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TITLE: Immune Correlate + Guided Design of Monoclonal Therapeutics for HIV Remission

PRINCIPAL INVESTIGATOR: Dr. Galit Alter, PhD

CONTRACTING ORGANIZATION: Massachusetts General Hospital

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5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)

Massachusetts General Hospital
Ragon Institute of MGH, MIT, and Harvard
400 Technology Square
Cambridge, MA 02139

8. PERFORMING ORGANIZATION REPORT NUMBER
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U.S. Army Medical Research and Development Command
Fort Detrick, Maryland 21702-5012

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

Current HIV-specific broadly neutralizing antibodies (bNAbs), selected for their ability to recognize the virus itself, fail to sufficiently kill infected cells and have only had a very modest impact on the HIV reservoir size in humans. Spontaneous control of viral rebound does infrequently occur during natural infection (post-treatment controllers) and seems to require specific functional antibody profiles with unique antigen specificities. These antibodies shall be identified and extracted from individuals who are undergoing antiretroviral treatment interruption and be functionally optimized to enhance the rapid and highly effective deletion of virally infected cells with the goal to develop "anti-reservoir" monoclonals that may be used as stand-alone therapeutics. In three aims, this project will define the correlates of humoral immunity that track with viral remission following treatment interruption followed by development of a library of and functionally enhanced novel monoclonal antibodies poised to recognize and kill reactivated latently HIV infected cells as novel therapeutics for HIV cure strategies. From existing sample banks (The Thai Red Cross AIDS Research Centre and United States Military HIV Research Program, Walter Reed Army Institute of Research) we selected individuals who controlled or did not control viral rebound after antiretroviral treatment interruption. To define the antigen-specific titer characteristics, an array of different HIV antigens was used to measure the antigen-specific antibody isotype and IgG subclass titer in all available patients and the most relevant and targeted antigens for the functional assays were identified. While patients that initiated treatment during the chronic phase of infection developed a robust humoral immune response against the virus, early antiretroviral treatment during the acute phase of infection abolished or at least dampened such a response. Interestingly, after treatment interruption, titers stayed relatively stable potentially explained by the lacking recall of memory cells. In some individuals, however, an increase in anti-p24 and anti-gp140 IgG was detectable. Whether, this may separate the cohort into subsets of patients with differing clinical outcomes will be determined next. To further delineate the functions which track with delayed rebound/viral control, we measured the Antibody Dependent Complement Deposition (ADCD) capacity and again we observed substantial differences in complement depositing activity across the patients and across timepoints. To determine if there is a functional signature that will track with antibody responses in individuals with controlled virus after ATI, we will next examine, using system's serology, the entire spectrum of antibody functionalities, including Antibody Dependent Cellular Cytotoxicity (ADCC), Antibody Dependent Cellular Phagocytosis (ADCP), Antibody Dependent Neutrophil Phagocytosis (ADNP) etc. In addition, antibodies will be isolated from post-treatment controllers and equipped with the most promising functional properties as identified in our system's serology approach. Together, this strategy will advance the development of novel monoclonal therapeutics during the upcoming funding period.

15. SUBJECT TERMS

NONE LISTED

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			USAMRDC
Unclassified	Unclassified	Unclassified	Unclassified	39	19b. TELEPHONE NUMBER *(include area code)*

TABLE OF CONTENTS

1. **INTRODUCTION:** *Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.*

Current HIV-specific broadly neutralizing (bNAbs), selected for their ability to recognize the virus itself, fail to kill all infected cells and have only had a very modest impact on the HIV reservoir size in humans. Spontaneous control of viral rebound seems to require specific functional antibody profiles with unique antigen specificities. These antibodies shall be identified and extracted from individuals who are undergoing antiretroviral treatment interruption and be functionally optimized to enhance the rapid and highly effective deletion of virally infected cells. These "anti-reservoir" monoclonals may be used as a stand-alone therapeutic or used to guide the development of a therapeutic vaccine able to drive a functional cure against this deadly pathogen.

2. **KEYWORDS:** *Provide a brief list of keywords (limit to 20 words).*

HIV, latency, HIV reservoir, treatment interruption control, broadly neutralizing antibodies, Systems Serology, HIV control.

3. **ACCOMPLISHMENTS:** *The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction.*

What were the major goals of the project?
List the major goals of the project as stated in the approved SOW. If the application listed milestones/target dates for important activities or phases of the project, identify these dates and show actual completion dates or the percentage of completion.

Specific Aim 1:	Define the correlates of humoral immunity that track with viral remission following treatment interruption
Specific Aim 2:	Develop and down select a library of novel monoclonal antibodies poised to recognize and kill reactivated latently HIV infected cells
Specific Aim 3:	Develop and test functionally enhanced "reservoir-targeting" monoclonal antibodies to cure HIV

What was accomplished under these goals?
For this reporting period describe: 1) major activities; 2) specific objectives; 3) significant results or key outcomes, including major findings, developments, or conclusions (both positive and negative); and/or 4) other achievements. Include a discussion of stated goals not met. Description shall include pertinent data and graphs in sufficient detail to explain any significant results achieved. A succinct description of the methodology used shall be provided. As the project progresses to completion, the emphasis in reporting in this section should shift from reporting activities to reporting accomplishments.

This study aims to partner with investigators at the Military HIV Research Program (MHRP) to generate novel monoclonal therapeutics, that will be able to specifically target the cellular HIV reservoir, thereby supporting reservoir eradication and potentially resulting in (functional) cure of individuals infected with HIV. We selected samples from existing sample banks (The Thai Red Cross AIDS Research Centre and United States Military HIV Research Program, Walter Reed Army Institute of Research) including individuals who controlled or did not control viral rebound after antiretroviral treatment interruption. The samples are derived from studies in patients from Thailand that were treated soon after (hyper)acute HIV infection (Fiebig stage I-IV) (cohort 1) or treated in the chronic phase of the infection (cohort 2). A total of 82 plasma and 33 PBMC samples of HIV patients at different timepoints before and during therapy interruption were shipped in June 2019.

During the previous funding period (see last annual report) we used the Systems Serology approach to define the specific correlates of humoral immunity that track with viral remission following treatment interruption ('Specific Aim 1'). We systematically explored the potential of the patient's antibodies to induce antibody-dependent complement deposition (ADCD), neutrophil phagocytosis (ADNP), monocyte phagocytosis (ADCP) and NK cell activation (ADNKA) against the three selected antigens. Interestingly, when normalized to their individual IgG titer delayed rebounder exhibit an overall augmented humoral immune response for ADCP, ADNP and ADNKA for the three tested antigens. Strikingly, the increased NK cell activation and engagement of FcγR2a by gp140 (clade AE) specific IgG in delayed rebounding patients was particularly important for the separation of the two groups in a computational machine learning model. These functions were among the top 4 selected features to discriminate early and delayed rebounder in the random forest model. In a co-correlation network analysis showing significant correlation of the selected features, NK cell activation was highly correlated for all antigens and interestingly also to cellular phagocytosis (ADCP) ($|r|>0.7$ and $p<0.05$).

During this funding period we continued experimental work for the development and down selection of a library of novel monoclonal antibodies poised to recognize and kill reactivated latently HIV infected cells ('Specific Aim 2'). Conventional library generation involves baiting, flow cytometric sorting, and BCR sequencing of B cells with a specificity against soluble HIV antigens (e.g. monomeric or trimeric spike antigens). However, the monoclonal antibody library generated under this aim should be specific to HIV antigens that are expressed on the surface of HIV infected cells and we used a novel unconventional approach for which we adopted an assay that was first described by Connors et.al. (doi:10.1038/nprot.2013.117) (**Figure 1**).

