Therapeutic Immune Reprogramming in Cancer: Targeting Dysfunctional, Suppressive, and Senescent Immune States

Award Amount and Performance Period

- Award amount: Up to $480,000, including up to 20% indirect costs
- Performance period: November 1, 2026 – October 31, 2028

Background and Purpose

Historically, amfAR's research initiatives have focused on finding a cure for HIV. Four decades of HIV research have reshaped our understanding of the immune system, and insights from HIV have been leveraged in adjacent fields, including cancer immunology.

Innovation can be bi-directional and reciprocal. Seminal findings in cancer immunology have also furthered understanding of HIV biology.

To facilitate this reciprocal innovation, **amfAR seeks proposals that investigate strategies to reprogram dysfunctional, suppressive, senescent, or otherwise ineffective immune states in cancer**.

More specifically, this Request for Proposals (RFP) is intended to support mechanistic, preclinical, and translational studies that test how anti-tumor immunity can be restored, redirected, or amplified in cancers shaped by chronic antigen exposure, viral oncogenesis, immune dysfunction, or highly immunogenic tumor biology.

exclusion, stromal barriers, and tissue niches that maintain dysfunctional cell states. It is critical to move beyond descriptive profiling and test interventions capable of changing immune-cell state or tumor microenvironment function.

Responsive projects may use a range of immune-reprogramming strategies, including but not limited to: RNA-based technologies, targeted delivery platforms, cytokine or chemokine modulation, epigenetic or transcriptional perturbation, engineered immune-cell approaches, antibody- or ligand-directed immune modulation, organoid or explant-based perturbation systems, and computationally guided target discovery.

Application Process and Deadlines

1. Applicants must complete a project synopsis by registering for an account, or signing in if you already have one, through our Grants portal. Once logged in, click on Funding Opportunities from the portal menu.
2. The amfAR Research Department verifies applicants' eligibility and reviews synopses based on relevance, potential impact, and alignment with amfAR's mission.
3. A selected number of applicants will be invited to submit a full application. We regret that we are unable to discuss every submission with applicants.
4. All invited applications are evaluated and scored through external peer–review process.

Areas of Interest

Responsive applications may focus on one or more of the following areas:

1. **Reversal of dysfunctional or senescent immune states**
   Studies that test strategies to reverse, bypass, or remodel exhausted, senescent, suppressed, or terminally dysfunctional conventional or non-conventional T cells, NK cells, B cells, dendritic cells, macrophages, or other immune populations in cancer.
2. **Reprogramming suppressive tumor microenvironments**
   Studies that target myeloid suppression, immune exclusion, stromal barriers, cytokine and chemokine circuits, impaired antigen presentation, regulatory immune populations, or other mechanisms that prevent productive anti-tumor immunity.
3. **Selective expansion, recruitment, or activation of anti-tumor immune populations**
   Studies that identify and test methods to evaluate, expand, recruit, activate, or redirect immune-cell populations with anti-tumor activity.
4. **RNA-enabled and other targeted immune-modulatory approaches**
   Studies using mRNA, self-amplifying RNA, circular RNA, siRNA, antisense oligonucleotides, RNA-guided perturbation systems, lipid nanoparticles, targeted delivery vehicles, or related platforms to modulate immune-cell state or tumor microenvironment function.

non-productive states.

6. **Perturbation screens and target discovery**
   Studies using CRISPR, RNA-based perturbation, pooled genetic screens, chemical biology, single-cell perturb-seq, spatial perturbation systems, or computational modeling to identify actionable immune-reprogramming targets.
7. **Human-relevant models of immune reprogramming**
   Studies using patient-derived organoids, tumor–immune co-cultures, tumor slice cultures, lymphoid organoids, humanized models, or *ex vivo* human tumor systems to test immune-reprogramming mechanisms.
8. **Combination immunotherapy strategies**
   Studies testing immune reprogramming in combination with checkpoint blockade, therapeutic vaccination, adoptive cell therapy, antibodies, radiation, targeted therapy, or other cancer treatments, provided that the immune-reprogramming mechanism is central to the proposal.

Cancers of Interest

Projects may address cancers in which immune dysfunction, chronic antigen exposure, viral antigen expression, inflammation, or immunogenic tumor biology create a strong rationale for immune reprogramming or functional enhancement. Examples include, but are not limited to:

- HPV-associated cancers, including anal, cervical, oropharyngeal, vulvar, vaginal, and penile cancers
- EBV-associated lymphomas and other EBV-associated malignancies
- KSHV/HHV-8-associated malignancies, including Kaposi sarcoma and primary effusion lymphoma
- HBV- or HCV-associated liver cancer
- HTLV-1 associated malignancies
- Lung or colorectal cancers, particularly studies focused on immune dysfunction, antigen presentation, or myeloid-mediated suppression
- Immunogenic hematologic malignancies, including myeloma, when the project has a clear immune-reprogramming rationale

General Requirements

The proposed research must be conducted or validated either *in vivo*, in humans or disease-relevant animal models or *ex vivo*, in disease-relevant cells or tissues of either animal or human origin. Interventions tested exclusively in cell lines or in “healthy” primary cells will not be considered responsive to this RFP.

cancer-relevant model.

Valuable outputs could include

- Biomarkers predictive of immune response
- Datasets that define cell state trajectories
- Computational methods, including those leveraging Artificial intelligence/Machine Learning approaches, that facilitate interpretation of dynamic immune states
- Biological targets relevant to immune dysfunction and rescue
- Highly translational human models.

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Deadlines

- **Synopsis submission deadline**: June 29, 2026, 3 PM (ET)
- **Invitation to submit full grant application:** July 13, 2026
- **Deadline to submit full application:** August 17, 2026, 3 PM (ET)

Eligibility

Any biomedical researcher holding a research or clinical doctoral degree who is affiliated with a nonprofit research institution, anywhere in the world, is eligible to apply.

For more information regarding Target Grants, please refer to our Frequently Asked Questions.

To provide additional information and answer questions, amfAR will host an informational webinar on Tuesday, June 16 at 2:00 PM ET. Interested applicants can register here.

Future requests for proposals

Sign up today to receive alerts about new requests for proposals (RFPs) when they are posted online.

amfAR's mission is to end the global AIDS epidemic through innovative research.