The MR4 Collection in BEI Resources: Placing Tools in the Hands of the Malaria Researcher

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SUPPORTING INFECTIOUS DISEASE RESEARCH

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Standwell C. Nkhoma, PhD; Amel O.A. Ahmed, PhD; Sharmeen Zaman, BS; Angela Robertson, MS; Sujatha Rashid, PhD; Rebecca Bradford, MS, MBA; and Robert E. Molestina, PhD
ATCC, 10801 University Boulevard, Manassas, VA 20110, USA

Abstract: BEI Resources (https://www.beiresources.org), a program supported by the National Institute of Allergy and Infectious Diseases (NIAID) and managed by ATCC, provides NIAID-qualified researchers worldwide with a centralized biorepository for the acquisition, production, characterization, preservation, storage, and distribution of unique, scientifically relevant and quality-assured biomaterials for infectious diseases, including malaria, and standardized protocols. Research materials for inclusion into the program are carefully selected, vetted, and approved by NIAID to ensure that they meet the growing needs of the research community. The collection of the Malaria Research and Reference Reagent Resource Center (MR4) is available through BEI Resources and includes well-characterized reference strains of *Plasmodium falciparum*, rodent malaria parasites, malaria antibodies, live mosquito vectors, mosquito-derived reagents, mosquito cell lines, nucleic acids, and fluorescent reporter parasite lines.

Background

- BEI Resources provides NIAID-qualified researchers worldwide with a central repository for the acquisition, authentication, and distribution of a broad range of unique and quality assured infectious disease research materials that aid in the development and evaluation of therapeutics and diagnostics (Figure 1).
- To access these reagents, researchers should be registered with BEI Resources and can order through the BEI Resources web catalog, www.beiresources.org.
- BEI Resources offers an opportunity for the scientific community to deposit materials. Advantages of depositing material: (i) Promotes access to the material and use of the material; (ii) Relieves researchers of the burdens of distributing materials; (iii) Protects intellectual property of the depositor; (iv) Ensures quality control of the materials; (v) Offers secure storage of materials; and (v) Ensures regulatory compliance in shipping.

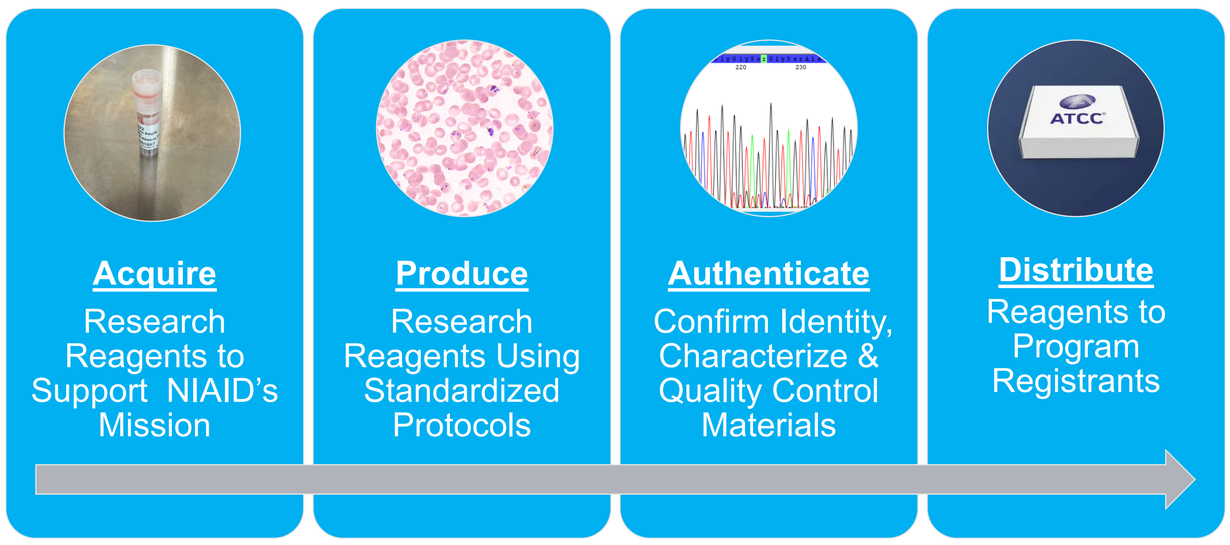

Figure 1: Role of BEI Resources in supporting malaria research. BEI Resources acquires high-value biomaterials from researchers around the world. It then produces adequate quantities of each biomaterial based on the projected scientific demand. Biomaterials are authenticated to confirm their identity and distributed to NIAID-qualified researchers to support malaria research.