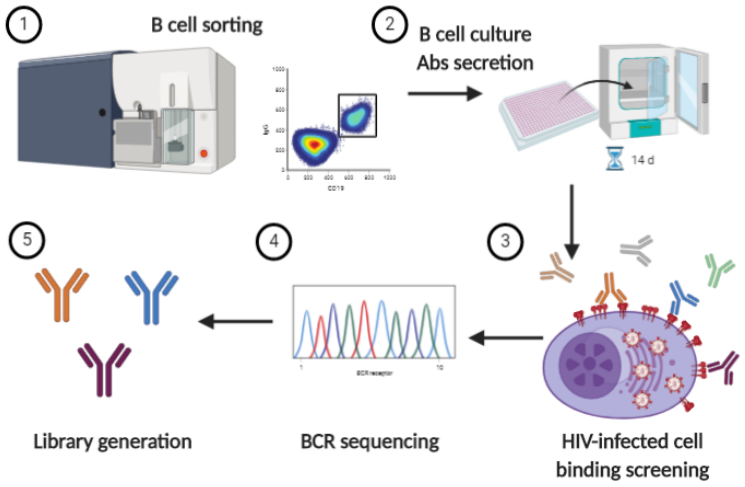

***Figure 1**: Scheme of the experimental procedure to generate a library of monoclonal antibodies specific for HIV antigens expressed on the surface of HIV infected cells.*

Our selection strategies aimed to discover novel mAbs poised to recognize and bind to (latently) HIV infected cells. In the original project idea, we aimed to include PBMC donors from our post-treatment cohort. However, due to low cell concentrations of the provided samples sorting from these samples was not feasible. As an alternative we resort to high concentration PBMC samples from Elite Controllers provided by the Ragon Institute Cellular Immunology Database (CIDB). For the selection process we specifically developed an antibody:cell binding assay using a latently infected cell line (ACH-2) or infected primary cells. PMA stimulated ACH-2 cells or infected primary cells (3 days post infection) were incubated with different dilution of HIV controller derived plasma. Antibody labeled cells were then detected by using a fluorescently tagged secondary probe and analyzed by flow cytometry.

To begin to select donors with enhanced potential to bind to infected cells plasma antibodies from a total of 24 Elite Controllers were screened for binding to ACH-2 (**Figure 2**). The top five binders were then further tested for binding to JRCSF or NL4-3 HIV-1 infected primary cells (**Figure 2**). Plasma samples no 12 and 13 both of which represent different timepoints from the same individual showed greatest binding with low background and this donor was selected for library generation.

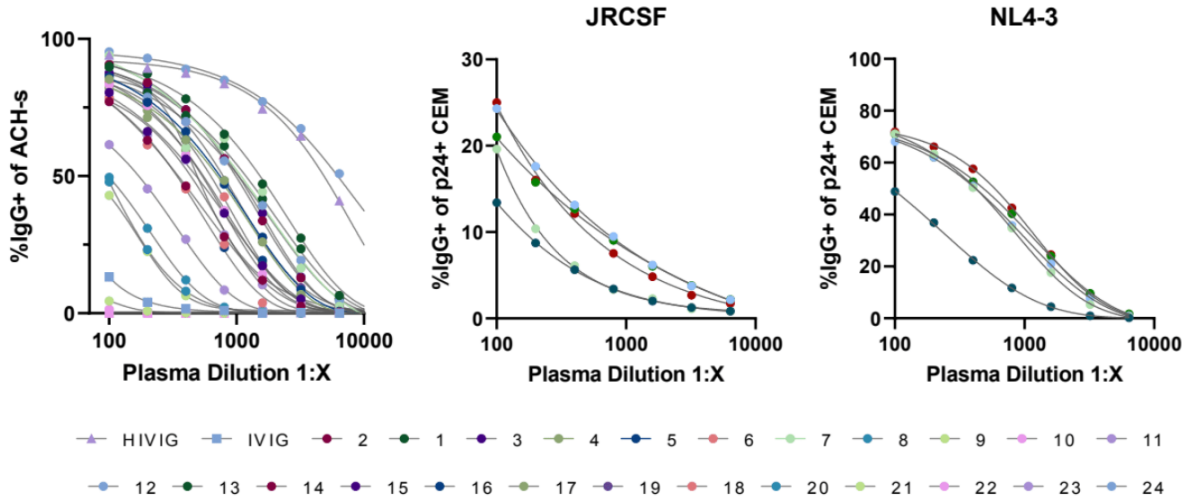

Figure 2*: Antibodies from 24 Elite controller were tested for the potential to bind to HIV infected cells. ACH-2 cells were stimulated overnight with PMA (left panel), or primary cells infected with JRCSF (middle panel) or NL4-3 (right panel) before incubation with 2fold serial diluted plasma (dilution ranging from 1:100 to 1:12,800). Pooled IgG from HIV infected (HIVIG) or healthy individuals (IVIG) was used as positive and negative control, respectively.*

IgM-/IgD-/IgA-/CD19+ B cells from the PBMC sample of the selected individual were seeded into wells of 384 well plates at low cell density (4 cells per well) and cultured along with CD40L expressing 3T3 feeder cells and stimulated with a cytokine cocktail for 14 days. During this period B cells proliferate and secrete their B cell receptor into the supernatant. The initial low cellular density ensures low clonal heterogeneity per well which allows us to obtain individual BCR sequences. After incubation supernatants were harvested for screening reactivity against HIV-infected cells as described above. B cells were lysed in RNA lysis buffer and stored at -80C to allow BCR sequencing for library generation from wells with positive screening result. While the sorting and culture of B cells has been completed, we are currently in the process of supernatant screening and identification of positive wells for BCR sequencing.

As proposed under AIM 3, we will generate monoclonal antibodies, identified under AIM 2 with respective Fc modifications using a high throughput cloning platform, Golden Gate, to ligate all antibody fragments into a pUC19 vector in a single reaction, as previously reported (Gunn et al,

Immunity 54: 815-828 e815.51). This method, termed Rationally Engineered and Functionally Optimized Monoclonal antibodies (REFORM), allows the rapid generation of antibody plasmids encoding different Fc variants with the same Fab binding domain. As an example, using a monoclonal antibody against HIV, unrelated to this project, we have generated 62 different isotypes or Fc variants and tested these for Fc-mediated functionality, ie antibody dependent complement deposition (ADCP), antibody dependent neutrophilic and cellular phagocytosis (ADNP and ADCP, respectively), and NK-cell function (IFNg, Mip-1b secretion and degranulation by CD107a expression) ***(Figure 3)***. This approach will be applied to the antibodies identified in AIM2 and the functional features that best match the profiles identified in AIM1 will be selected for further downstream testing.

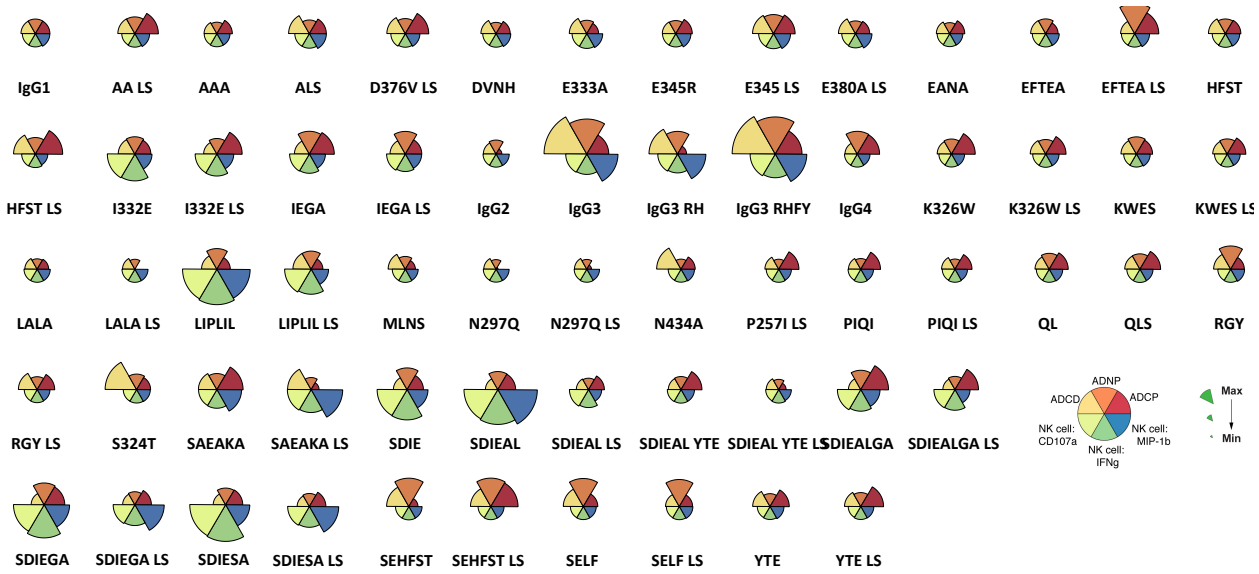

Figure 3*: Antibodies' functional signatures based on isotype or Fc-modification as shown by flor-plots. The colors of the petals match the examined function, and the petal size relates to the magnitude. IgG1 is the unmodified wild-type antibody.*

What opportunities for training and professional development has the project provided?
If the project was not intended to provide training and professional development opportunities or there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe opportunities for training and professional development provided to anyone who worked on the project or anyone who was involved in the activities supported by the project. "Training" activities are those in which individuals with advanced professional skills and experience assist others in attaining greater proficiency. Training activities may include, for example, courses or one-on-one work with a mentor. "Professional development" activities result in increased knowledge or skill in one's area of expertise and may include workshops, conferences, seminars, study groups, and individual study. Include participation in conferences, workshops, and seminars not listed under major activities.

