

## **Growth Inhibition Assay (GIA) Reference Center**

### **The Project: Expand GIA Services**

As part of a comprehensive effort to properly evaluate the potential of new malaria vaccine candidates, the PATH Malaria Vaccine Initiative (MVI) is expanding its support for a range of laboratory tools, including those that employ the growth inhibition assay (GIA) at the US National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health.

Established in 2004 with MVI support, the purpose of the GIA Reference Center has evolved from support for a primarily research assay to support for an assay that is used more widely as a decision-making tool in the assessment of candidate vaccines that target the malaria parasite at its most destructive—when it enters human red blood cells.

The GIA Reference Center measures and assesses the ability of blood-stage vaccines to induce an antibody response—one that inhibits the ability of malaria parasites to infect and replicate in human red blood cells. MVI has used GIA as a potency assay to compare the immunogenicity of various blood-stage vaccine candidates.

### **The Potential: More Reliable Assays to Evaluate New Vaccine Candidates**

Experience shows that properly evaluating the potential of new vaccine candidates requires reliable and sensitive laboratory tools. MVI is therefore eager to direct significant resources toward developing and refining assays. As such, several areas at GIA have been identified for assay improvement, including the treatment of human samples and the development of reference reagents.

*Human samples:* The quality of serum is a major concern. Purification of the immune globulin IgG from serum can eliminate some of the variability introduced by the use of serum. Also, difficulties arise in attempting to purify IgG from small volumes of serum such as that available from children and infants. Proposed activities include identification of quality criteria that serum, plasma, or IgG samples need to meet for use in GIA. MVI also proposes to compare approaches in terms of reliability and capacity to deal with small volumes and to distribute standard operating procedures (SOPs) to participating labs.

*Reference reagents:* Standard reference reagents for controls when measuring human samples are needed. An independent critique on the development of this assay argued that a bank of serum samples should be collected from protected individuals living in endemic areas and that these samples should be tested individually in GIA assays before pooling. This standard reagent could be stored and made available to the malaria community either as whole serum or as purified IgG.

*Parasites:* Experts have pointed to parasite culture conditions and the percentage of infected red blood cells at the start of the assay as important sources of variation that should be agreed

upon by the community. The consensus is to use a selected set of strains and a single source of parasite for each strain.

*Proficiency testing:* A type of proficiency testing that would help to relate results obtained in different laboratories is needed. One suggested approach would be to run a proficiency panel in which different labs would run GIAs using common reagents, standards, and coded samples. MVI proposes to harmonize not only the SOPs of different labs but also the ways in which data are reported and which reagents are used in the assays.

*Parasite detection read out:* A number of different assays are used for detection of parasite-infected red blood cells. While some are capable of detecting live parasites, others appear to detect dead parasites. The choice of a method should allow for some degree of automation and treatment of large numbers of samples. MVI plans to establish criteria for selection of optimal parasite detection.

In addition to these proposed improvements, MVI has initiated a series of discussions with NIAID, the World Health Organization, the US Agency for International Development, the Walter Reed Army Institute of Research, the European Malaria Vaccine Initiative, and others to establish a solid plan for improving the reliability and significance of the center.

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**The PATH Malaria Vaccine Initiative (MVI)** is a global program established at PATH through an initial grant of \$50 million from the Bill & Melinda Gates Foundation. MVI's mission is to accelerate the development of malaria vaccines and ensure their availability and accessibility in the developing world. MVI's vision is a world free from malaria. For more information, please visit [www.malariavaccine.org](http://www.malariavaccine.org). **PATH** is an international, nonprofit organization that creates sustainable, culturally relevant solutions that enable communities worldwide to break longstanding cycles of poor health. By collaborating with diverse public- and private-sector partners, PATH helps provide appropriate health technologies and vital strategies that change the way people think and act. PATH's work improves global health and well-being. For more information, please visit [www.path.org](http://www.path.org).