Research Reagents Available to the Malaria Scientific Community

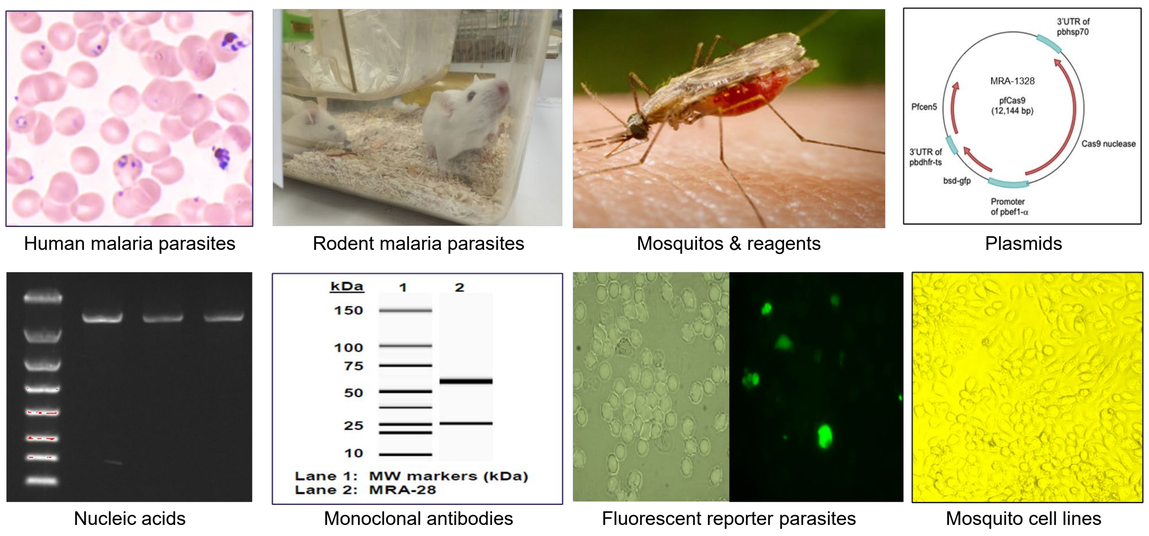

Figure 2: Research materials available to the malaria scientific community. Research biomaterials available through BEI Resources include reference strains of the human malaria parasite, *Plasmodium falciparum*, rodent malaria parasites (*P. berghei*, *chabaudi*, *yoelii*, and *vinckei*), malaria antibodies, live mosquito vectors, mosquito-derived reagents, mosquito cell lines, nucleic acids, and fluorescent reporter parasite lines. Plasmid map for MRA-1328 was adapted from Payungwoung *et al., Parasitology International* 67(5), 605–608.