Nothing to report

How were the results disseminated to communities of interest?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the results were disseminated to communities of interest. Include any outreach activities that were undertaken to reach members of communities who are not usually aware of these project activities, for the purpose of enhancing public understanding and increasing interest in learning and careers in science, technology, and the humanities.

Nothing to report

Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives.

We will continue with the experimental work in order to accomplish the goals described in aim 2 and 3. In particular we will complete the generation of a library of monoclonal antibodies from the individuals, antibodies will be tested for the potential to bind latently infected and reactivated cells. Furthermore, the selected clones will be functionally optimized by Fc engineering to enhance killing activity for downstream testing.

4. What was the impact on the development of the principal discipline(s) of the project?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how findings, results, techniques that were developed or extended, or other products from the project made an impact or are likely to make an impact on the base of knowledge, theory, and research in the principal disciplinary field(s) of the project. Summarize using language that an intelligent lay audience can understand (Scientific American style).

Nothing to report

What was the impact on other disciplines?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the findings, results, or techniques that were developed or improved, or other products from the project made an impact or are likely to make an impact on other disciplines.

Nothing to report

What was the impact on technology transfer?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe ways in which the project made an impact, or is likely to make an impact, on commercial technology or public use, including:

- *transfer of results to entities in government or industry;*
- *instances where the research has led to the initiation of a start-up company; or*
- *adoption of new practices.*

Nothing to report

Describe how results from the project made an impact, or are likely to make an impact, beyond the bounds of science, engineering, and the academic world on areas such as:

- *improving public knowledge, attitudes, skills, and abilities;*
- *changing behavior, practices, decision making, policies (including regulatory policies), or social actions; or*
- *improving social, economic, civic, or environmental conditions.*

Nothing to report

5. **CHANGES/PROBLEMS:** *The PD/PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, "Nothing to Report," if applicable:*

Nothing to report

Changes in approach and reasons for change
Describe any changes in approach during the reporting period and reasons for these changes. Remember that significant changes in objectives and scope require prior approval of the agency.

Nothing to report

Actual or anticipated problems or delays and actions or plans to resolve them
Describe problems or delays encountered during the reporting period and actions or plans to resolve them.

Nothing to report

Changes that had a significant impact on expenditures
Describe changes during the reporting period that may have had a significant impact on expenditures, for example, delays in hiring staff or favorable developments that enable meeting objectives at less cost than anticipated.

Nothing to report

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents
Describe significant deviations, unexpected outcomes, or changes in approved protocols for the use or care of human subjects, vertebrate animals, biohazards, and/or select agents during the

reporting period. If required, were these changes approved by the applicable institution committee (or equivalent) and reported to the agency? Also specify the applicable Institutional Review Board/Institutional Animal Care and Use Committee approval dates.

Significant changes in use or care of human subjects

Nothing to Report

Significant changes in use or care of vertebrate animals

Nothing to Report

Significant changes in use of biohazards and/or select agents

Nothing to Report

6. PRODUCTS: *List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state "Nothing to Report."*

- **Publications, conference papers, and presentations**
  Report only the major publication(s) resulting from the work under this award.

  Journal publications. *List peer-reviewed articles or papers appearing in scientific, technical, or professional journals. Identify for each publication: Author(s); title; journal; volume: year; page numbers; status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

  Title: **Viral rebound kinetics correlate with distinct HIV antibody features**
  Authors: Bartsch YC, Loos C, Rossignol E, Fajnzylber JM, Yuan D, Avihingsanon A, Ubolyam S, Jupimai T, Hirschel B, Ananworanich J, Lauffenburger DA, Li JZ, Alter G, Julg B.
  Journal: mBio. 2021 Mar 9;12(2):e00170-21. doi: 10.1128/mBio.00170-21. PMID: 33688003; PMCID: PMC8092214.
  Status: Published
  acknowledgement of federal support: yes

  Books or other non-periodical, one-time publications. *Report any book, monograph, dissertation, abstract, or the like published as or in a separate publication, rather than a periodical or series. Include any significant publication in the proceedings of a one-time conference or in the report of a one-time study, commission, or the like. Identify for each one-time publication: author(s); title; editor; title of collection, if applicable;*

bibliographic information; year; type of publication (e.g., book, thesis or dissertation); status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).

Nothing to report

Other publications, conference papers and presentations. *Identify any other publications, conference papers and/or presentations not reported above. Specify the status of the publication as noted above. List presentations made during the last year (international, national, local societies, military meetings, etc.). Use an asterisk (*) if presentation produced a manuscript.*

Nothing to report

- **Website(s) or other Internet site(s)**
  List the URL for any Internet site(s) that disseminates the results of the research activities. A short description of each site should be provided. It is not necessary to include the publications already specified above in this section.

Nothing to report

- **Technologies or techniques**
  Identify technologies or techniques that resulted from the research activities. Describe the technologies or techniques were shared.

Nothing to report

- **Inventions, patent applications, and/or licenses**
  Identify inventions, patent applications with date, and/or licenses that have resulted from the research. Submission of this information as part of an interim research performance progress report is not a substitute for any other invention reporting required under the terms and conditions of an award.

Nothing to report

- **Other Products**
  Identify any other reportable outcomes that were developed under this project. Reportable outcomes are defined as a research result that is or relates to a product, scientific advance, or research tool that makes a meaningful contribution toward the understanding, prevention, diagnosis, prognosis, treatment and /or rehabilitation of a disease, injury or condition, or to improve the quality of life. Examples include:
  - *data or databases;*
  - *physical collections;*
  - *audio or video products;*
  - *software;*
  - *models;*
  - *educational aids or curricula;*
  - *instruments or equipment;*
  - *research material (e.g., Germplasm; cell lines, DNA probes, animal models);*
  - *clinical interventions;*
  - *new business creation; and*
  - *other.*

Nothing to report

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate "no change".

Name: Galit Alter, PhD
Project Role: PI
Researcher Identifier (e.g. ORCID ID): 0000-0002-7680-9215
Nearest person month worked: 0.5 CM
Contribution to Project: Dr Alter has provided oversight of the project and supervised Dr Bartsch in design and execution of the sample analysis
Funding Support: Complete only if the funding support is provided from other than this award.)

Name: Boris Juelg, MD PhD
Project Role: Co-I
Researcher Identifier (e.g. ORCID ID): 0000-0002-4687-9626
Nearest person month worked: 0.6 CM
Contribution to Project: Dr Juelg has provided oversight of the project and supervised Dr Bartsch in design and execution of the sample analysis
Funding Support: Complete only if the funding support is provided from other than this award.)

Name: Yannic Bartsch, PhD
Project Role: Post-doctoral fellow
Researcher Identifier (e.g. ORCID ID): 0000-0002-3844-3056
Nearest person month worked: 6.6 CM
Contribution to Project: Dr Bartsch is performing the experiments.
Funding Support: Complete only if the funding support is provided from other than this award.)

Name: Evan Rossignol, PhD
Project Role: Post-doctoral fellow
Researcher Identifier (e.g. ORCID ID): 0000-0002-5347-4301
Nearest person month worked: 4.0 CM
Contribution to Project: Dr Rossignol is developing the B-cell screening technology
Funding Support: Complete only if the funding support is provided from other than this award.)

Name: Hacheming Compere
Project Role: Research technician
Researcher Identifier (e.g. ORCID ID): 0000-0002-0774-8623
Nearest person month worked: 11.0 CM
Contribution to Project: Mr Compere is supporting the experimental work, ie conducting experiments, sample
management etc related to this project.
Funding Support: NA

Name: Kang, Jaewon
Project Role: Research technician
Researcher Identifier (e.g. ORCID ID): 0000-0003-0846-4611
Nearest person month worked: 12.0 CM
Contribution to Project: Mr Kang is supporting the experimental work, ie conducting experiments, sample
management etc related to this project.
Funding Support: NA

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?
If there is nothing significant to report during this reporting period, state "Nothing to Report." If the active support has changed for the PD/PI(s) or senior/key personnel, then describe what the change has been. Changes may occur, for example, if a previously active grant has closed and/or if a previously pending grant is now active. Annotate this information so it is clear what has changed from the previous submission. Submission of other support information is not necessary for pending changes or for changes in the level of effort for active support reported previously. The awarding agency may require prior written approval if a change in active other support significantly impacts the effort on the project that is the subject of the project report.

