (B) As part of a recent study, serum and plasma samples have been derived from a cohort of horses who had received a glycemic diet challenge. With this opn2EXPERTS question we seek to understand the causal relationship between equine metabolic syndrome and the equine specific pathology. We also wonder whether the samples can be used as part of translational and comparative approaches?

Boehringer Ingelheim Animal Health (BI-AH) pursues animal health & well-being, innovation, and sustainability. BI-AH has performed a global (AU, DE, SE, UK, US) clinical study on oral glycemic challenges employed as diagnostics for equine ID and banked serum and plasma samples of ID and healthy non-ID equids. Horses and ponies underwent a standardized feeding (oral glycemic challenge pellets) with repeated blood sampling for 3 hours to assess the postprandial responses (glucose and insulin). Included equids covered a broad range of postprandial insulinemic responses from physiological to highly

pathological. A complete sample set will be comprised of 400 individual samples derived from 108 enrolled horses and ponies. Subsets would also be available upon request. Comprehensive metadata including demographics, phenotypic characteristics such as precise body morphometrics and anamnesis with a focus on previous episodes of laminitis and further related endocrinopathies are available. The studies have been approved or registered with the responsible authorities. Samples were collected with standardized protocols.

By making our internal samples available via this opn2EXPERTS question, we hope to trigger innovative approaches to improve our understanding of the pathologic mechanisms underlying metabolic syndrome. Despite the equine origin of sample materials, we are open to various aspects and comparative approaches to promote a multi-species deep dive into the pathophysiology of the metabolic syndrome in general. We are convinced that new insights will provide another clue to the puzzle of EMS and laminitis and will further accelerate optimization of diagnostics and development of innovative therapeutic options – even beyond horses.

What potential solutions could be in scope?

Research groups eligible for this opn2EXPERTS call should be in possession of and must remain in compliance with all necessary permits, approvals, licenses, and other authorizations required by applicable (local) legislation for the handling of biological samples, in particular equine blood samples.

Boehringer Ingelheim Animal Health can help with additional details if required, e.g., for import permits or fulfilling Nagoya protocol requirements.

Potential approaches to answer our question include, but are not limited to the following:

- A well-structured proposal outlining a new and compelling scientific approach.
- Translational and comparative approaches Similarities or differences in pathomechanisms known in e.g., human metabolic syndrome or diabetic complications in other species are highly welcome and could be prioritized.
- Anything that can be investigated in / with serum or plasma samples.
- The proposal should be highly feasible, based on established and existing methods and assays and involve tools or reagents that are either available or which can be easily produced.

• We expect that the project will be executed in your laboratory and will take advantage of existing technologies and assays.

What potential solutions would be out of scope?

The following will be considered out of scope:

- Proposals that are considered primarily fee for service.
- Projects that are based on technologies that require first substantial establishment and validation (no previous hands-on experience) will be deprioritized.

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 Translational Veterinary Science Research team of Boehringer Ingelheim Animal Health. Access to the equine serum or plasma samples will include additional metadata (e.g. demographics, phenotypic and clinical characteristics and laboratory data of insulin and glucose readings).

In addition to the outlined in-kind funding and depending on the nature of your proposal, there will be additional funding available of up to 20,000 euros in total for the best projects that will be selected. Your funding request and rationale should be outlined in your proposal and we suggest that your initial funding request is structured in milestones.

An agreement for the transfer and use of the material will need to be established mutually. It will provide full transparency about each partner's rights & obligations. As part of the agreement it will be acknowledged that you will be the owner of any potential new intellectual property; however, Boehringer Ingelheim will have a right of first refusal. Furthermore, you will be encouraged to publish following the terms of the collaboration agreement.

To maintain the highest degree of transparency 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 kindly ask for your upfront consent, in case our scientific jury selects your answer.

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.
- A novel, testable working hypothesis distinct from those previously published.
- 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 wellthought-through project.
- Proven track record in the required field(s) of expertise.

What information should be included in your answer submission?

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

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 **January 27, 2022 11:59 pm PST at** the very latest
- Phase 2 Our review of all proposals will be completed by end of February 2022 and scientists will be informed beginning of beginning of March 2022.
- Phase 3 Potential collaboration starting date in Q2/2022

Submitting a collaboration proposal

- Check the outline of the opn2EXPERTS "Elucidating mechanisms of metabolic syndrome" 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 <u>FAQ</u> section on opnMe.com to learn more about our opn2EXPERTS program.

References

1. Durham A. E., Frank N., McGowan C. M., Menzies-Gow N. J., Roelfsema E., Vervuert I., Feige K., Fey K. ECEIM consensus statement on equine metabolic syndrome. *J Vet Intern Med* **2019**, 33(2):335-349. DOI: 10.1111/jvim.15423, PubMed.