opnMe by Boehringer Ingelheim

opn2EXPERTS – Tumor microenvironment crosstalk in mCRC

How would you propose to decipher the crosstalk between tumor-stromal-immune cells that initiate and perpetuate immune suppressive tumor microenvironment of metastatic colorectal cancer?

Answers to this question including a proposal for collaboration can only be considered if they arrive no later than December 20, 2022, 11:59 pm PST.

Boehringer Ingelheim

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

Colorectal cancer (CRC) is the third most common cancer diagnosed in both men and women each year in the United States. Metastasis is the major cause of death in patients with CRC and is often associated with resistance to immunotherapy.

The growth of tumor cells depends on its soil, the tumor microenvironment (TME). In the TME, the stromal cells including cancer associated fibroblast cells (CAFs) crosstalk to tumor cells and immune cells and may form multi-cellular hubs that drive cancer stemness and immune escape[1]. The mechanisms that orchestrate and maintain this crosstalk in the metastatic CRC TME are potentially actionable drug targets to enable novel therapies. The challenge to identify and validate molecular targets in the metastatic CRC TME has been: 1) an incomplete understanding of the cellular and molecular mechanisms underlying the crosstalk between tumor-stromal-immune cells causing immune-suppressive TME in the metastatic CRC, and 2) proper models to screen and validate immune-suppressive stromal and CAF targets are lacking.

We seek human *in vitro* translational and *in vivo* models that faithfully recapitulate aspects of the immune suppressive TME of metastatic CRC (defined *in vivo* models, cell line 2 or 3D, explant, etc.) to help identify new potential therapeutic targets (such as genes, proteins, or pathways). Eventually these models should enable testing and characterizing therapeutic strategies in reverting immune suppression of the TME in patients to prevent metastasis and improve immunity against colorectal cancers.

What potential solutions could be in scope?

- Innovative and translational *in vitro* systems or *in vivo* models that recapitulate the TME of metastatic CRC in human to allow the identification and validation of targets that sustain and mediate an immunosuppressive TME, thereby enabling immune activation and suppressing tumor growth.
- Covering, but not limited to:
  1. *In vitro* culture using primary immune cells and tumor cell lines (2D or 3D) or primary material that recapitulate human metastasis CRC TME and tumor-stromal-immune cell crosstalk for the identification of potential starting points (genes, proteins, pathways) for new therapies.
  2. *In vivo* screens using an in vivo model of metastatic CRC with translational value.

Applications containing preliminary evidence and characterization of the initiation and perpetuation of immune suppressive TME of metastatic CRC and applications containing human translational models will be prioritized.

What potential solutions would be out of scope?

The following will be considered out of scope:

- *in vitro* and *in vivo* models in which CRC metastasis is not reproducible, poorly characterized or without demonstrated relevance/link to human biology or only unique or specific to nonhuman species.
- Proposals without any preliminary/supporting data
- Proposals that are considered primarily fee for service

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 Cancer Immunology and Immune Modulation Discovery 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.

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.
- 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 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.

Applications containing preliminary evidence and characterization of the initiation and perpetuation of an immune suppressive TME of metastatic CRC and applications containing human translational models will be prioritized.

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 20, 2022, 11:59 pm PST** at the very latest
Phase 2	Our review of all proposals will be completed by mid-February 2023 and scientists will be informed after that.
Phase 3	Potential collaboration starting date in Q1/2023

Submitting a collaboration proposal

- Check the outline of the opn2EXPERTS "Tumor microenvironment crosstalk in mCRC" question 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.

Reference

1. Pelka K., Hofree M., Chen J. H., Sarkizova S., Pirl J. D., Jorgji V., Bejnood A., Dionne D., Ge W. H., Xu K. H., Chao S. X., Zollinger D. R., Lieb D. J., Reeves J. W., Fuhrman C. A., Hoang M. L., Delorey T., Nguyen L. T., Waldman J., Klapholz M., Wakiro I., Cohen O., Albers J., Smillie C. S., Cuoco M. S., Wu J., Su M-J., Yeung J., Vijaykumar B., Magnuson A. M., Asinovski N., Moll T., Goder-Reiser M. N., Applebaum A. S., Brais L. K., DelloStritto L. K., Denning S. L., Phillips S. T., Hill E. K., Meehan J. K., Frederick D. T., Sharova T., Kanodia A., Todres E. Z., Jané-Valbuena J., Biton M., Izar B., Lambden C. D., Clancy T. E., Bleday R., Melnitchouk N., Irani J., Kunitake H., Berger D. L., Srivastava A., Hornick J. L., Ogino S., Rotem A., Vigneau S., Johnson B. E., Corcoran R. B., Sharpe A. H., Kuchroo V. K., Ng K., Giannakis M., Nieman L. T., Boland G. M., Aguirre A. J., Anderson A. C., Rozenblatt-Rosen O., Regev A., Hacohen N. Spatially organized multicellular immune hubs in human colorectal cancer *Cell* **2021**, 184(18):4734-4752.e20. DOI: 10.1016/j.cell.2021.08.003, PubMed.