South East Asia Research Collaboration in HIV (SEARCH) Thai Red Cross AIDS Research Centre: This subcontract has not performed any work since the inception of this award. Dr. Eugène Kroon has not devoted any effort and no billable work has been performed. We therefore are terminating the subcontract agreement with this organization.
Other Support forms for Drs. Alter and Juelg are provided below.

OTHER SUPPORT

ALTER, GALIT
ACTIVE

*Title: COVID-19: ANIMAL MODELS
Major Goals: The goal of this project is to determine functional antibody response in the setting of SARS-Cov-2 infection.
*Status of Support: Active (NEW)
Project Number: INV-006131
Name of PD/PI: Alter, G.
*Source of Support: Bill and Melinda Gates Foundation
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 04/01/2020 – 03/31/2022
* Total Award Amount (including Indirect Costs): $100,000
* Person Months per budget period.

Year (YYYY)	Person Months (##.##)
2. 2021	0.12 calendar

*Title: GH-VAP: Systems serology platform
Major Goals: The goal of this project is to establish The Alter Laboratory as part of The Gates Foundation Global Health Vaccine Accelerator Platforms (GH-VAP). Previously established/qualified Systems Serology assays will be made available to The Gates Foundation collaborators/community to define the role of the innate immune system in recruiting antibodies to provide protection from infection across multiple pathogens.
*Status of Support: Active
Project Number: INV-001650
Name of PD/PI: Alter, G.
*Source of Support: Bill and Melinda Gates Foundation
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 11/21/2019 - 09/30/2022
* Total Award Amount (including Indirect Costs): $847,660
* Person Months per budget period.

Year (YYYY)	Person Months (##.##)
2. 2020	0.12 calendar
3. 2021	0.12 calendar
4. 2022	0.12 calendar

*Title: Consortia for Innovative AIDS Research in Nonhuman Primates/Humoral Immunology Core
Major Goals: The goal of this program is to define the immunological mechanisms that lead to prevention and eradication in the non-human primate model of HIV.
*Status of Support: Active
Project Number: 1UM1AI124377-05
Name of PD/PI: Barouch, D.
*Source of Support: NIH
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 05/01/2016 – 04/30/2022
* Total Award Amount (including Indirect Costs): $1,232,730
* Person Months per budget period.

Year (YYYY)	Person Months (##.##)
6. 2021	0.12 calendar

*Title: Combined Immunologic Approaches to Cure HIV-1 - Focus 2
Major Goals: The goal of this project is to develop next-generation “killer” monoclonal antibodies to aggressively purge the HIV reservoir following reactivation.
*Status of Support: Active
Project Number: 5UM11AI126603-05
Name of PD/PI: Barouch, D.
*Source of Support: NIH
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 07/01/2016 – 06/30/2022
* Total Award Amount (including Indirect Costs): $1,738,471
* Person Months per budget period.

Year (YYYY)	Person Months (##.##)
6. 2021	0.12 calendar

*Title: Combined Immunologic Approaches to Cure HIV-1 – SRS Core
Major Goals: The goal of this project is to profile the vaccine-induced humoral immune responses induced by therapeutic vaccination in both non-human primates and humans to define the reservoir-depleting activity of these responses.
*Status of Support: Active
Project Number: 5UM1AI126603-05
Name of PD/PI: Barouch, D.
*Source of Support: NIH
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 07/01/2016 – 06/30/2022
* Total Award Amount (including Indirect Costs): $708,081
* Person Months per budget period.

Year (YYYY)	Person Months (##.##)
6. 2021	0.12 calendar

*Title: Therapeutic vaccination and PD-1 blockade in treated HIV disease
Major Goals: The goals of this program are to define the safety and immunogenicity of novel DNA vaccine in HIV-infected adults on antiretroviral therapy and to determine if DP-1 inhibition during vaccination improves immunogenicity.
*Status of Support: Active
Project Number: 5U01AI131296-04
Name of PD/PI: Deeks, S.
*Source of Support: NIH
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 04/01/2017 – 03/31/2022
* Total Award Amount (including Indirect Costs): $129,278
* Person Months per budget period.

Year (YYYY)	Person Months (##.##)
5. 2021	0.12 calendar

*Title: Optimization of Broadly Neutralizing Antibodies for HIV Eradication
Major Goals: The goal of this project is to develop a bi- or tetra-specific Fc-engineered single monoclonal antibody the covers global viral diversity and drive the rapid and highly effective clearance of reactivated latently infected cells to test in vivo in NHP following viral reactivation.
*Status of Support: Active
Project Number: R01AI129797-05
Name of PD/PI: Alter, G./Barouch, D.
*Source of Support: NIH
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 08/01/2017 – 07/31/2022
* Total Award Amount (including Indirect Costs): $1,150,929
* Person Months per budget period.

Year (YYYY)	Person Months (##.##)
5. 2021	0.48 calendar

*Title: Consortium for Viral systems Biology (CViSB)-Project 1
Major Goals: The goal of this project is to use an integrated systems-level identification and investigations of the host determinants of patient outcomes in Lassa virus and Ebola virus infection.
*Status of Support: Active (THIS AWARD)
Project Number: 5U19AI135995-04
Name of PD/PI: Anderson, K.
*Source of Support: NIH
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 02/01/2018 – 01/31/2023
* Total Award Amount (including Indirect Costs): $751,168
* Person Months per budget period.

Year (YYYY)	Person Months (##.##)
3. 2020	0.12 calendar
4. 2021	0.12 calendar
5. 2022	0.12 calendar

*Title: IPCAVD 4
Major Goals: The goal of this IPCAVD program is to develop Ad26/Env vaccines for HIV-1 by a highly collaborative and multifaceted research program involving leading investigators in academia and industry.
*Status of Support: Active
Project Number: 5U19AI128751-04
Name of PD/PI: Barouch, D.
*Source of Support: NIH
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 02/01/2018 – 01/31/2023
* Total Award Amount (including Indirect Costs): $1,499,979
* Person Months per budget period.

Year (YYYY)	Person Months (##.##)
4. 2021	0.24 calendar
5. 2022	0.24 calendar

*Title: Immune Correlate + Guided Design of Monoclonal Therapeutics for HIV Remission
Major Goals: The goal of this project is to define the specific antibody profile that tracks with cellular reservoir control to rationally design a therapeutic strategy able to effectively eliminate the viral reservoir and drive viral remission at a global level.
*Status of Support: Active (THIS AWARD)
Project Number: W81XWH1810579
Name of PD/PI: Alter, G.
*Source of Support: DoD
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 09/30/2018 – 09/29/2022
* Total Award Amount (including Indirect Costs): $1,754,195
* Person Months per budget period.

Year (YYYY)	Person Months (##.##)
3. 2020	0.24 calendar
4. 2021	0.24 calendar
5. 2022	0.24 calendar

*Title: Antibody mediated protective immunity against cholera
Major Goals: The goal of this project is to improve our understanding of host-pathogen interactions during cholera, result in better immunologic correlates of vaccine protection, and impact strategies for improving vaccines for cholera and potentially other mucosal infections.
*Status of Support: Active
Project Number: 5R01AI137164-03
Name of PD/PI: Harris, J.
*Source of Support: NIH
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 09/14/2018 – 08/31/2023
* Total Award Amount (including Indirect Costs): $3,865,697
* Person Months per budget period.

Year (YYYY)	Person Months (##.##)
3. 2020	0.12 calendar
4. 2021	0.12 calendar
5. 2022	0.12 calendar

*Title: Consortium for Immunotherapeutics against Emerging Viral Threats - Core D
Major Goals: The goal of this project is to use systems serology and antibody engineering to improve against filovirus, arenavirus, and alphavirus.
*Status of Support: Active
Project Number: 5U19AI42790-03
Name of PD/PI: Saphire, E.
*Source of Support: NIH/NIAID
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 05/01/2019 - 04/30/24
* Total Award Amount (including Indirect Costs): $658,223
* Person Months per budget period.

