

Grand Challenges **China**

New Interventions for Global Health

Request for Proposals

Scope

Under this new Grand Challenge we seek original, transformative, and innovative concepts for vaccines and therapeutics to ameliorate the acquisition, progression, or transmission of infectious diseases that disproportionately affect the world's poorest citizens. To this end, the Bill & Melinda Gates Foundation (Gates Foundation) and the National Natural Science Foundation of China (NSFC) will support up to six research programs that involve collaborations between investigators in Chinese-based institutions and those in institutions based in other countries. These grants will be for four years and up to US\$1M, with the Gates Foundation funding and managing the non-Chinese portion of the collaborations, and the NSFC funding and managing the Chinese portion of the collaborations.

For more information on the eligibility, scope, timeline, and process of this program, please see the [Frequently Asked Questions](#) document.

Background

Vaccines have been a cornerstone of global health campaigns to prevent, control and eliminate/eradicate infectious diseases. This has been most notably demonstrated in the smallpox eradication campaign, and in the current efforts to eradicate polio. However, many diseases of global importance still lack vaccines that are highly efficacious and safe, and can induce long-term immunity.

In recent years, vaccinology has seen tremendous advances in knowledge and technology for interrogation of the structure of protective antigens, definition of antigen-specific host immune responses at the cellular and molecular levels, and elicitation of protective immune response against desired targets in the relevant tissues. These tools may enable us to develop effective vaccines for diseases lacking such.

Antibiotics and anti-viral therapies have also been central to infectious disease treatment, control programs and elimination campaigns for many diseases. However, treatments for many diseases that affect the world's poorest are often inadequate. There is no treatment for some diseases. Others are expensive, have serious side-effects, or are contraindicated when co-infections exist. Still others have treatment courses that are long or complicated, resulting in non-compliance and therefore the emergence of resistance.

For many diseases, the emergence of resistance can be avoided by the use of combination drug therapy. However, these combinations can be costly, difficult to formulate, and necessitate generation of additional drugs as resistance continues to emerge. This perpetuates the costly and time-consuming cycle of drug discovery, validation, optimization, and production. We need efficient ways of generating and analyzing new chemical diversity. We need new ways to create drugs that are less likely to be made

ineffective by pathogen evolution, which would enhance the useful lifespan of anti-microbial agents, and reduce the frequency of treatment failures. Finally, we need sensitive but reliable assays to determine drug efficacy in target pathogens or host targets, all in the proper context.

Target Diseases and Pathogens

This RFP is focused on identifying new interventions in a small set of diseases of relevance to global health, considering strategic alignment with other funders and current investments within the NSFC and the Gates Foundation. Consequently, only proposals addressing these specific indications will be considered.

Vaccines

What we are looking for

The goal of this challenge is to solicit novel concepts and candidates for vaccines that can serve as transformative tools in the efforts to prevent, control or eliminate diseases of our interest. We are particularly interested in approaches to induce unnatural immunity to pathogens to achieve long-lasting immunity across multiple strains, species and/or sub-species, utilizing recent advances made in structural biology, bioinformatics and molecular immunology. Our ultimate goal is to enable a path to move the best vaccine concepts and candidates into clinical development. The scope of vaccine concepts could include ideas specific to the subset of global health pathogens described below, or broad, paradigm-shifting concepts in vaccinology, should they also have potential applicability to those specific pathogens.

Target pathogens:

- *Human immunodeficiency virus* – only approaches that aimed at providing sustained protection will be considered
- *Mycobacterium tuberculosis*

A few of the many options to be considered include:

- Applications of new knowledge of structure-based immunogen design.
- New approaches to target common antigenic components shared by multiple strains that may evolve over time and/or multiple species or sub-species
- Novel vaccine concepts that can prevent infection, and block transmission
- Novel vaccine concepts, targets and constructs inspired by new understanding about the mechanism by which a targeted organism induces protective immunity by the human host
- New vaccine concepts that target specific tissue or cell types for appropriate induction of local and systemic immunity
- Novel vaccines designed specifically for populations with high disease burden or risk of infection
- New experimental systems or models for rapidly testing vaccines and predicting their efficacy

We will not consider funding for:

- Projects not relevant to the diseases listed above
- Identification of antigens without preliminary proof or hypothesis that developing such antigens radically improves protective efficacy
- Projects targeting molecular pathways targeted by currently available antigens or adjuvants currently in clinical development



- Vaccine concepts not based on an explicit hypothesis or rationale for improved performance over those candidates currently in development
- Approaches that represent incremental improvements to conventional solutions
- Basic studies of pathogen or human biology without a clear component that tests the potential for translation into specific and practical health solutions

