

# Strengthening Research Environments and Capacity: NCI's Global Training for Research and Equity in Cancer (GlobTREC) program

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# Conflicts

Nothing to Disclose



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## Goals

Primary focus on LMICs  
for CGH-led programs

### Research

Support innovative, impactful research that (a) addresses key scientific issues in global cancer control and/or (b) leverages unique or unusual scientific opportunities afforded by collaboration with global partners.

### Research training

Support cancer research training that enables equitable, impactful scientific collaboration with global partners.

### Dissemination

Promote the integration of current scientific knowledge into global cancer control policies and practice.

### Partnerships

Represent the NCI and promote its engagement with key partners in global cancer research and control.

## Strategic Priorities

### Improve Global Cancer Research Skills

SP1. Increase participation of LMIC investigators in existing NCI-supported cancer research curricula.

SP2. Identify key curricular gaps for aspiring global cancer investigators and address these gaps in collaboration with intramural and extramural partners, ideally through virtual learning platforms to increase access by diverse learners worldwide.

### Support Global Cancer Investigators

SP3. Increase NCI career development awards to young investigators working in LMIC settings.

SP4. Continue strategic co-funding to FIC research training awards that complement NCI-administered research training awards.

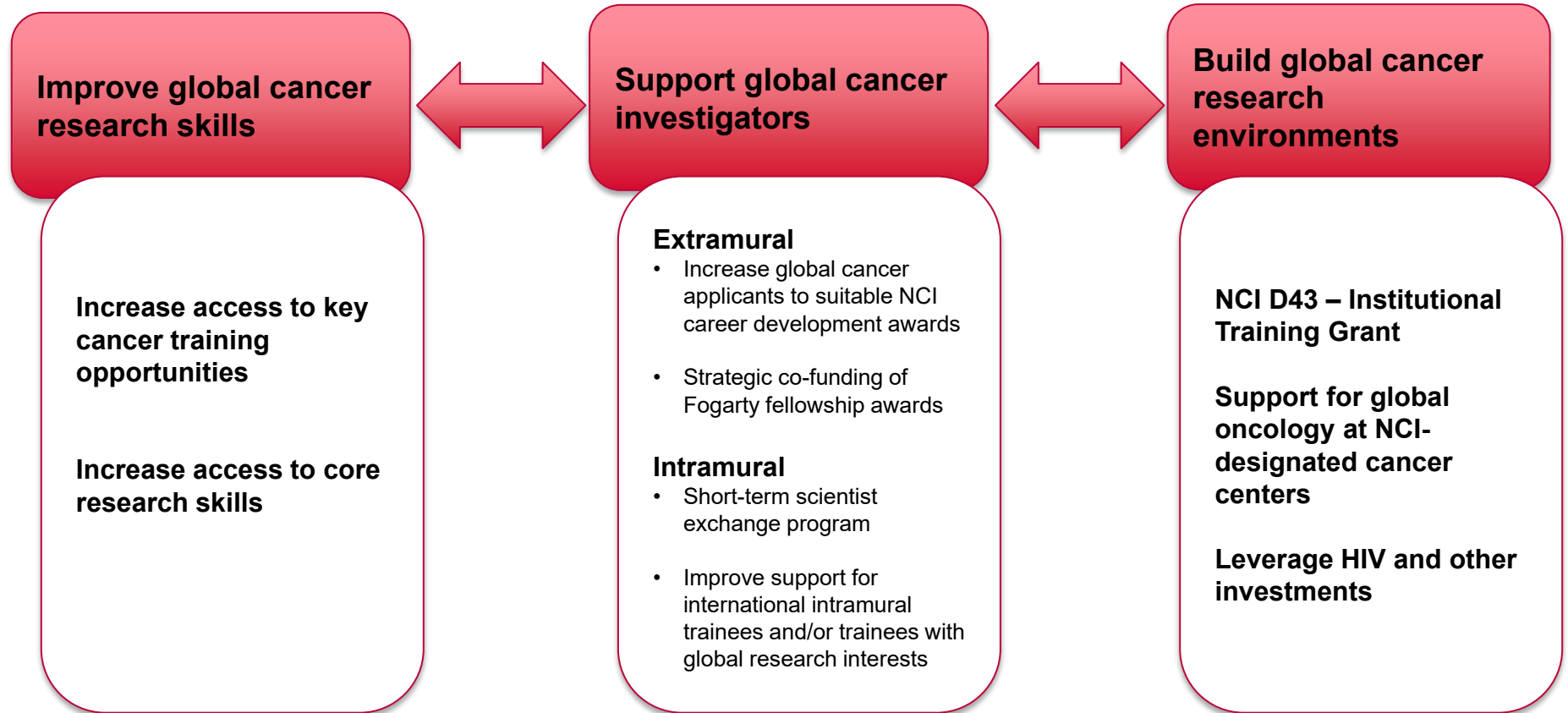
### Build Global Cancer Research Environments