Year (YYYY)	Person Months (##.##)
3. 2021	0.96 calendar
4. 2022	0.96 calendar
5. 2023	0.96 calendar

*Title: Center for Influenza Vaccine Research in High Risk Populations
Major Goals: The goal of this proposal is to determine immunological correlates of protection in influenza infection in naturally infected human populations and in human and animal challenge models post vaccination.
*Status of Support: Active
Project Number: 75N93019C00052
Name of PD/PI: Ross, T.

*Source of Support: NIH/NIAID
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 09/10/2019 – 09/30/2026
* Total Award Amount (including Indirect Costs): $2,469,888
* Person Months per budget period.

Year (YYYY)	Person Months (##.##)
2. 2020	0.55 calendar
3. 2021	0.55 calendar
4. 2022	0.55 calendar
5. 2023	0.55 calendar
6. 2024	0.55 calendar
7. 2025	0.55 calendar

*Title: Immune Mechanisms of Protection against Mycobacterium Tuberculosis Center (IMPAc-TB)

Major Goals: The goal of this proposal is probe the potential biological role of antibodies in driving anti-microbial control and to generate antibodies and engineer monoclonals to further dissect the mechanistic role of antibodies in bactericidal activity.

*Status of Support: Active
Project Number: 75N93019C00071
Name of PD/PI: Fortune, S.
*Source of Support: NIH/NIAD
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 09/30/2019 – 02/28/2023
* Total Award Amount (including Indirect Costs): $2,290,109
* Person Months per budget period.

Year (YYYY)	Person Months (##.##)
3. 2021	0.84 calendar
4. 2022	0.84 calendar

*Title: Defining the Fc-correlates of protection against influenza

Major Goals: The goal of this proposal is to define the influenza-specific Fc-humoral profiles that associate with protection against influenza and the development of neutralizing antibody breadth to guide next generation design of a universal influenza vaccine.

*Status of Support: Active
Project Number: 5R01AI146785
Name of PD/PI: Alter, G.
*Source of Support: NIH/NIAID
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 03/11/2020 – 02/28/2025
* Total Award Amount (including Indirect Costs): $2,949,879
* Person Months per budget period.

Year (YYYY)	Person Months (##.##)
2. 2021	0.48 calendar
3. 2022	0.48 calendar
4. 2023	0.48 calendar
5. 2024	0.48 calendar

*Title: Demystifying the antiviral activity of the IgG3+ antibody response
Major Goals: The goal of this project is to explore and define the specificity/functionality of IgG3+ B cell responses and the mechanism, by which the immune system programs such potent antiviral humoral immunity.
*Status of Support: Active
Project Number: 5R37AI80289-12
Name of PD/PI: Alter, G.
*Source of Support: NIH/NIAID
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 01/09/2020 – 12/31/2024
* Total Award Amount (including Indirect Costs): $3,225,602
* Person Months per budget period.

Year (YYYY)	Person Months (##.##)
2. 2021	0.67 calendar
3. 2022	0.67 calendar
4. 2023	0.67 calendar

*Title: Demystifying the antiviral activity of the IgG3+ antibody response
Major Goals: This proposal seeks to define the humoral correlates and mechanisms of action against COVID-19 in mice, ferrets, and monkeys
*Status of Support: Active
Project Number: 3R37AI080289-12S1
Name of PD/PI: Alter, G.
*Source of Support: NIH
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 04/10/2020 – 12/31/2022
* Total Award Amount (including Indirect Costs): $773,527
* Person Months per budget period.

Year (YYYY)	Person Months (##.##)
1. 2021	0.48 calendar
2. 2022	0.48 calendar

*Title: Multiplexed Antigen-Specific Antibody Fc Profiling on a Chip for Point-of-Care Diagnosis of TB in HIV-infected Children
Major Goals: The goal of this proposal is to develop an inexpensive, simple, reliable TB-specific antibody-based point-of-care diagnostic to manage TB disease in children under the age of 5.
*Status of Support: Active
Project Number: 5R01AI152158-02
Name of PD/PI: Alter, G.
*Source of Support: NIH

*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 05/06/2020 - 04/30/2025
* Total Award Amount (including Indirect Costs): $4,583,793
* Person Months per budget period.

Year (YYYY)	Person Months (##.##)
2. 2021	0.96 calendar
3. 2022	0.96 calendar
4. 2023	0.96 calendar
5. 2024	0.96 calendar

*Title: Mapping and dissecting the role of antibodies in Mtb control
Major Goals: This proposal aims to define the specificities, functional profiles, and anti-microbial mechanism(s) of antibodies that prevent progression to TB.
*Status of Support: Active
Project Number: 1R56AI155149-01
Name of PD/PI: Alter, G.
*Source of Support: NIH
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 09/01/2020 – 08/31/2022
* Total Award Amount (including Indirect Costs): $815,165
* Person Months per budget period.

Year (YYYY)	Person Months (##.##)
1. 2020	0.48 calendar
2. 2021	0.12 calendar

*Title: Functional profiling of OSP-specific and other antibodies during shigella infection
Major Goals: The goal of this project is to further evaluate the functional attributes of anti-shigella antibodies and their correlation with protection, especially among young children in resource-limited settings.
*Status of Support: Active (NEW)
Project Number: 1R01AI155414-01
Name of PD/PI: Ryan, E.
*Source of Support: NIH
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 09/22/2020 – 08/31/2025
* Total Award Amount (including Indirect Costs): $3,613,163
* Person Months per budget period.

Year (YYYY)	Person Months (##.##)
1. 2020	0.12 calendar
2. 2021	0.12 calendar
3. 2022	0.12 calendar
4. 2023	0.12 calendar
5. 2024	0.12 calendar

*Title: Differential Humoral Immune response in Children and Adults with COVID-19
Major Goals: The goal of this project is to define the concentration and type of antibody responses to coronaviruses in pediatric and adult sera
*Status of Support: Active (NEW)
Project Number: 280870.5116745.0011
Name of PD/PI: Alter, G.
*Source of Support: Boston Children's Hospital
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 08/01/2020-04/30/2022
* Total Award Amount (including Indirect Costs): $24,968
* Person Months per budget period.

Year (YYYY)	Person Months (##.##)
2. 2021	0.12 calendar

*Title: Defining functional humoral correlates of immunity to guide vaccine design
Major Goals: The proposal aims to dissect and define the correlates of immunity that track with protection from malaria infection following irradiated sporozoite vaccination as well as dissect the role of pre-existing immunity in shaping these vaccine-induced immune responses
*Status of Support: Active (NEW)
Project Number: 1R01AI151178-01A1
Name of PD/PI: Alter, G.
*Source of Support: NIH
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 11/24/2020 - 10/31/2025
* Total Award Amount (including Indirect Costs): $4,023,237
* Person Months per budget period.

Year (YYYY)	Person Months (##.##)
1. 2020	0.77 calendar
2. 2021	0.77 calendar
3. 2022	0.77 calendar
4. 2023	0.77 calendar
5. 2024	0.77 calendar

*Title: Immunologic Signatures of SARS-CoV-2 Vaccination and Disease
Major Goals: This project seeks to define the humoral correlates of immunity following infection as well as the durability of this protective humoral immunity both following natural infection or vaccination to inform vaccine development.
*Status of Support: Active (NEW)
Project Number: 5U01CA260476-01
Name of PD/PI: Alter, G./Barouch. D.
*Source of Support: NIH
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 09/30/2020-08/31/2022
* Total Award Amount (including Indirect Costs): $642,600
* Person Months per budget period.

Year (YYYY)	Person Months (##.##)
1. 2020	0.96 calendar
2. 2021	0.96 calendar

*Title: Harvard University Center for AIDS Research Co-Director
Major Goals: The scope of this award is to provide administrative and senior leadership support to Harvard University's Center for AIDS Research
*Status of Support: Active
Project Number: 5P30AI060354-17 (NEW)
Name of PD/PI: Alter, G.
*Source of Support: NIH
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 08/01/2020-07/31/2024
* Total Award Amount (including Indirect Costs): $22,374
* Person Months per budget period.

