opnMe by Boehringer Ingelheim

opn2EXPERTS – Elucidate CD73's potential role in lung injury and repair

Using novel *in vitro* cellular systems utilizing human patient biopsies, how would you propose to elucidate the role by which CD73 acts on pathologic mechanisms in the context of lung injury and repair?

Answers to this question including a proposal for collaboration can only be considered if they arrive no later than December 16, 2021 11:59 pm PST.

Boehringer Ingelheim

Table of contents

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

Chronic lung diseases are the second leading cause of death in the world. Despite the emergence of current therapeutics, the diseases are ultimately fatal.

Adenosine is a potent regulator of tissue repair that is elevated in response to injury or stress. High levels of extracellular adenosine have been shown to be associated with the progression of injury and its levels are reduced in the resolution phases in different repair models. Therefore, strategies to target this pathway are emerging as a promising new avenue for tissue repair and regeneration. CD73 plays a central role in adenosine production as it converts extracellular AMP to immunosuppressive adenosine. This led us to identify a novel humanized antagonistic anti-CD73 monoclonal antibody (BI-4153, also known as mAb19[1]) that inhibits the enzymatic activity of CD73 and reduces adenosine levels. A novel, complex cellular system that recapitulates lung injury and repair processes is necessary to elucidate CD73's mode of action in the disease pathogenesis.

What potential solutions could be in scope?

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

1. A strong scientific proposal with a new and compelling scientific idea to investigate CD73 functions in lung injury and repair processes.
2. A novel in vitro human system enabling investigation of the communication between different cell types.
3. A novel and feasible working hypothesis and experimental plan distinct from those previously published.

What potential solutions would be out of scope?

4. Proposals focusing on mechanisms of action that are unique or specific to non-human species.
5. Proposals for cell systems lacking applications to the disease setting.
6. Proposals that address lung injury and repair from an oncology perspective are out of scope as well.

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

We are open to all proposals that can fully or partially meet its requirements. Selected scientists will be able to access our potent anti-CD73 mAb in sufficient quantities to validate

their hypothesis. Collaborating scientists will have the opportunity to directly collaborate with Boehringer Ingelheim's drug discovery research team.

An appropriate funding for the prospective collaboration period is available. The exact funding request should be outlined in the submitted proposal. As a framework, we suggest that the initial funding request is structured in milestones and does not exceed 200,000 euros per submitted proposal.

Furthermore, 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?

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.
- Outline 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.
- Framing the questions and the innovation aspects which includes a well thought- through project plan with key decision points (e.g. clear Go/No-Go criteria).
- Contain a defined funding request. The project should be structured in milestones and planned with key decision points. 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 including access to a laboratory.

The collaborative priorities for Boehringer Ingelheim's therapeutic areas are shown in the following table:

Oncology and Immuno-Oncology	Proposals which focus on oncology or immuno-oncology are out of scope of this opn2EXPERTS question.
Cardiometabolic diseases	Liver diseases • Non-alcoholic steatohepatitis (NASH), liver fibrosis, cirrhosis, portal hypertension Retinopathies • Geographic atrophy/dry and wet AMD • Diabetic retinopathy/DME and related retinal diseases Novel obesity treatments achieving weight loss > 10% CKD and heart failure Breakthrough treatments for type 2 diabetes, such as pancreas regeneration options
CNS diseases	Novel treatment options for neuropsychiatric diseases such as: • Schizophrenia: Cognitive Impairment, Negative Symptoms, (Relapse Prevention) • Major Depression • Cognition: Reward, Motivation & Emotion, Disease Progression • Borderline Personality Disorder
Immunology & Respiratory	Systemic sclerosis-scleroderma (SSc) SSc-Interstitial Lung Disease (ILD) Inflammatory bowel diseases such as Crohn's disease including specific approaches for fistulizing and refractory ileal Crohn's disease and ulcerative colitis Interstitial pulmonary fibrosis (IPF)/PF-ILD: Block of pro-fibrotic signaling beyond standard of care Disease-modifying therapies for respiratory indications Approaches to induce lung regeneration and repair mechanisms Aberrant epithelial sensing

	Epithelial-fibroblast interactions Macrophage repair function
Research Beyond Borders	Gene Therapy: Novel therapeutic concepts/targets, which are amenable to AAV-based gene therapy. Technology advancement in the field of tissue selective AAV capsid variants with translational potential to man; innovative technology, which allows spatio-temporal control of cargo expression, increased cargo size or modulation of immune response to AAV capsids and/or DNA cassettes; human tissue/organ models for translational screening or characterization of AAVs. Regenerative Medicine: Focus on biology underlying endogenous mechanisms & master switches to regenerate tissues. The proposed therapeutic concept should be supported by preclinical in vivo data with a clear translational path to patients. Therapeutic fields of interest include, but are not limited to, tissue such as bone, cartilage, spinal cord and thymus. Emerging Therapeutic Concepts: Open to new and disruptive ideas in uncharted therapeutic spaces to treat diseases for which there are no effective therapies, including rare diseases. New Therapeutic Technologies: Capture emerging technologies/modalities that will change medical practice e.g. exosomes and extracellular vesicles.

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 **December 16, 2021 11:59 pm PST** the very latest
Phase 2	Our review of all proposals will be completed by end of January 2022 and scientists will be informed during February 2022.
Phase 3	Potential collaboration starting date in Q2/2022.

Submitting a collaboration proposal

7. Check the outline of the opn2EXPERTS question to "Elucidate CD73's potential role in lung injury and repair" on opnMe.
8. Alternatively, you may click the "Get Answer Template" banner to access the collaboration submission template.
9. Follow the instructions to upload your submission document (requires login or registration).
10. The upload allows you to attach additional application files if desired.
11. You will be able to access your final submitted collaboration proposal in your personal dashboard and follow its review status.
12. Please also visit the FAQ section on opnMe.com to learn more about our opn2EXPERTS program.

Reference

13. Wurm M., Schaaf O., Reutner K., Ganesan R., Mostböck S., Pelster C, Böttcher J., de Andrade Pereira B., Taubert C., Alt I., Serna G., Auguste A., Stadermann K. B., Delic D., Han F., Capdevila J., Nuciforo P. G., Kroe-Barrett R., Adam P. J., Vogt A. B., Hofmann I. A novel antagonistic CD73 antibody for inhibition of the immunosuppressive adenosine pathway. *Mol Cancer Ther* **2021**. DOI: 10.1158/1535-7163.MCT-21-0107, PubMed.