Therapeutics:

What we are looking for:

With this topic we also seek to explore new therapeutic options to treat infectious diseases and other conditions that disproportionately burden those living in low-resource settings. We are particularly interested in approaches that would target specific pathogen populations that are either bottlenecks in the pathogen's life-cycle or that are significant contributors to disease or transmission, but may be difficult to treat with current agents. Areas of focus include: exploiting novel sources of chemical diversity not typically found in conventional small molecule libraries, including novel chemical approaches to the manipulation and optimization of complex molecules and natural products; development and prosecution of screening approaches that target pathogens in a realistic environment; and taking advantage of recent scientific and technical advances for target identification, validation, and deconvolution.

Target Diseases:

- Tuberculosis
 - New agents or approaches with the potential for shortening treatment duration
- Malaria
 - *Plasmodium falciparum* and *Plasmodium vivax*
 - Liver-stage and gametocyte-active agents, and multi-stage active compounds
- Diarrheal Disease in infants caused by:
 - *Cryptosporidium hominis*
 - *Cryptosporidium parvum*

A few of the many possible options to be considered include (non-exclusive):

- Development of assays which allow high-throughput screening of pathogenic organisms under conditions that reflect their natural in vivo environment
- Approaches to target typically challenging organisms – e.g. intracellular or non-replicating *M. tuberculosis*, malaria parasite hypnozoites or gametocytes
- Development of broad and generalizable methods for the optimization of active natural compounds and other complex molecules

We will not consider funding for:

- Proposals not directed at one of the pathogens/diseases included in the priority list above.
- Screening of natural product extracts or other unrefined sources of chemical matter
- Identification and prosecution of new drug targets without a clear rationale for how drugs against such targets would fill a gap in our current therapeutic armamentarium
- Basic research into pathogen biology without a compelling rationale for how such research can be rapidly translated into a new therapeutic discovery approach



- Community-based interventions aimed at improving adherence to drug treatment regimens;
- Development of broad-spectrum antibiotic or antiviral compounds.

Grand Challenges

Definition

Grand Challenges is a family of initiatives fostering innovation to solve key problems in global health and development for those most in need. It seeks to establish a portfolio of projects with complementary approaches that encompass multiple types of innovation, including innovation in biological research, medical health technology and product development, service delivery, and behavior change. Grand Challenges initiatives therefore seek to:

- Engage diverse investigators, including those outside of the areas that might traditionally be associated with the initiative
- Encourage partnerships that bring together investigators from diverse organizations, including for-profit institutions, non-governmental organizations, academic and health research institutions, foundations, and civil society groups

History

Today, a variety of funding partners use “Grand Challenges” to accelerate research, creating an expanding network of funding and research partnerships spanning diverse topics. Below are some key examples highlighting how the Grand Challenges family has grown over time:

- In 2003, the Bill & Melinda Gates Foundation launched [Grand Challenges in Global Health](#), a US\$450 million research initiative that came to include multiple funding partners and, in 2007, it launched [Grand Challenges Explorations](#) (GCE), an accelerated program providing small, initial grants for exploratory research
- In 2010, the Canadian government funded [Grand Challenges Canada](#) to support global health researchers in low- and middle-income countries and in Canada through multiple grant programs.
- In 2011, USAID launched [Grand Challenges for Development](#), an initiative that brought the Grand Challenges approach to diverse new areas, including agriculture and child reading, through multiple grant programs
- In 2012, the Gates Foundation and the Brazilian government established [Grand Challenges Brazil](#), a partnership to fund researchers in Brazil through GCE and, to date, the grant program [Reducing the Burden of Preterm Birth](#).
- In 2013, the Gates Foundation and the Indian government launched [Grand Challenges India](#), a partnership to fund researchers in India through GCE and, to date, the grant programs [Achieving Healthy Growth through Agriculture and Nutrition](#) and [Reinvent the Toilet Challenge – India](#)
- In 2015, the [African Academy of Sciences](#) and the [New Partnership for African Development](#) launched [Grand Challenges Africa](#). Grand Challenges Africa will build on the global success of Grand Challenges programs in India, Brazil and South Africa, as well as the strong base of Africa Grand Challenges grantees funded by the Bill & Melinda Gates Foundation, Grand Challenges Canada and USAID.
- In 2015, the Gates Foundation and the [National Natural Science Foundation of China](#) launched Grand Challenges China, a partnership to fund infectious disease collaborations between Chinese and non-Chinese researchers