Year (YYYY)	Person Months (##.##)
2. 2021	0.48 calendar
3. 2022	0.6 calendar
4. 2023	0.6 calendar

*Title: Consortium for Immunotherapeutics against Emerging Viral Threats/Supplement: Jump to warp speed: Understanding mechanisms of antibody action to mitigate risk and maintain efficacy
Major Goals: Under this proposal we aim to define the Fc-correlates of immunity of SARS-Cov-2 monoclonal antibodies to guide monoclonal therapeutic and vaccine design
*Status of Support: Active (NEW)
Project Number: 3U19AI142790-02S1
Name of PD/PI: Saphire, E.
*Source of Support: NIH
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 07/27/2020 - 04/30/2022
* Total Award Amount (including Indirect Costs): $317,718
* Person Months per budget period.

Year (YYYY)	Person Months (##.##)
2. 2021	0.12 calendar

*Title: Discovery and development of antibody therapeutics for SARS-CoV-2 and other high-risk emerging viruses
Major Goals: The Alter Lab will profile monoclonal antibodies categorized as neutralizers: B3819, non-neutralizers (CR3022)20, and other novel antibodies from Dr. Abraham to define the mechanistic correlates of immunity against SARS-CoV-2.
*Status of Support: Active (NEW)
Project Number: 223827.5229200.0006
Name of PD/PI: Alter, G.
*Source of Support: AbbVie
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 12/01/2020-11/30/2023
* Total Award Amount (including Indirect Costs): $1,512,000
* Person Months per budget period.

Year (YYYY)	Person Months (##.##)
2. 2021	0.12 calendar
3. 2022	0.12 calendar
4. 2023	0.12 calendar
5. 2024	0.12 calendar

*Title: Statement of Work No. 2: Systems Serology and Antibody Effector Function
Major Goals: The Alter lab will conduct Systems Serology to survey the characteristics of the humoral immune response
*Status of Support: Active (NEW)
Project Number: A09406
Name of PD/PI: Alter, G.
*Source of Support: International AIDS Vaccine Initiative (IAVI)
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 11/01/2020 - 06/30/2023
* Total Award Amount (including Indirect Costs): $40,415
* Person Months per budget period.

Year (YYYY)	Person Months (##.##)
2. 2021	0.05 calendar
3. 2022	0.05 calendar

*Title: Statement of Work No. 3: Systems Serology and Antibody Effector Function
Major Goals: The Alter lab will conduct Systems Serology to survey the characteristics of the humoral immune response
*Status of Support: Active (NEW)
Project Number: A09564
Name of PD/PI: Alter, G.
*Source of Support: International AIDS Vaccine Initiative (IAVI)
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 02/01/2021 - 06/30/2023
* Total Award Amount (including Indirect Costs): $104,134
* Person Months per budget period.

Year (YYYY)	Person Months (##.##)
1. 2021	0.05 calendar
2. 2022	0.05 calendar

*Title: TB-induced immunity in HIV-infected and uninfected individuals
Major Goals: The goal of this project is to study the impact of HIV coinfection on reshaping Mtb specific immunity mediated by antibodies.
*Status of Support: Active (NEW)
Project Number: 1R56AI147950-01
Name of PD/PI: Goldfield, A.
*Source of Support: NIH
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 04/01/2020-12/31/2022
* Total Award Amount (including Indirect Costs): $84,000
* Person Months per budget period.

Year (YYYY)	Person Months (##.##)
2. 2021	0.12 calendar
3. 2022	0.12 calendar

*Title: Early recognition of Pulmonary Tuberculosis among HIV-exposed, HIV-infected, and HIV-unexposed Ugandan children using novel imaging and immune-based diagnostics
Major Goals: The goal of this project is to define CD4+ and CD8+ T cell, and B cell responses to primary Mtb-infection associated with asymptomatic containment of infection versus progression to disease.
*Status of Support: Active (NEW)
Project Number: 1R01AI157807-01A1
Name of PD/PI: Lancioni, C.
*Source of Support: NIH
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 04/15/2021 - 03/31/2026
* Total Award Amount (including Indirect Costs): $621,600
* Person Months per budget period.

Year (YYYY)	Person Months (##.##)
1. 2021	0.12 calendar
2. 2022	0.12 calendar
3. 2023	0.12 calendar
4. 2024	0.12 calendar
5. 2025	0.12 calendar

*Title: (Restricted Supplment SARS-CoV-2 Variant Testing) Defining the Fe-correlates of protection against influenza
Major Goals: The goal of this study is to profile the evolution of the breadth of the VOC-specific Fc-effector functions of vaccine induced antibodies across vaccine platforms.
*Status of Support: Active (NEW)
Project Number: 3R01AI146785-02W1
Name of PD/PI: Alter, G.
*Source of Support: NIH-National Institutes of Health
*Primary Place of Performance: MGH
Project/Proposal Start and End Date: 08/17/2021 - 02/28/2023
* Total Award Amount (including Indirect Costs): $499,721
* Person Months per budget period.

Year (YYYY)	Person Months (##.##)
1. 2021	0.12 calendar

*Title: I4C 2.0: Immunotherapy for Cure
Major Goals: The goal of this study is to identify markers of HIV reservoir
*Status of Support: Active (NEW)
Project Number: 1UM1AI164556-01
Name of PD/PI: Barouch, D.
*Source of Support: NIH/NIAID
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 07/01/2021 - 06/30/2026
* Total Award Amount (including Indirect Costs): $1,680,000
* Person Months per budget period.

Year (YYYY)	Person Months (##.##)
1. 2021	0.36 calendar
2. 2022	0.36 calendar
3. 2023	0.36 calendar
4. 2024	0.36 calendar
5. 2025	0.36 calendar

*Title: Pediatric Adolescent Virus Eradiation (PAVE) Martin Delaney Collaboratory
Major Goals: To probe the functional antibody responses involved in HIV immunity to support the rational design of therapeutics or vaccines to counteract this pathogen
*Status of Support: Active (NEW)
Project Number: 1UM1AI164566-01
Name of PD/PI: Persaud, D.
*Source of Support: NIH
*Primary Place of Performance: MGH
Project/Proposal Start and End Date: 07/01/2021 - 06/30/2026
* Total Award Amount (including Indirect Costs): $510,500
* Person Months (Calendar/Academic/Summer) per budget period.

Year (YYYY)	Person Months (##.##)
1. 2021	0.12 calendar
2. 2022	0.12 calendar
3. 2023	0.12 calendar
4. 2024	0.12 calendar
5. 2025	0.12 calendar

*Title: Maternal Determinant of Infant Immunity
Major Goals: The Alter lab will perform and evolve the systems serology platform to dissect the impact of pregnancy, placental transfer, and early life on shaping antibody profiles.
*Status of Support: Active (NEW)
Project Number: 1U19AI145825-01A1
Name of PD/PI: Alter, Galit
*Source of Support: University of Maryland
*Primary Place of Performance: MGH
Project/Proposal Start and End Date: 07/12/2021 - 02/28/2026
* Total Award Amount (including Indirect Costs): $3,188,570
* Person Months per budget period.

Year (YYYY)	Person Months (##.##)
1. 2021	0.48 calendar
2. 2022	0.48 calendar
3. 2023	0.48 calendar
4. 2024	0.48 calendar
5. 2025	0.48 calendar

COMPLETED

*Title: Development of a novel class of broadly functional antibodies (bFAbs) that can kill the viral reservoir within lymphoid sanctuaries
Major Goals: The overall goal of this project is to develop an innovative monoclonal therapeutic strategy to cure HIV
*Status of Support: Completed
Project Number: Unassigned
Name of PD/PI: Alter, G.
*Source of Support: Gilead Sciences, Inc.
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 11/15/2016 – 12/31/2021

*Title: IgG Fc Assessment Services/Fc Ab Core
Major Goals: This project aims to establish and develop high-throughput, standardized assays to profile vaccine-induced antibody responses
*Status of Support: Completed
Project Number: OPP1146996
Name of PD/PI: Alter, Galit
*Source of Support: Bill and Melinda Gates Foundation
*Primary Place of Performance: MGH
Project/Proposal Start and End Date: 07/01/2016 - 12/31/2021

*Title: Ab mediated innate immune mechanisms
Major Goals: This project aims to define the independent or synergistic function of C-term-specific antibodies.
*Status of Support: Completed
Project Number: Unassigned
Name of PD/PI: Alter, G.
*Source of Support: PATH
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 06/01/2020-10/31/2021