SP5. Support institutional capacity for global cancer research training, particularly at NCI-designated cancer centers and their LMIC institutional partners.

SP6. Serve as a resource for NCI intramural trainees from foreign countries and those with global cancer research interests.

SP7. Work with other funders to increase non-NIH support for early career global cancer researchers.

# Toward a more comprehensive global cancer research training strategy



# Building Global Cancer Research Environments (NCI CGH, CCT, OCC)

## Institutional Training Grant – Global Training for Research and Equity in Cancer (GlobTREC)

<https://grants.nih.gov/grants/guide/rfa-files/RFA-CA-20-031.html>

- Build on collaborations in global research and training- Uses NIH D43 funding mechanism
- Support pre- and post-doctoral training of US and LMIC scientists
  - Degree/Certificate; mentored research experience; mentored research
- Facilitate research leadership/mentorship at US and LMIC institutions
- LMIC trainees: pre and postdoc level; US trainees: postdoc only
- Provide durable funding (5 years) to allow multi-disciplinary training programs to address cancer research priorities in LMICs
  - 250K/yr in Direct Costs – Tuition, Stipend, Mentored research projects, Mentor effort, Travel

## Selection of the D43 Mechanism

- Institutional training: 5-year program that allows multi-disciplinary training
- Unlike National Research Service Award (NRSA) training mechanisms, support of foreign scientists allowed
- Funding mechanism with a track record of success at NCI, Fogarty (AIDS training; NCD research training)

### Attributes of a D43 grant

- **Identifies** training needs to advance specific aims within US-LMIC collaboration
- **Develops** a program/plan of activities to support identified needs
- **Facilitates** trainee development and institutional capacity building
- **Lays foundation** for future collaborative research and career independence

# Collaborations on GlobTREC Projects



 Round 1 (2021-2026)

 Round 2 (2022-2027)

# Highlights of the GlobTREC Program

- Research Training in key areas of cancer research relevant to LMICs.
  - Cancer Genomics. Bioinformatics, Epidemiology, Clinical Trials, Oncology Nursing, Implementation Science
  - 9 doctoral and 11 master's candidates enrolled; Mentored research
  - 35 postdoctoral scientists, which includes 24 clinician scientists
  - Workshop and curricula
- LMIC-based research training.
- Leveraging regional research networks.
- Initial success of early career scientists.
- Leveraging resources to strengthen institutional capacity.
- Leveraging international workshops and symposia to expand GlobTREC learning
  - ASGCR; AORTIC; CReDO workshop in India



# Highlights of the GlobTREC Program

## **Preliminary feedback from trainees**

- Mentorship
- Institutional capacity building
- Addressing locally relevant questions

## **Establishment of a Community of Practice**

- Virtual Online Community
- Peer-led and developed
- Meetings every other month
- Basecamp as a platform for resource sharing and communication

