opnMe by Boehringer Ingelheim

opn2EXPERTS – Spatial multi-omics profiling of fibrotic diseases

How would you propose to leverage novel spatial multi-omics to investigate molecular and cellular mechanisms driving human fibrotic disease suitable for computational analyses?

Answers to this question including a proposal for collaboration can only be considered if they arrive no later than May 15, 2024, 11:59 pm PST.

Boehringer Ingelheim

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

Spatial transcriptomics as a sequencing technology has been immensely popular in the last few years across many areas of biomedical research. With the straightforward implementation of commercial kits, many academic and industry groups have been able to introduce spatially resolved RNA-sequencing to their research projects. With this approach becoming relatively commonplace, we are looking towards the next revolutionary advancement in spatial technology that will allow us to improve disease understanding and ultimately lead to the development of novel therapeutics.

Spatial multi-omics can be seen as the next frontier in sequencing-based methods, as it integrates several layers of information from the same tissue section and pieces together a more complete understanding of the underlying biology. More specifically, spatial sequencing of RNA can be combined with spatial profiling of the epigenome, chromatin accessibility, and protein expression from the same tissue by clever use of tissue barcoding. Aligning these layers of information allows a comprehensive understanding of biological processes at an unprecedented resolution.

As part of this opnMe call, we aim to apply spatial multi-omics methods to the study of human fibrotic diseases. Fibrosis is a complex process contributing to many inflammatory diseases such as pulmonary fibrosis, Crohn's disease, scleroderma, metabolic-associated steatohepatitis, chronic kidney disease, as well as cancer. We are interested in the pathogenesis of fibrosis and consider it crucial that we improve our understanding of the spatial context of fibrosis. Fibrosis encompasses complex underlying processes including stromal cell activation, inflammation, senescence, cell-cell interaction, transcriptional and epigenetic regulation, etc. which are dependent on the spatial context of the tissue neighborhoods, microenvironments, and the fibrotic niche, and fail to be fully addressed by one-dimensional methods.

The aim of this proposal is to identify and invite research collaborators with shared interests in fibrosis and expertise in spatial technology to investigate on this exciting topic with a potential for new entry points for the discovery of novel therapeutics against fibrotic diseases.

The main scope of a joint collaborative project phase will be the computational integration of multi-omics data layers using novel analytical pipelines, tailored towards the purpose of advancing disease understanding.

In summary, leveraging novel spatial multi-omics, how would you propose to investigate molecular and cellular mechanisms driving human fibrotic disease suitable for computational analyses?

What potential solutions could be in scope?

- A proposal for building a computational pipeline to analyze an existing multi-omics dataset from human fibrotic tissue
- A proposal to generate a novel multi-omics dataset from human fibrotic tissue plus creating a computation pipeline for analysis
- A submission should explore two or more of the following: spatial epigenetics, spatial chromatin accessibility, spatial transcriptomics, spatial proteomics, high-plex imaging, or other omics types from the same tissue section
- Proposals that enable access to human tissue from fibrotic disease

What potential solutions would be out of scope?

- Solutions that require de novo set up of spatial multi-omics skill sets at site of proposing scientist
- Multi-omics data set generation required at Boehringer Ingelheim
- Non-human tissue and tissue outside the scope of human fibrotic disease

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 Global Computational Biology and Data Science team of Boehringer Ingelheim with extensive experience in spatial multi-omics data analysis. In addition, benefit from the expanded human disease experience of our scientists in the fields of pulmonary fibrosis, Crohn's disease, scleroderma, metabolic-associated steatohepatitis, chronic kidney disease, and cancer.

As an additional incentive specific to this opn2EXPERTS call, you can also 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 250,000 euros annually for a maximum duration of two years per submitted project in total (including direct, indirect, 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).

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

We are seeking research collaboration proposals that address our question. Proposals that flag existing data and results in the domain of fibrotic diseases would be prioritized (please only share non-confidential results as part of your application). Additional success criteria are:

- The successful proposal will point to an existing human fibrosis multi-omics dataset and develop a computational analysis pipeline or,
- Be ready to generate a novel human fibrosis multi-omics dataset and implement a plan for developing a computation analysis pipeline
- The successful proposal would provide a clear path indicating what types of data, disease indication, and methodology would be included
- The submitted scientist/group must have the capability of generating and/or providing spatial multi-omics datasets
- The proposal will explore two or more of the following: spatial epigenetics, spatial chromatin accessibility, spatial transcriptomics, spatial proteomics, high-plex imaging, or other omics types from the same tissue section
- If generating new data, access to a wet lab and sequencing facilities is required
- Data analysis can/will be a collaborative effort with Boehringer Ingelheim computational biologists
- 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 annually for a maximum duration of two years per submitted project in total
- The tissues evaluated must be from patients with fibrotic disease covered by an ethics protocol
- Computational multi-omics analyses would represent an upside that could lead to further prioritization of the project proposal

What information should be included in your answer submission?

As part of your submission, you should outline your capability of providing or generating spatial multi-omics datasets from human fibrotic diseases. Please outline your previous expertise in this area as part of proposal.

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 **May 15, 2024, 11:59 pm PST at** the very latest.
Phase 2	Our review of all proposals will be completed by end June 2024 and scientists will be informed after that.
Phase 3	Start of discussions for the collaboration agreement in Q3/2024.

Submitting a collaboration proposal

- Check the outline of the opn2EXPERTS "Spatial multi-omics profiling of fibrotic diseases" 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. Liu Y., Yang M., Deng Y., Su G., Enninful A., Guo C. C., Tebaldi T., Zhang D., Kim D., Bai Z., Norris E., Pan A., Li J., Xiao Y., Halene S., Fan R. High-Spatial-Resolution Multi-Omics Sequencing via Deterministic Barcoding in Tissue *Cell.* **2020**, 183(6):1665-1681.e18. DOI: 10.1016/j.cell.2020.10.026, PubMed.
2. Deng Y., Bartosovic M., Ma S., Zhang D., Kukanja P., Xiao Y., Su G., Liu Y., Qin X., Rosoklija G. B., Dwork A. J., Mann J. J., Xu M. L., Halene S., Craft J. E., Leong K. M., Boldrini M., Castelo-Branco G., Fan R. Spatial profiling of chromatin accessibility in mouse and human tissues *Nature*. **2022**, 609(7926):375-383. DOI: 10.1038/s41586-022-05094-1, PubMed.
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4. Zhang D., Deng Y., Kukanja P., Agirre E., Bartosovic M., Dong M., Ma C., Ma S., Su G., Bao S., Liu Y., Xiao Y., Rosoklija G. B., Dwork A. J., Mann J. J., Leong K. W., Boldrini M., Wang L., Haeussler M., Raphael B. J., Kluger Y., Castelo-Branco G., Fan R. Spatial epigenome-transcriptome co-profiling of mammalian tissues *Nature*. **2023**, 616(7955):113-122. DOI: 10.1038/s41586-023-05795-1, PubMed.