*Title: Differential Humoral Immune response in Children and Adults with COVID-19
Major Goals: The goal of this project is to define the concentration and type of antibody responses to coronaviruses in pediatric and adult sera
*Status of Support: Completed
Project Number: 280870.5116745.001
Name of PD/PI: Alter, G.
*Source of Support: Boston Children's Hospital
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 08/01/2020-10/31/2021

*Title: Vaccine Enterprise Comprehensive Antibody Vaccine Immune Monitoring Consortium
Major Goals: This project aims to establish and develop high-throughput, standardized assays to profile vaccine-induced antibody responses
*Status of Support: Completed
Project Number: OPP1146996
Name of PD/PI: Montefiori, D.
*Source of Support: Bill and Melinda Gates Foundation
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 07/01/2016 – 06/30/2021

*Title: Defining Humoral Correlates of Mycobacterial Immunity in TB Resistors
Major Goals: The goal of this project is to identify unique humoral immune responses in individuals who resist TB infection that may contribute to protection from infection or progression of disease in an effort to guide future vaccine design.
*Status of Support: Completed
Project Number: OPP 1151840
Name of PD/PI: Alter, G.
*Source of Support: Bill and Melinda Gates Foundation
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 11/30/2016-06/30/2021

*Title: Integration of Systems Serology with OMICs analysis to generate models of vaccine response in endemic areas of parasitic infection.
Major Goals: The goal of this proposal is to comprehensively analyze analysis of the functionality of HepB antibody responses in helminth-infected subjects to determine the impact of Schistosoma infection on the qualitative features of the humoral immune response.
*Status of Support: Completed
Project Number: 5U19AI128910-02
Name of PD/PI: Haddad, E.
*Source of Support: NI0
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 06/01/2020 - 05/31/2021

*Title: Herpesviral Recombinant Vectors for Vaccine Vectors and Study of Coronaviral Pathogenesis
Major Goals: The antibody signatures will be used to develop an antibody based diagnosis based on Tb-specific antibody glycan modifications.
*Status of Support: Completed
Project Number: 280870.5117101.0032
Name of PD/PI: Knipe, D.
*Source of Support: Massachusetts Consortium on Pathogen Readiness
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 05/01/20 – 04/30/21

*Title: Systems Serology and Antibody Effector Function
Major Goals: The goal of this study is to develop assays to evaluate induction antibody-mediated effector functions from NK cells, monocytes, and neutrophils against antigenic targets from Lassa virus.1
*Status of Support: Completed
Project Number: A08529
Name of PD/PI: Gupta, S.
*Source of Support: International AIDS Vaccine Initiative (IAVI)
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 06/24/2020 - 12/31/2020

*Title: An unbiased OMICs approach to identify mechanisms of Cocaine regulation of the HIV reservoir
Major Goals:
*Status of Support: Completed
Project Number: 5R01DA043263-05
Name of PD/PI: Sekaly, R.
*Source of Support: Case Western Reserve University
*Primary Place of Performance: MGH
Project/Proposal Start and End Date: 09/15/2016 - 09/30/2020

*Title: Resetting immune homeostasis: a non-invasive approach towards HIV eradication
Major Goals:
*Status of Support: Completed
Project Number: 5U01Al131295-03
Name of PD/PI: Sekaly, R.
*Source of Support: Case Western Reserve University
*Primary Place of Performance: MGH
Project/Proposal Start and End Date: 08/09/2017 - 09/30/2020

*Title: Protective role of monoclonal antibodies in the control of MTB infection
Major Goals: The goal of this project is to identify the potential causal role of antibodies in MTB control in vivo in an effort to guide future vaccine design.
*Status of Support: Completed
Project Number: OPP 1156795
Name of PD/PI: Alter, G.
*Source of Support: Bill and Melinda Gates Foundation
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 11/30/2016-06/30/2021
* Total Award Amount (including Indirect Costs): $982,576
* Person Months per budget period.

Year (YYYY)	Person Months (##.##)
5. 2020	0.12 calendar

OVERLAP
None

IN-KIND

*Summary of In-Kind Contribution: Post-doctoral fellow, Nicholas Webb, PhD, who conducts research activities in the Alter lab. Salary support from 5T32AI007386-27 at Dana Farber Cancer Institute
*Status of Support: Active
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 05/01/2021 – 04/31/2023
*Person Months (Calendar/Academic/Summer) per budget period: 12 calendar
*Estimated Dollar Value of In-Kind Information: $119,160

*Summary of In-Kind Contribution: Post-doctoral fellow, Leela Davies, MD, PhD, who conducts research activities in the Alter lab. Salary supported by the Doris Duke Charitable Foundation
*Status of Support: Active
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 07/01/2021 – 06/30/2023
*Person Months (Calendar/Academic/Summer) per budget period: 12 calendar
*Estimated Dollar Value of In-Kind Information: $220,000

*Summary of In-Kind Contribution: Post-doctoral fellow, Jonathan Herman, MD, PhD, who conducts research activities in the Alter lab. Salary supported by the Doris Duke Charitable Foundation
*Status of Support: Active
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 07/01/2021 – 06/30/2023
*Person Months (Calendar/Academic/Summer) per budget period: 12 calendar
*Estimated Dollar Value of In-Kind Information: $220,000

*Summary of In-Kind Contribution: Post-doctoral fellow, Patricia Grace, PhD, who conducts research activities in the Alter lab. Salary and professional development expenses supported by the Harvard Chan Yerby Fellowship Program
*Status of Support: Active
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 07/01/2021 – 06/30/2022
*Person Months (Calendar/Academic/Summer) per budget period: 12 calendar
*Estimated Dollar Value of In-Kind Information: $73,500

*Summary of In-Kind Contribution: Post-doctoral fellow, Mariana Spatola, PhD, who conducts research activities in the Alter lab. Salary and miscellaneous research expenses supported by the Swiss National Funding for Scientific Research
*Status of Support: Active
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 11/01/2020 – 04/30/2022
*Person Months (Calendar/Academic/Summer) per budget period: 9.6 calendar
*Estimated Dollar Value of In-Kind Information: $50,000

*Summary of In-Kind Contribution: Post-doctoral fellow, Biana Bernshtein, PhD, who conducts research activities in the Alter lab. Allowances for living, child, travel, and research supported by the International Human Frontier Science Program
*Status of Support: Pending
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 04/01/2021 – 03/31/2024
*Person Months (Calendar/Academic/Summer) per budget period: 12 calendar
*Estimated Dollar Value of In-Kind Information: $238,632

*Summary of In-Kind Contribution: Post-doctoral fellow, Lisa Bebell, PhD, who conducts research activities in the Alter lab. Salary and miscellaneous research expenses supported by the William F. Milton Fund of Harvard University
*Status of Support: Pending
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 07/01/2021 – 06/30/2022
*Person Months (Calendar/Academic/Summer) per budget period: 12 calendar
*Estimated Dollar Value of In-Kind Information: $50,000

OTHER SUPPORT

Juelg, Boris

ACTIVE

*Title: Immune Correlate + Guided Design of Monoclonal Therapeutics for HIV Remission
*Major Goals: The goal of this project is to define the specific antibody profile that tracks with cellular reservoir control to rationally design a therapeutic strategy able to effectively eliminate the viral reservoir and drive viral remission at a global level.
*Status of Support: Active
Project Number: W81XWH1810579
Name of PD/PI: Alter, Galit
*Source of Support: U.S. Army Medical Research Acquisition Activity
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 09/2018-09/2022
* Total Award Amount (including Indirect Costs): $1,754,195
* Person Months (Calendar/Academic/Summer) per budget period.

Year	Person Months
1. 2022	0.6

*Title: Consortium for Immunotherapeutics against Emerging Viral Threats
*Major Goals: The overall goal is to move promising antiviral monoclonals without delays into early product development.
*Status of Support: Active
Project Number: 5U19AI142790-03
Name of PD/PI: Juelg, Boris D.
*Source of Support: La Jolla Institute for Immunology
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 05/2019-04/2024
* Total Award Amount (including Indirect Costs): $22,268
* Person Months (Calendar/Academic/Summer) per budget period.

Year	Person Months
1. 2022	0.24
2. 2023	0.24
3. 2024	0.24

*Title: Optimizing HIV-specific T-cell responses by therapeutic vaccination
*Major Goals: Proposal examines the potential of a novel vaccine strategy to enhance the body's immune response to better control the virus and destroy HIV infected cells.
*Status of Support: Active
Project Number: 5R01AI138790-03
Name of PD/PI: Juelg, Boris D.
*Source of Support: NIH
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 12/2018-11/2024

* Total Award Amount (including Indirect Costs): $3,367,316

* Person Months (Calendar/Academic/Summer) per budget period.