## **Early challenges**

- Delays in initiation of training due to COVID-19, visa delays
- Eligibility criteria is limited to US-based institutions with LMIC partners
- Limited geographic variation among awardees (7 in Africa, 1 in Latin America)
- Low success rate (11/52 unique applications funded)

# Summary of NIH global research training programs

NIH IC	Grant Mechanism and Program Name	# of Awards
<b>Institutional research training awards</b>		
NCI	D43 <a href="#">NCI's Global Training for Research and Equity (GlobTREC)</a>	8
NCI	R25 <a href="#">Cancer Research Education Grants Program – Research Experiences</a>	64 (6 with proposed training in LMICs)
FIC	D43 <a href="#">Launching Future Leaders in Global Health Research Training Program (LAUNCH)</a>	7 (0 specific to cancer)
FIC	D43 <a href="#">Chronic, Noncommunicable Disease and Disorders Research Training (NCD-Lifespan)</a>	56 ( <a href="#">3 specific to cancer</a> )
FIC	D43 <a href="#">Fogarty HIV Research Training Program for Low- and Middle-Income Country Institutions</a>	97 ( <a href="#">3 specific to cancer</a> )
FIC	D43 <a href="#">HIV-associated Noncommunicable Diseases Research at LMIC institutions</a>	26 ( <a href="#">4 specific to cancer</a> )
FIC	D43 <a href="#">Global Infectious Diseases Research Training Program</a>	45 ( <a href="#">1 specific to cancer</a> )
FIC	R25 <a href="#">International Research Ethics Education and Curriculum Development Award</a>	34 (0 specific to cancer)

# Supporting Global Cancer Research Investigators

## Collaborating with NIH global research training programs

NIH IC	Grant Mechanism and Program Name	# of Awards
<b>Individual research training awards</b>		
FIC	K01 <a href="#">International Research Scientist Development Award (IRSDA) for US Scientists</a>	45 ( <a href="#">7 specific to cancer</a> )
All	K08 <a href="#">Mentored Clinical Scientists Research Career Development Award</a>	15 to scientists in LMICs ( <a href="#">9 specific to cancer</a> )
FIC	K43 <a href="#">Emerging Global Leader Award for LMIC Scientists</a>	89 ( <a href="#">11 specific to cancer</a> )

# Supporting Global Cancer Research Investigators

## Fogarty's International Research Scholar Development Award -K01 ( Rect. Dates: March 2022, 2023)

<https://www.fic.nih.gov/Programs/Pages/research-scientists.aspx>

K01TW010271	Metabolic Syndrome and Epigenetic Markers of Breast Cancer in Nigerian Women (PI: Akinyemiju)
K01TW011191	Understanding Methotrexate Dosing, Pharmacokinetics, and Toxicities for Burkitt Lymphoma in Malawi (PI: Westmoreland)
K01TW011481	Fidelity and adaptation of breast cancer resource-stratified treatment guidelines in Botswana (PI: Martei)
K01TW012174	Adaptation and Pilot of a Peer-Facilitated Self-Help Plus Stress Management Intervention for Breast Cancer Patients in Viet Nam (PI: Le)

## Fogarty International Center - Emerging Global Leader Award – K43 (Rect Dates: Nov 2021, 2022, 2023)

<https://www.fic.nih.gov/Programs/Pages/emerging-global-leader.aspx>

K43TW011095	Biomarkers of Kaposi sarcoma recrudescence in Zambia (PI: Ngalamika)
K43 TW010721	Treatment response and microRNA profiles in triple negative breast cancer patients receiving standard chemotherapy (TARMAC) (PI: Ntekim)
K43TW011387	Novel Prostate Cancer Cell Lines to Address Prostate Cancer Disparity in Black Men (PI: Badal)
K43 TW011961	A clinical prediction rule for identifying South African colorectal cancer patients who will fail to engage in oncology care (PI: Moodley)
K43 TW011942	Early life aflatoxin B1 exposure and epigenetic programming in Nigerian Newborns (PI: Rotimi)

