opn2EXPERTS - Elucidate the role of sFRP2 in lung or skin fibrosis

How would you propose to elucidate and validate the role of sFRP2 in the context of lung or skin fibrosis whereby sFRP2 may either lead to disease progression or inhibition of resolution?

Answers to this question including a proposal for collaboration can only be considered if they arrive no later than July 11, 2023 12:59 pm PST.

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

Idiopathic pulmonary fibrosis (IPF) is a chronic and progressive lung disease of unknown cause, with high mortality. Currently, there are two approved antifibrotic drugs – nintedanib and pirfenidone – that slow, but do not stop the progression of fibrosis. Therefore, additional treatments are needed to inhibit or even revert the disease.

Secreted Frizzled related protein 2 (sFRP2) is a protein that has been implicated in the WNT signaling pathway, which plays a role in tissue development and repair. Furthermore, sFRP2 was described to have a role in cardiac fibrosis and tumor progression. An increased expression of sFRP2 was also found in myofibroblasts from systemic sclerosis (SSc) patients. However, the contribution to lung or skin fibrosis progression or resolution remains unclear. Offered pathways, all known to be involved in fibrotic conditions, such as WNT-FRZD receptor interaction, BMP1 interaction, or interference with SMAD signaling were proposed previously, however it is unclear if the binding to those proteins leads to disease progression, or if progression is caused by yet unknown mechanisms or interaction

partners. Although the name sFRP2 suggests a relation to WNT, beta-catenin, and Frizzled signaling, we do not necessarily think the solution is (solely) in the WNT space.

As part of our current opnMe call, we look forward to receiving creative ideas to decipher the contribution of sFRP2 in lung or skin fibrosis. Furthermore, we aim to elucidate the mode of action/ binding partner that leads to the pathologic phenotype, in best case including proximity markers. The ideal solution should deliver a potential starting point for novel therapeutic interventions against sFRP2 in lung or skin fibrosis.

What potential solutions could be in scope?

- Any unconventional, but feasible scientific idea that provides a link between sFRP2 and lung or skin fibrosis progression or influence of resolution using cellular systems and/or *in vivo* models
- Any unconventional, but feasible scientific idea that allows identifying and validating (novel) sFRP2 interacting partner(s), responsible for the pathologic phenotype, in the context of lung or skin fibrosis
- Identification and validation of proximity marker(s): Pathway or players that provide a mechanistic link between sFRP2 and fibrosis
- In our opinion, a thorough validation will include an in-depth analysis package consisting of biochemical, and biophysical analyses
- Any unconventional but feasible approach should be based on existing assays and available tools in your laboratory
- Initial data are a plus, but conceptually proposals might be acceptable

What potential solutions would be out of scope?

- Purely computational approaches
- Proposals without major focus on lung or skin fibrosis
- Proposals focusing on mechanisms of action that are unique or specific to non-human species
- Proposals for cell systems lacking applications to the disease setting
- Purely descriptive binding partners, without linkage to pathology

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 Immunology and Respiratory Discovery Research team of Boehringer Ingelheim. As an incentive specific to this opn2EXPERTS call, we offer an exclusive access to non-commercial, quality reagents and tools to validate your submitted hypotheses, should your proposal be selected by our scientific review team. In addition, 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 200,000 euros 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).

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.
- Anything considerably longer than 2 years will be excluded

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 confidential 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 **July 11, 2023 11:59 pm PST** at the very latest.
Phase 2	Our review of Proposals will be completed towards end of September and scientists will be informed after that.
Phase 3	Potential collaboration starting date late Q3/2023 or Q4/2023

Submitting a collaboration proposal

- Check the outline of the opn2EXPERTS "Elucidate the role of sFRP2 in lung or skin fibrosis" on opnMe or alternatively,
- Click the "Download your answer submission template" banner to access the collaboration submission template.
- Follow the instructions upload your submission document (requires login or registration).
- The upload allows you to attach additional application files if you want to.

- 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. Wu Y., Liu X., Zheng H., Zhu H., Mai W., Huang X., Huang Y. Multiple Roles of sFRP2 in Cardiac Development and Cardiovascular Disease. *Int J Biol Sci* **2020**; 16(5):730-738. DOI: 10.7150/ijbs.40923, PubMed.
2. van Loon K., Huijbers E.J.M., Griffioen A.W. Secreted frizzled-related protein 2: a key player in noncanonical Wnt signaling and tumor angiogenesis. *Cancer Metastasis Rev* **2021**, 40, 191–203. DOI: 10.1007/s10555-020-09941-3, PubMed.
3. Tabib T., Huang M., Morse N., Papazoglou A., Behera R., Jia M., Bulik M., Monier D. E., Benos P. V., Chen W., Domsic R., Lafyatis R. Myofibroblast transcriptome indicates SFRP2hi fibroblast progenitors in systemic sclerosis skin. *Nat Commun* **2021**, 12, 4384. DOI: 10.1038/s41467-021-24607-6, PubMed.