opnMe by Boehringer Ingelheim

Role of TLR5 in tumor immune evasion

Using suitable models, how would you propose to validate the role of TLR5 in cancer immune evasion associated with chronic inflammation?

Answers to this question including a proposal for collaboration can only be considered if they arrive no later than March 17, 2026, 11:59 pm PST.

Boehringer Ingelheim

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

Acute inflammation supports anti-tumor immunity by activating myeloid cells and T cells. In contrast, chronic inflammation not only promotes tumor initiation, progression, and metastasis, but also facilitates immune evasion and therapy resistance in the tumor microenvironment, largely driven by activation of pattern recognition receptors (PRRs) on myeloid cells and inflammatory mediators such as IL-6, IL-1β, TNF-α, and IFNα [1]. The therapeutic potential of inhibiting these receptors or cytokines to improve anti-tumor immune response is emerging but not yet fully explored due to lack of suitable systems to model chronic inflammation. Establishment of *in vitro* and *ex vivo* human/mouse models of chronic inflammation can allow evaluation of the role of known inflammatory markers as well as screening and identification of new therapeutic targets.

TLR5 is a well characterized PRR and has a dual role in cancer: acute TLR5 activation can enhance innate immune functions, long-term anti-tumor memory T cell responses and responses to immunotherapy [2], whereas chronic TLR5 signaling may impair dendritic cell differentiation, promote immunosuppressive myeloid subsets, and reduce CD8+ T cell function, ultimately limiting the efficacy of checkpoint therapies [3]. Inhibition of TLR5 has been shown in preclinical models to reduce tumor growth and may help overcome immune resistance in selected patient populations [4]. However, there are currently no active clinical or preclinical TLR5 inhibitor programs in oncology indications.

Developing *in vitro* and *ex vivo* human and mouse models of chronic inflammation is essential to clarify the tumor-promoting mechanisms associated with TLR5 and to identify patient populations that may benefit from TLR5 inhibition. These models will also facilitate the discovery of new inflammatory markers and therapeutic targets.

We invite proposals to develop or apply models that define the role of chronic inflammation—specifically TLR5 activation and inhibition—in cancer progression and immune evasion and to discriminate from any acute immune enhancing activity function. Selected projects may receive access to custom TLR5 antagonists and direct collaboration with the Oncology Research Team.

What potential solutions could be in scope?

Proposals that can define the immune settings that determine the role of TLR5-driven inflammation in the seemingly opposing directions. This can be achieved by using

- Immune cell-based models of chronic inflammation (myeloid cells/T cells/tumor cells)
- Human and mouse *in vitro* and *ex vivo* models
- Syngeneic and humanized *in vivo* tumor models

What potential solutions would be out of scope?

- *in silico* models
- Non-mouse; non-human models

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 Oncology Research Team of Boehringer Ingelheim.

As an incentive specific to this opn2EXPERTS call, we offer exclusive access to custom biological tools and reagents, in particular well-characterized TLR5 antagonists, from our research activities 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 300,000 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).

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

Our scientific review will address the following key success criteria for selecting winning proposals:

The objective of the proposed solution must be to understand and validate the role of TLR5 activation in opposing immune context (tumor preventing vs tumor promoting). It must be based on a compelling scientific hypothesis and address the in-scope and out-of-scope criteria of this call.

Outlining of the technical feasibility, and potentially existing data or previous publications that support feasibility / experience with outlined technology, based on existing and established models.

Ideally, the proposed solution is backed up by relevant (preliminary) data, and it should be based on established and existing methods, assays and involve tools, reagents, or data that are accessible.

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 does not exceed 300,000 Euros per submitted project in total.

Information regarding intellectual property / third party infringement used in the context of the submission.

The access to relevant infrastructure to implement the proposed solution is a prerequisite of a collaboration with Boehringer Ingelheim.

Ability to reach tangible results within a timeframe of approximately two years to reach the next decision point.

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 **March 17, 11:59 pm PST at** the very latest.
Phase 2	Our review of all proposals will be completed by mid-May 2026 and scientists will be informed after that.
Phase 3	Start of discussions for the collaboration agreement in Q3/2026.

Submitting a collaboration proposal

- Check the outline of the opn2EXPERTS "Role of TLR5 in tumor immune evasion" 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. Nishida A., Andoh A. The Role of Inflammation in Cancer: Mechanisms of Tumor Initiation, Progression, and Metastasis *Cells* **2025**, 14(7):488. DOI: 10.3390/cells14070488, PubMed.
2. Gonzalez C., Williamson S., Gammon S. T., Glazer S., Rhee J. H., Piwnica-Worms D. TLR5 agonists enhance anti-tumor immunity and overcome resistance to immune checkpoint therapy *Commun Biol*. **2023**, 6(1):31. DOI: 10.1038/s42003-022-04403-8, PubMed.
3. McGinty M. T., Putelo A. M., Kolli S. H., Feng T-Y., Dietl M. R., Hatzinger C. N., Bajgai S., Poblete M. K., Azar F. N., Mohammad A., Kumar P., Rutkowski M. R. TLR5 Signaling Causes Dendritic Cell Dysfunction and Orchestrates Failure of Immune Checkpoint Therapy against Ovarian Cancer *Cancer Immunol Res*. **2025**, 13(5):696-711. DOI: 10.1158/2326-6066.CIR-24-0513, PubMed.
4. Rutkowski M. R., Stephen T. L., Svoronos N., Allegrezza M. J., Tesone A. J., Perales-Puchalt A., Brencicova E., Escovar-Fadul X., Nguyen J. M., Cadungog M. G., Zhang R., Salatino M., Tchou J., Rabinovich G. A., Conejo-Garcia J. R. Microbially driven TLR5-dependent signaling governs distal malignant progression through tumor-promoting inflammation *Cancer Cell*. **2015**, 27(1):27-40. DOI: 10.1016/j.ccell.2014.11.009, PubMed.