Year	Person Months
1. 2022	3.84
2. 2023	3.84
3. 2024	3.84

*Title: Harvard University Center for AIDS Research

*Major Goals: The main goal is to provide expansive infrastructure support for HU CFAR investigators conducting clinical and basic science research related to HIV, associated coinfections and HIV prevention.

*Status of Support: Active

Project Number: 5P30AI060354-18

Name of PD/PI: Juelg, Boris D.

*Source of Support: President and Fellows of Harvard College

*Primary Place of Performance: Massachusetts General Hospital

Project/Proposal Start and End Date: 08/2019-07/2024

* Total Award Amount (including Indirect Costs): $1,108,029

* Person Months (Calendar/Academic/Summer) per budget period.

Year	Person Months
1. 2022	0.72
2. 2023	0.72
3. 2024	0.72

*Title: Ad26 Based Therapeutic Vaccines for HIV

*Major Goals: The overall goal is to evaluate therapeutic vaccination in combination with latency reversal agents and broadly neutralizing antibodies for HIV eradication strategies.

*Status of Support: Active

Project Number: 5U01AI145801-02

Name of PD/PI: Juelg, Boris D.

*Source of Support: Beth Israel Deaconess Medical Center

*Primary Place of Performance: Massachusetts General Hospital

Project/Proposal Start and End Date: 05/2020-04/2024

* Total Award Amount (including Indirect Costs): $146,446

* Person Months (Calendar/Academic/Summer) per budget period.

Year	Person Months
1. 2022	3.60
2. 2023	3.60

*Title: Boston Covid-19 Recovery Cohort (BCRC)
*Major Goals: The goal of the study is to rapidly improve understanding of recovery after SARS-CoV-2 infection and to prevent and treat PASC.
*Status of Support: Active
Project Number: OT2HL161847-01
Name of PD/PI: Bassett, Ingrid V.
*Source of Support: Brigham and Women's Hospital, Inc.
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 10/2021-05/2025
* Total Award Amount (including Indirect Costs): $11,187,365
* Person Months (Calendar/Academic/Summer) per budget period.

Year	Person Months
1. 2022	0.60
2. 2023	0.60
3. 2024	0.60

*Title: COVID 19: CTA: Management of patients with COVID-19 in a Large, Academic Medical Center
*Major Goals: The overall goal is to assess the efficacy of Remdesivir outside of a randomized controlled trial setting.
*Status of Support: Active
Project Number:
Name of PD/PI: Hohmann, Elizabeth L
*Source of Support: Gilead Sciences, Inc.
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 07/2021-07/2026
* Total Award Amount (including Indirect Costs): $50,000
* Person Months (Calendar/Academic/Summer) per budget period.

Year	Person Months
1. 2022	0.12

*Title: Combination bFAb and CAR T Cell Control of Persistent HIV
*Major Goals: Propose to develop a combination immunotherapy comprising engineered bFAbs and HIV-specific Dual-CAR T cells to control persistent HIV following cessation of ART.
*Status of Support: Active
Project Number: 110199-70-RGRL
Name of PD/PI: Allen, Todd M
*Source of Support: The Foundation for AIDS Research (AMFAR)
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 07/2021-06/2022
* Total Award Amount (including Indirect Costs): $200,000
* Person Months (Calendar/Academic/Summer) per budget period.

Year	Person Months
1. 2022	0.60

*Title: A randomized, double-blinded, placebo-controlled, dose-ranging phase 1 clinical trial to evaluate the safety and immunogenicity of recombinant HIV Envelope protein BG505 SOSIP.664 with AS01B adjuvant in healthy, HIV-1 uninfected adults
*Major Goals: This study will evaluate the safety and immunogenicity of recombinant HIV Envelope protein BG505 SOSIP.664 with AS01B adjuvant in healthy, HIV-1 uninfected adults
*Status of Support: Active
Project Number:
Name of PD/PI: Juelg, Boris D.
*Source of Support: The Ragon Institute of MGH, MIT, and Harvard
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 12/2018-01/2022
* Total Award Amount (including Indirect Costs): $722,171
* Person Months (Calendar/Academic/Summer) per budget period.

Year	Person Months
1. 2022	1.56

COMPLETED
*Title: Development of a novel class of broadly functional antibodies (bFAbs) that can kill the viral reservoir within lymphoid sanctuaries
*Major Goals: The overall goal of this project is to develop an innovative monoclonal therapeutic strategy to cure HIV.
*Status of Support: Active
Project Number: PA-HIV-16-0061
Name of PD/PI: Alter, Galit
*Source of Support: Gilead Sciences, Inc.
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 11/2016-12/2021
* Total Award Amount (including Indirect Costs): $2,842,222
* Person Months (Calendar/Academic/Summer) per budget period.

Year	Person Months
1. 2018	0.60
2. 2019	0.60
3. 2020	0.60
4. 2021	0.60

*Title: A Phase 1 Study to Evaluate the Safety/Tolerability and Immunogenicity of a Heterologous Ad26 Mosaic Vector Vaccine Regimen in Virologically Suppressed HIV-1 Infected Adults on cART
*Major Goals: This study evaluates the safety/tolerability and immunogenicity of a heterologous Ad26 Mosaic vaccine in HIV-1 infected adults on cART
*Status of Support: Active
Project Number:
Name of PD/PI: Juelg, Boris D.
*Source of Support: The Ragon Institute of MGH, MIT, and Harvard
*Primary Place of Performance: Massachusetts General Hospital

Project/Proposal Start and End Date: 09/2015-12/2021
* Total Award Amount (including Indirect Costs): $751,309
* Person Months (Calendar/Academic/Summer) per budget period.

Year	Person Months
1. 2015	0.12
2. 2016	0.12
3. 2017	0.12
4. 2018	0.12
5. 2019	0.12
6. 2020	0.12
7. 2021	0.12

PENDING
*Title: Autologous chimeric antigen receptor engineered T cell immunotherapy for desensitization in patients awaiting kidney transplantation.
*Major Goals: This project proposes to evaluate the combination therapy with CART-19 and CART-BCMA as a novel desensitization measure in kidney transplant candidates
*Status of Support: Pending
Project Number:
Name of PD/PI: Markmann, James F
*Source of Support: Trustees of the University of Pennsylvania
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 07/2023-06/2028
* Total Award Amount (including Indirect Costs): $1,424,027
* Person Months (Calendar/Academic/Summer) per budget period.

Year	Person Months
1. 2023	0.12
2. 2024	0.12
3. 2025	0.12
4. 2026	0.12
5. 2027	0.00

*Title: Maternal 'Omics to Maximize Immunity: Project 2 – The pregnancy AdaptOME
*Major Goals: The goal of this study is to decode the principles of immune induction in pregnant and lactating women in response to vaccination.
*Status of Support: Pending
Project Number:
Name of PD/PI: Alter, Galit
*Source of Support: Massachusetts Institute of Technology
*Primary Place of Performance: Massachusetts General Hospital
Project/Proposal Start and End Date: 03/2022-02/2027

* Total Award Amount (including Indirect Costs): $3,997,845
* Person Months (Calendar/Academic/Summer) per budget period.

Year	Person Months
1. 2022	0.60
2. 2023	0.60
3. 2024	0.60
4. 2025	0.60
5. 2026	0.60

IN-KIND

None

OVERLAP

None

Location of Organization: (if foreign location list country)
Partner's contribution to the project (identify one or more)

- *Financial support;*
- *In-kind support (e.g., partner makes software, computers, equipment, etc., available to project staff);*
- *Facilities (e.g., project staff use the partner's facilities for project activities);*
- *Collaboration (e.g., partner's staff work with project staff on the project);*
- *Personnel exchanges (e.g., project staff and/or partner's staff use each other's facilities, work at each other's site); and*
- *Other.*

From The Henry Jackson Foundation:
Organization Name: HIV Netherlands Australia Thailand (HIV-NAT)
Location: Bangkok, Thailand
Contribution: In-kind support to provided clinical samples and obtain necessary regulatory approvals.
Organization Name: South East Asia Research Collaboration in HIV (SEARCH)
Location: Bangkok, Thailand
Contribution: In-kind support to provide clinical samples and obtain necessary regulatory approvals.

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: Not applicable

QUAD CHARTS: Not applicable

APPENDICES: