

# opn2EXPERTS - Improved tumor site penetration and retention of biologics

Utilizing protein engineering or novel formulation approaches, how would you propose to improve penetration and retention of biologics in order to increase their local concentration within the tumor?

Answers to this [question](#) including a proposal for collaboration can only be considered if they arrive no later than November 29, 2023, 11:59 pm PST.

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

Antibodies and protein-based therapies such as cytokines have become a cornerstone in the therapeutic guidelines of a wide range of diseases. In particular, they held much promise for cancer therapy. Unfortunately, despite the significant progress that has been made in past decades, the effect of those drugs remains unsatisfactory. A common barrier that limits the efficacy of all protein-based therapies is poor uptake and distribution within solid tumors, which results in suboptimal exposure to portions of the tumor, development of resistance, and tumor progression<sup>1</sup>. The main factors responsible for poor penetration and distribution of biologics are related to intratumoral vasculature, stroma/matrix, and cellular barriers. In the case of antibodies, low intratumoral concentration is in addition driven by the level of antigen expression and rapid antigen turnover<sup>2</sup>.

To date, significant body of evidence has been generated which points to the critical parameters of large molecules that are responsible for their low tumor concentration upon systemic application. Most of the available data are highly antibody-centered and include size, affinity, avidity, and charge among other physicochemical properties to determine tumor penetration and retention<sup>3</sup>.

Identification of factors which limit tumor penetration and distribution or retention of biologics in solid tumors led to experimental testing of various strategies. Most prominent approaches tested to date include delivery systems (e.g., nanoparticles), strategies that focus on targeting specific components which impact tumor growth and survival (e.g., normalization of vasculature, disruption of extracellular matrix) as well as physical treatments (e.g., hyperthermia or application of ultrasound). Unfortunately, none of the strategies proposed to overcome penetration/retention limitations have translated into the clinic. As a result, novel approaches which would increase penetration into the tumor and/or retention at the tumor site would significantly improve the therapeutic index of such molecules.

With our call, we seek ideas to significantly enhance the amount of available biological drug within the tumor via increased tumor penetration and/or retention or combinations thereof. Applications with *in vitro* / *ex vivo* systems that enable testing of different strategies will be prioritized. Ultimately, proposed solution(s) shall lead to improved efficacy in a disease relevant model.

## What potential solutions could be in scope?

- Any approaches targeting penetration obstacles such as, but not limited to:
  - vasculature,
  - extracellular matrix or cellular barriers
- Solutions increasing retention of biologics at the tumor site supported by (preliminary) *in vivo* or *ex vivo* experimental evidence
- Proposed approaches that lead to increased local drug concentration upon systemic delivery (either by increasing in-rate or decreasing off-rate or combination thereof). Proposed solutions shall be broadly applicable to large molecules and not limited to antibodies. In addition, protein engineering solutions will be favored. Innovative formulation approaches that lead to an increase of local biologics drug concentration upon systemic delivery would be also in scope.
- Please note that we will only consider project proposals which can be completed within 24 months or less. Within this period, you should be able to generate confirmation about your hypothesis based on predefined experimental milestones, as well as publishable results.

## What potential solutions would be out of scope?

The following will be considered out of scope:

- Test systems to validate without any clear hypothesis that leads to increased uptake
- Approaches that have previously failed clinical testing
- Proposals without any preliminary/supporting data
- Furthermore, the following approaches are out of scope:
  - Local administration (e.g. intratumoral); systemic delivery must be guaranteed
  - Gene therapy / mRNA expression in the tumor
  - Affinity/avidity-driven solutions based on antigen binding (proposed solutions shall be applicable to a broad range of proteins and not limited to antibodies)
  - Strategies involving physical treatment (e.g., hyperthermia)
- 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 experts of the Cancer Immunology and Immune Modulation and Biotherapeutics Discovery Research teams of Boehringer Ingelheim. You can expect appropriate funding for the prospective collaboration period and 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.

## 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 project proposal that can be completed within 24 months or less
- A novel, testable working hypothesis distinct from those previously published
- Outline of the technical feasibility of the innovative proposed approach, potentially supported by a few publications that support feasibility and display experience with the outlined technology, based on established techniques and/or 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 milestones and decision points (e.g. clear Go/No-Go criteria)
- Contain a defined funding request. 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

## 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 **November 29, 2023, 11:59 pm PST** at the very latest.
- Phase 2 Our review of all proposals will be completed by mid-February 2024 and scientists will be informed after that.
- Phase 3 Potential collaboration starting date in Q2/2024

## Submitting a collaboration proposal

- Check the outline of the opn2EXPERTS “[Improved tumor site penetration and retention of biologics](#)” 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. Cruz E., Kayser V. Monoclonal antibody therapy of solid tumors: clinical limitations and novel strategies to enhance treatment efficacy. *Biologics*. **2019**, 13:33-51. [DOI: 10.2147/BTT.S166310](#), [PubMed](#).
2. Bordeau B. M., Balthasar J. P. Strategies to enhance monoclonal antibody uptake and distribution in solid tumors. *Cancer Biol Med*. **2021**, 18(3):649-664. [DOI: 10.20892/j.issn.2095-3941.2020.0704](#), [PubMed](#).
3. Thurber G. M., Zajic S. C., Wittrup K. D. Theoretic criteria for antibody penetration into solid tumors and micrometastases. *J Nucl Med*. **2007**, 48(6):995-9. [DOI: 10.2967/jnumed.106.037069](#), [PubMed](#).