

- 1 ISO certification crowns FIND's quality management systems
- 1-2 New strides towards a simple molecular test for diagnosis of sleeping sickness
- 2 SBRI and FIND collaborate in selection of diagnostic reagents for trypanosome antigens
- 3 Fighting malaria with improved rapid diagnostic tests
- 4 FIND welcomes Global Health Fellows
- 4 Senator Mary Henry honors FIND with a visit
- 4 Experts gather in Riga for IUATLD's 4th European Congress

## ISO certification crowns FIND's quality management systems



Since its launch in 2003, FIND has strived to put in place standard operating procedures in all areas of its operations as a means for achieving quality performance. On 29 June 2007, the foundation's quality management systems (QMS) were audited by the SWISS TS / TÜV-Süd authority who confirmed that

the organizational procedures implemented throughout FIND were compliant with the International Standardization Organization (ISO) standards.

Following this successful audit, FIND was awarded ISO 13485:2003 for Medical Devices, Quality Management Systems, and Requirements for Regulatory Purposes, and ISO 9001:2000 for Quality Management Systems, and Requirements.

Dr. Giorgio Roscigno, Chief Executive Officer, stated: "This is a very important cornerstone in the history of FIND. We have strived from the

very beginning to establish quality management practices that are identical to those used by for-profit industries. We are particularly proud of this achievement, especially because we have implemented these standards in a non-profit diagnostics organization and have established outstanding quality assurance norms."

The ISO certification is indication that FIND has taken a giant stride in their quality and project management of the design, development and manufacture of in vitro diagnostics, as well as evaluation and demonstration of the devices for roll-out in developing country health systems. ■

## New strides towards a simple molecular test for diagnosis of sleeping sickness

Today experts stress that the parasitologic tests used for diagnosis of human African trypanosomiasis (HAT), or sleeping sickness,

have low sensitivity, and that current serologic tests have inadequate specificity. Possible solutions to address these challenges include

the detection of trypanosomal DNA from a patient's blood, urine or saliva. Using this method would also be a significant improvement



Scientists at both Obihiro (left) and Murdoch (right) Universities who are working with FIND to optimize reagents for HAT LAMP tests

on parasitological examination. Loop-mediated isothermal amplification (LAMP) of DNA also represents a promising new molecular technique that shows high sensitivity and specificity. Target DNA is amplified under isothermal conditions, meaning that the test can be carried out with minimal equipment.

Positive samples are identified visually either through the formation of a white precipitate or through a colour reaction. LAMP can also be used for the simultaneous analysis of large

numbers of samples, and can be performed by staff with minimal experience in molecular biology. This test may also be useful for confirming cure in treatment follow-up.

During the past year, FIND has been working with Murdoch and Obihiro Universities to develop and evaluate HAT diagnostic tests based on the LAMP technology. Sets of primers that are specific to the subgenus *Trypanozoon*, *T.b. rhodesiense* and *T.b. gambiense* have been designed, and tests are being optimized using

DNA from various members of the sub-genus *Trypanozoon*, with great success. The most sensitive and specific primer sets are being validated using samples from HAT patients.

The tests have been reproduced successfully in laboratories in endemic countries, including Tanzania, Uganda and Kenya. This work is giving sufficiently promising results to support adaptation of the LAMP technique for diagnosis of HAT and has increased the prospects for a commercial test being developed in 2008. ■

## FIND and SBRI collaborate in selection of diagnostic reagents for trypanosome antigens

Among the most commonly used tools for the diagnosis of sleeping sickness is a serological test for exposure to the parasite *Trypanosoma brucei gambiense*. A limitation of such tests is their inability to distinguish active infections from past or subclinical exposures. A direct test for parasite proteins in blood samples would offer better specificity for active infection. Unfortunately, past attempts to develop such assays have not been successful, mainly due to inadequate sensitivity. New molecular sensing methods developed in recent years could offer better sensitivity for detection of parasite protein. Many such methods are inexpensive and easy to use at point of care, even in remote locations such as the ones where sleeping sickness occurs. With these innovations, detection of pathogen protein has become a more attractive option for diagnosis of infectious diseases.

However, a critical bottleneck remains: whereas diagnostic platforms are extensively optimized, the same is not always true of the detection reagents that go into them. Binding reagents that specifically recognize target molecules in patient samples constitute

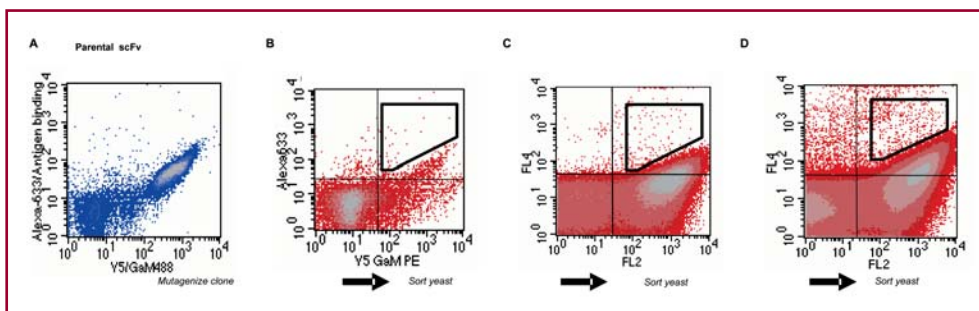
the core of any “state of the art” diagnostic test. When proteins are being detected, the most commonly used probes are antibodies, the proteins produced by mammals that confer pathogen-specific protection against disease. Very often, the sensitivity of a diagnostic test is limited by an inadequate affinity of antibodies for their molecular targets.