Malaria Protocols & Training Aids Available to the Scientific Community

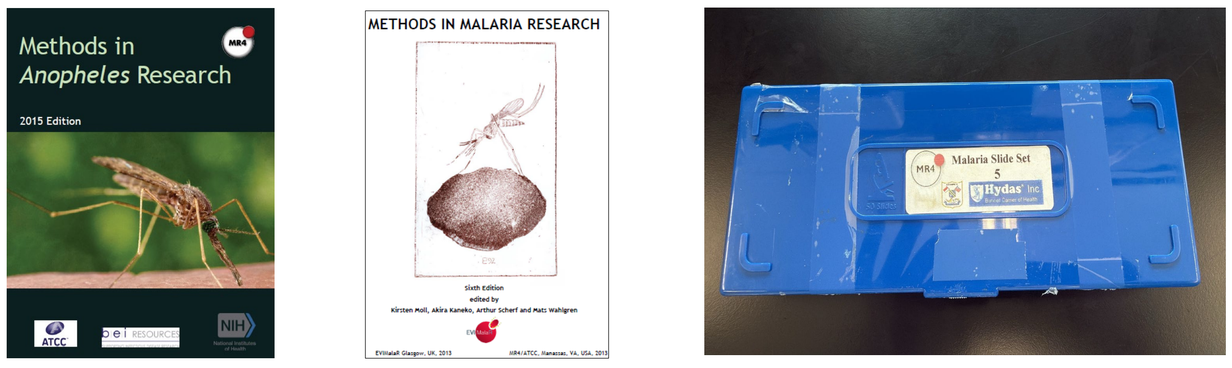

Figure 3: Research protocols and training aids available to the scientific community. BEI Resources provides insectary manuals for mosquitoes containing an array of insectary management and experimental protocols for vector biology (www.beiresources.org/Catalog/VectorResources.aspx). Free protocols for conducting mosquito vector research and malaria parasitology are available in the Methods in *Anopheles* Research and Methods in Malaria Research, respectively. Additionally, for training purposes, reference sets of malaria slides with bench aids are available.

Authentication

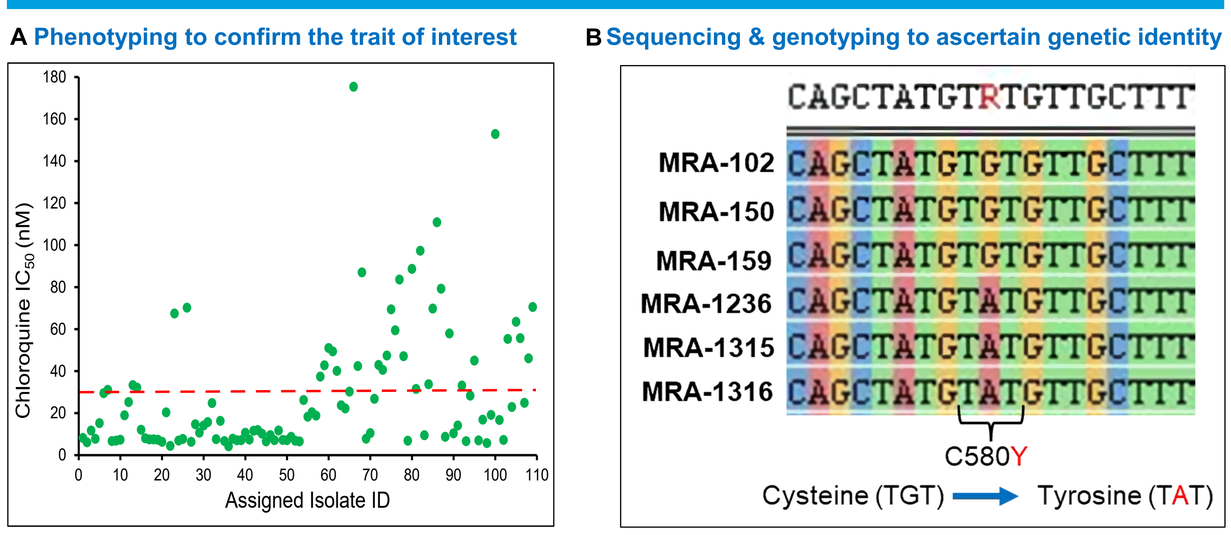

Figure 4: Authentication of BEI Resources malaria strains. (A) A dot plot depicting *in vitro* chloroquine (CQ) susceptibility data of 109 malaria strains. IC_{50} assays measure the drug concentration that inhibits drug-treated parasites by 50% relative to the untreated controls. The red dotted line is a previously established threshold for resistance with parasites above the line deemed resistant and those below CQ-susceptible. (B) Results from sequencing the K13 gene that mediates *P. falciparum* resistance to the antimalarial drug artemisinin. While MRA-102, MRA-150, and MRA-159 bear the wild-type amino acid cysteine, MRA-1236 and its two constituent parasite lineages (MRA-1315 & MRA-1316) bear the resistance-conferring mutant tyrosine at codon 580.

