



GHDx Course 4 Fellowship Projects

Opportunities for Fully Funded Fellowships in Laboratory Point-of-Care Diagnostics for Global Health

As an international participant in our POC Training Course 1 in 2008 or 2009, we invite you to apply for a 9-month fully funded fellowship in POC diagnostics for global health. We have listed several projects below from mentors who would like to participate in these projects. However, you also have the opportunity to propose your own project if you have identified someone in Seattle who has agreed to be your mentor. Unless otherwise indicated, all projects include a 6-month fully funded fellowship in the mentor's laboratory followed by a 3-month distanced mentorship in the fellow's home country. If you would like to apply, please send us a completed application form indicating the project of interest to you. General information on these fellowship opportunities and the application form can be found on the course website: <http://www.path.org/dxcenter/training-developers-and-users.php>.

We look forward to seeing our returning GHDx Course 1 participants take part in these exciting projects!

Pat Totten and Karen Stephens

Project 1

Development of Low-Cost Point-of-Care Diagnostics for Global Health

Mentor: Paul Yager, PhD, Professor and Chair, Bioengineering Department, University of Washington, Seattle

Work in the Yager laboratory will be related to the development of extremely low-cost diagnostic technology. Projects concern the development of instrument-free amplified immunoassays, nucleic acid amplification reactions, and the use of cellular phones to capture assay data. The main approach is to reformat complex chemical processes into a paper-based format. Fellows will follow their period of device development in the Yager laboratory with a period of interactive testing of the new technology in their home country, culminating in a joint publication.

Project 2

Development of Diagnostic Tests for *Mycobacterium tuberculosis*

Mentor: Jerry Cangelosi, PhD, Associate Member, Seattle BioMed (formerly SBRI, Seattle Biomedical Research Institute), Seattle

The Cangelosi laboratory at Seattle BioMed has training opportunities for up to two GHDx fellows. All projects are related to research and development of diagnostics for infectious diseases. Fellows will receive 6 months of training in the BSL2 and BLS3 laboratories at Seattle BioMed, followed by at least 3 months of continued, distance mentorship in their home setting. Distance mentorship will utilize internet bridges as well

as travel. Beyond the formal 9-month period, it is hoped that fellowships will lead to extended collaborations aimed at improving POC diagnosis of infectious diseases of global importance.

Seattle BioMed (<http://www.seattlebiomed.org/disease/diagnostics>) is the largest not-for-profit research organization in the United States that focuses exclusively on infectious disease research. Diagnostics research at Seattle BioMed emphasize biomarker discovery but extends to POC diagnostics through partnerships with test developers including PATH. Fellows will be mentored by Dr. Gerard Cangelosi, who has more than 18 years of experience in diagnostics development in the public and private research sectors. His work has resulted in 7 patents, 2 successful product launches, and over 50 publications in relevant areas.

Available projects include (but are not limited to):

1. Sample processing methods for molecular detection of *Mycobacterium tuberculosis* in sputum and other fluids. Building upon preliminary work in the lab, novel POC methods will be evaluated for extracting intact antigens and/or nucleic acids from *Mycobacterium* cells in human fluid samples.
2. Molecular viability testing of bacterial pathogens in samples. This project will expand upon a recently published "ratiometric pre-rRNA analysis" (RPA) method (Cangelosi, et al., *Appl Environ Microbiol* 76:960, 2010). The method was originally developed for water quality testing, and a GHDx fellow will work to transfer it to tuberculosis diagnosis and treatment monitoring.
3. Accelerated molecular probe pipeline. This novel biomarker discovery technology, developed at Seattle BioMed, is the focus of a new 5-year project aimed at identifying improved biomarkers for diagnosis of intestinal amoebiasis (<http://www.seattlebiomed.org/ampp>). A GHDx fellow will apply it to detecting biomarkers of tuberculosis and/or other infectious diseases.

Training will focus on laboratory research techniques and concepts. Fellows will present their work in a group setting at the end of their training period at Seattle BioMed. Moreover, all three projects are designed to "seed" new research efforts intended to culminate in publications, patents, and/or new diagnostic tests.