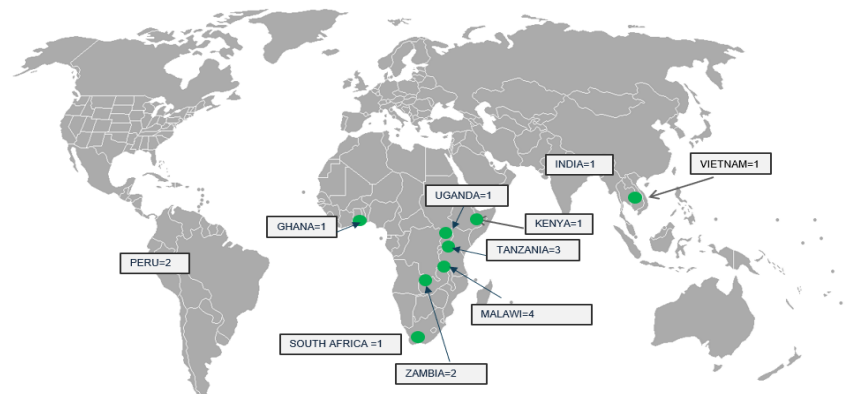
# Supporting Global Cancer Research Investigators

NCI K08 (NCI Center for Cancer Training): NCI Mentor Clinical Scientist Career Development Award - <https://www.cancer.gov/grants-training/training/funding/k08>

<b>K08CA228761</b>	Randomized controlled trial of an implementation science tool to increase cervical cancer screening in Mombasa, Kenya ( PI: McKenna)
<b>K08CA230170</b>	Prognostic value of quantitative HPV viral load in determining cervical cancer treatment response and recurrence (Botswana) (PI: Grover)
<b>K08CA263299</b>	A multi-faceted intervention to promote breast cancer hormone receptor testing in Tanzania (PI: Ng)
<b>K08CA271949</b>	Evaluation of triage strategies and screening intervals in a human papillomavirus based cervical cancer screening program in women living with human immunodeficiency virus in Botswana ( PI: Lockett)

## NCI CGH Mentored Research Supplements – Fogarty’s LAUNCH Fellows and Scholars

Mentored Research Supplements: Fogarty D43; 2018 to 2023 n=17

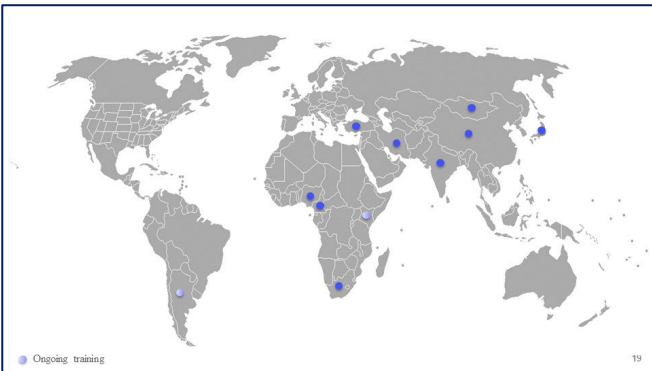


# Supporting Global Cancer Research Investigators

The Short-Term Scientist Exchange Program promotes collaborative research between established NCI investigators and foreign scientists to enhance global cancer research capacity at international institutions.

## Research Experiences at NCI Intramural Divisions

Short-term Scientist Exchange Program: <https://www.cancer.gov/about-nci/organization/cgh/research-training/stsep>



13 candidates, 8 countries  
(2 weeks – 6 months)  
Monthly stipend, no travel

> Mol Cancer Ther. 2021 May;20(5):846-858. doi: 10.1158/1535-7163.MCT-20-0476. Epub 2021 Feb 25.