Drug Response Phenotyping Workflow

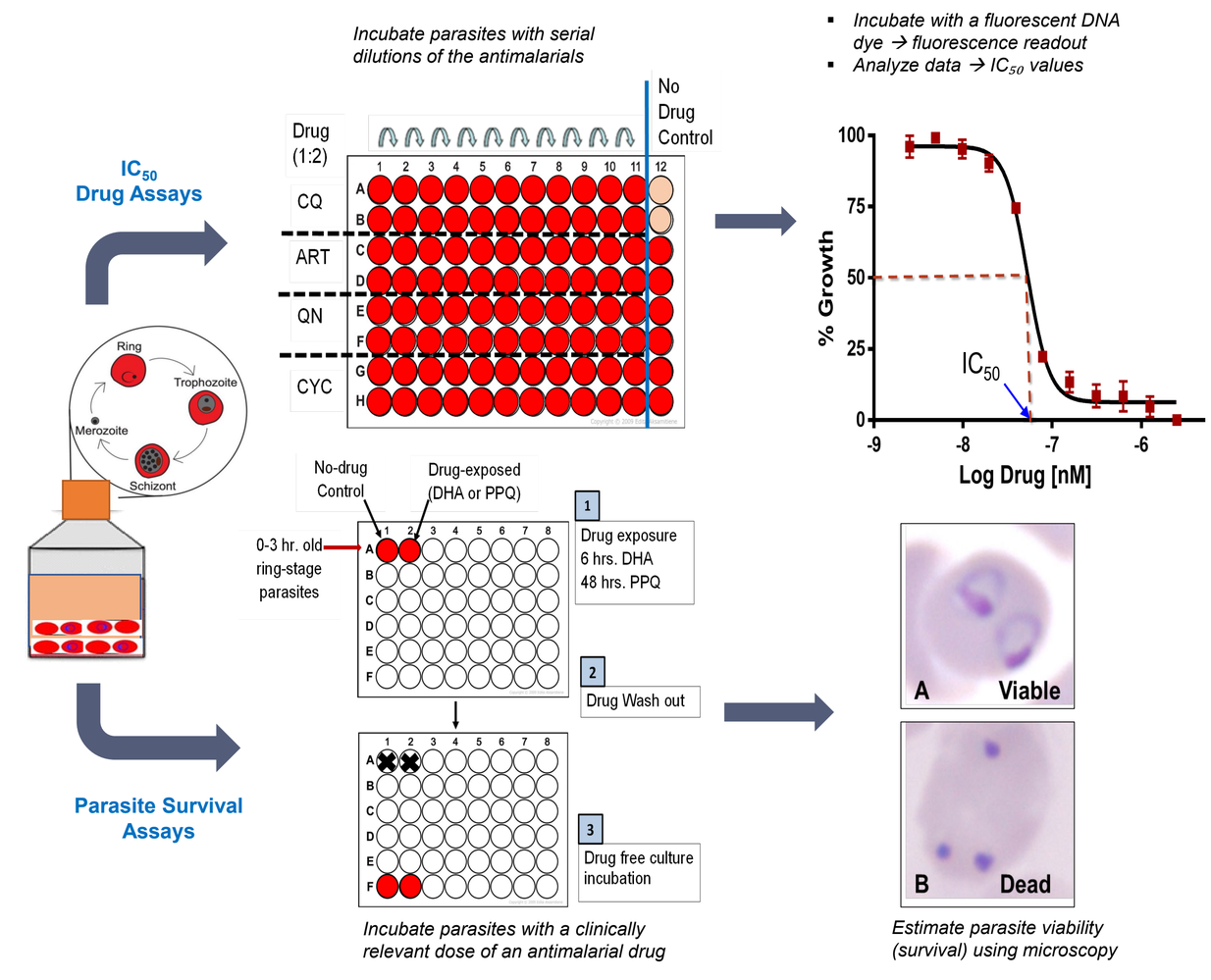

Figure 5: Schematic representation of antimalarial susceptibility tests for BEI Resources malaria strains. The drug susceptibility status of each reference strain is determined using standard IC_{50} assays (top panel) and/or parasite survival assays (bottom panel). Parasite survival assays measure the viability of parasites upon exposure to a pharmacologically relevant drug dose *in vitro*. Susceptibility data are reported on the Certificate of Analysis for each batch produced and show whether the strain is drug-susceptible or resistant.

Quality Control Tests

- **Assessment of parasite viability**: growth recovery and proliferation to >1.5% parasitemia within 96 hours of initiating the culture from a frozen vial.
- **Sterility testing**: Culture purity assessed by screening for microbial contamination using a comprehensive panel of bacterial and fungal media and by molecular screening for mycoplasma contamination using the Universal Mycoplasma Detection Kit (ATCC® 30-1012K™).

Acknowledgments

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ATCC 10801 University Boulevard, Manassas, Virginia 20110-2209 **Phone:** 800.638.6597 **Email:** Contact@BEIResources.org **Web:** www.atcc.org