Project 3

Pre-Analytical Specimen Processing for Molecular Diagnostics

Mentor: Gonzalo Domingo, Research Scientist, PATH, Seattle

Background and intent of mentorship: Among the many challenges for adopting molecular diagnostics in countries with limited resources are the costs and logistics for importation of reagents, disposables, and kits required for this class of tests. In the absence of local or regional kit producers, the price of importation of these kits is prohibitive. As an example, the same DNA extraction kit purchased in the United States for the price of US\$133 costs US\$301 in Kenya. To address the hurdle of costs of sample

processing, PATH is developing technology transfer packages to enhance and enable local and regional entities to produce reagents and kits for molecular diagnostics. The proposed mentorship covers a series of activities towards establishment of local capacities to develop and manufacture a portfolio of nucleic acid extraction kits that are more affordable to the local users. We are looking for applicants involved in diagnostic development with the capability to introduce the production of this class of products in their organizations. We propose to host the diagnostic developer at PATH.

Time frame and list of activities: In the months between July 1, 2010 and December 31, 2010, the candidate would undertake the following activities at PATH:

Assay research and development (in the PATH laboratory)

1. Development of analytical tools (component performance evaluation assays) for the development of the nucleic acid extraction kit (1.5-2 months).
2. Development of QA/QC SOPs for product quality evaluation (1.5-2 months).

Strategies for manufacturing and distribution

1. Harmonization of the markets requirement document (MRD) for the nucleic acid extraction kit addressing introduction and distribution aspects of the project (this involves engagement with the commercialization team) (0.5-1 months).
2. Harmonization of the product requirements document (PRD) addressing manufacturing aspects of the project (this involves engagement with the product manager) (0.5-1 month).

Upon return to the country of origin under this opportunity, the candidate will accomplish the following activities within 3 months

1. Transfer and implementation of performance evaluation assays.
2. Transfer and implementation of QA/QC SOPs.
3. Establishment of product development framework/plan for nucleic acid extraction kits including the development of an MRD and PRD for this class of products owned by the candidate's entity.

Project 4

Evaluate the Cultural and Operational Constraints Affecting the Distribution and Uptake of Rapid Diagnostic Tests in Kenyan Health Facilities

Mentors: Judd Walson, MD, Assistant Professor, Global Health, Medicine, and Pediatrics, University of Washington, Seattle

Background and goals of mentorship: The World Health Organization (WHO) recommends parasite-based diagnosis, with either microscopy or rapid diagnostic testing (RDT), be used for all cases in malaria-endemic regions, with the exception of young children in high transmission areas, or in times of severe malaria outbreaks in resource-poor areas. Despite the WHO recommendation, the standard of care in malaria-endemic areas of sub-Saharan Africa continues to be presumptive treatment based on clinical diagnosis of symptoms due to a lack of diagnostic equipment in most settings (Meya, 2007). To support the Kenyan Ministry of Health, Division of Malaria Control with their interest to explore how RDTs could be used at health facilities to improve treatment

decisions as outlined in the 2009 Malaria Operational Plan, we propose to conduct an evaluation of operational barriers to the use and uptake of RDTs in Kenya.

Specific activities: To evaluate the cultural and operational constraints affecting the distribution and uptake of RDTs in Kenyan health facilities. Specifically we will:

1. Evaluate the RDT market in Kenya and determine which RDTs are currently available for widespread use and what is the sensitivity and specificity of these tests.
2. Evaluate the availability and perceived utility of microscopy and RDTs, among different cadres of health care providers in Kenya.
3. Understand the barriers that health care workers face in withholding antimalarials among those patients with a negative RDT.
4. Investigate the feasibility of private sector drug dispensaries requiring a positive RDT before selling antimalarials.

Time frame: This project will require a 3- month mentorship in Seattle in which the participant would work to define the aims, develop questionnaires, and structure the survey followed by 6-9 months distance mentorship in Kenya to carry out the work.

Project 5

Propose Your Own Project!

This is your opportunity to learn the skills you really need, collaborate with the group that you have always wanted to work with, and receive continued mentoring when you return to your home country. On the application form on the course website (<http://www.path.org/dxcenter/training-developers-and-users.php>), describe the needs and impact of your project in your home country, include an outline of project activities, a proposed timeline, and a proposed mentor. Be sure to contact your mentor to make sure he/she is willing to participate in this project and has space in his/her laboratory.