### Robust Antitumor Activity and Low Cytokine Production by Novel Humanized Anti-CD19 CAR T Cells

Alka Dwivedi<sup>1</sup>, Athava Kanulkar<sup>2</sup>, Sarbani Ghosh<sup>3</sup>, Sriasthya Srinivasan<sup>1</sup>, Bajarang Vasant Kumbhar<sup>2</sup>, Ankesh Kumar Jaiswal<sup>1</sup>, Atish Kizhakeyl<sup>1</sup>, Sweety Asja<sup>1</sup>, Afrin Rafiq<sup>1</sup>, Sushant Kumar<sup>1</sup>, Albeena Nisar<sup>2</sup>, Deepali Pandit Patil<sup>2</sup>, Minal Vivek Poojary<sup>4</sup>, Hasimukh Jain<sup>5</sup>, Shripad D Banavali<sup>2</sup>, Steven L Highfill<sup>2</sup>, David F Stronck<sup>3</sup>, Nirali N Shah<sup>6</sup>, Terry J Fry<sup>7</sup>, Gaurav Nanula<sup>2</sup>, Rahul Purwar<sup>8</sup>

Affiliations \* expand  
PMID: 33632869 DOI: 10.1158/1535-7163.MCT-20-0476

#### Abstract

Recent studies have described the remarkable clinical outcome of anti-CD19 chimeric antigen receptor (CAR) T cells in treating B-cell malignancies. However, over 50% of patients develop life-threatening toxicities associated with cytokine release syndrome which may limit its utilization in low-resource settings. To mitigate the toxicity, we designed a novel humanized anti-CD19 CAR T cells by humanizing the framework region of single-chain variable fragment (scFv) derived from a murine FMC63 mAb and combining it with CD8 $\alpha$  transmembrane domain, 4-1BB costimulatory domain, and CD3 $\zeta$  signaling domain (h1CAR19-888C). Docking studies followed by molecular dynamics simulation revealed that the humanized anti-CD19 scFv (h1CAR19) establishes higher binding affinity and has a flexible molecular structure with CD19 antigen compared with murine scFv (mCAR19). *Ex vivo* studies with CAR T cells generated from healthy donors and patients with relapsed/refractory B-cell acute lymphoblastic leukemia (B-ALL) expressing either h1CAR19 or mCAR19 showed comparable antitumor activity and proliferation. More importantly, h1CAR19-888C T cells produced lower levels of cytokines (IFN $\gamma$ , TNF $\alpha$ ) upon antigen encounter and reduced the induction of IL6 cytokine from monocytes than mCAR19-888C T cells. There was a comparable proliferation of h1CAR19-888C T cells and mCAR19-888C T cells upon repeated antigen encounter. Finally, h1CAR19-888C T cells efficiently eliminated NALM6 tumor cells in a preclinical model. In conclusion, the distinct structural modification in CAR design confers the novel humanized anti-CD19 CAR with a favorable balance of efficacy to toxicity providing a rationale to test this construct in a phase I trial.

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## Training in cancer bioinformatics, genetic epidemiology and molecular diagnosis



University College Hospital  
Ibadan, Nigeria

# Improving Global Cancer Research Skills

## Research Education

- NIH Support of Conferences and Scientific Meeting (R13): <https://grants.nih.gov/grants/guide/pa-files/PA-24-141.html>

5R13CA221315-03	African Cancer Leaders Institute
1R13CA261076-01	5th Annual International Symposium: Improving Breast Cancer Management and Outcomes
1R13CA257481-01A1	Global Health Catalyst (GHC) Summit
1R13CA265019-01	Inaugural Conference on Implementation Science for Cancer Control in Africa

- Collaboration with CReDO workshop led by Tata Memorial in India.
  - Participation of NCI faculty; support of GlobTREC trainees
- Implementation Science: <https://cancercontrol.cancer.gov/is/training-eventshttps://grants.nih.gov/grants/guide/pa-files/PA-21-151.html>

# Please stay in touch!

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