### Advantages of antibody probes in cancer imaging and sleeping sickness diagnosis

New methods enable researchers to generate and optimize antibody probes in the laboratory. Ideal probes have high affinity for the target protein with no cross-reactivity, and are stable at working temperature. Engineered antibody fragments, such as single chain variable fragments (scFv), have additional advantages in terms of manufacturing economy. Moreover, because they are much smaller in size than naturally-occurring mammalian antibodies such as IgG, they can penetrate to molecular targets that cannot

be detected by traditional antibody probes. For these reasons, engineered antibody probes have become modern tools in cancer imaging and diagnosis.

FIND is working with the Seattle Biomedical Research Institute (SBRI) to apply scFv antibody engineering technology in the development of optimized antibody probes for trypanosome proteins in blood. Using a technology called yeast display, high-affinity probes for a number of *T. brucei* proteins will be generated, and those which are best suited for diagnostic detection in human samples will be identified. Finally, the sensitivity and stability of the probes for the chosen proteins will be further enhanced by antibody engineering methods. The outcome will be a set of antibody probes with characteristics of sensitivity, stability, and manufacturability that are superior to probes generated by traditional methods. This general approach has potentially broad applications in immunological test development beyond human African trypanosomiasis diagnostics. It will also facilitate the validation of novel biomarkers, a critical bottleneck in biomarker discovery. ■



**Figure: Affinity maturation of scFv antibodies.** Panel A shows a parental clone selected for binding to the recombinant HIV Ag gp140 at 50 nM, and affinity stained with 50 nM biotinylated Ag. Panels B through D show sequential selections conducted on the mutagenic library generated from this clone using Ag at 5 nM. The black box in the upper right quadrant was used as a sort gate, and the sorted cells became the population of each successive selection. Clones in the upper left quadrants were specific Ag-binding clones that stained poorly with the scFv expression stain, anti-c-myc, due to mutagenesis. The same approach is being used by SBRI for HAT.

## Fighting malaria with improved rapid diagnostic tests

**E**arly and accurate diagnosis, coupled with effective treatment is critical to the care and control of malaria. Recently developed rapid diagnostic tests represent an important advance, but must perform reliably to have an impact.

Dr. Mark Perkins, Chief Scientific Officer at FIND, agreed to discuss FIND's role in the fight against malaria.

### What were the main reasons for adding malaria to FIND's portfolio?

FIND seeks to work in areas where diagnostics can have a big impact on the lives of people in developing countries, and where making progress is technically feasible. Malaria is not only a huge global cause of morbidity and mortality, resulting in more than 300 million acute illnesses and at least one million deaths annually, it is also almost synonymous in the minds of many with its most common presenting symptom, fever. Of course, there are many causes of fever, and as many as two-thirds of people with fever treated for malaria have something else wrong with them. Accurate and early diagnosis is critical to malaria control, and to targeting often expensive therapy to the right patients. This is especially relevant with the powerful new artemisinin combination therapy (ACT). Without confirmation of cause, over-diagnosis and mistreatment are common, which wastes resources, fuels drug-resistance, and results in much morbidity from undertreatment of the true cause of illness in many.

FIND has a unique opportunity, in partnership with the World Health Organization (WHO)<sup>1</sup>, and others already active in this area, to provide mechanisms to increase the reliability of malaria rapid diagnostic tests (RDTs), to empower local users to ensure the quality of the products they are using, and improve malaria care and control.

### How is malaria usually diagnosed and how would you describe current testing methods?

Malaria has been classically diagnosed with microscopy. Unfortunately, this technology is

relatively complex and cumbersome to implement, and gives quite variable performance even with highly experienced microscopists. Over the past 15 years, RDTs have been developed that can accurately detect antigens from the malaria parasites in a fingerprick blood sample. These tests are much simpler to use than microscopy and are potentially a hugely important advance supporting disease control. Unfortunately, a number of factors, including poor test stability at high temperatures, sometimes inadequate manufacturing control from the large number of companies making them, geographic variability in target antigens, and improper storage or use of the tests, conspire to diminish the reliability of the tests in practice. This in turn decreases the confidence of both patient and care-giver in the test results, so that they may be disregarded entirely and treatment decisions be made on clinical grounds only.

### Is December 2006 the official date that malaria was incorporated into FIND's activities?

The announcement was made that FIND received approval for the project from the Bill and Melinda Gates Foundation on December 14. Full activity plans and detailed project descriptions were completed shortly thereafter. Additional funds were received towards the end of 2006 from the Dutch Ministry of Foreign Affairs to strengthen and extend the scope of the project.

### What projects are being developed and/or planned? Can you briefly describe some primary goals?

The overall goal of the project is to improve the performance and reliability of tests being used in the field. This will be achieved in a number of ways. First, by developing reference materials that will allow countries procuring tests, and health care workers using them, to determine the quality of purchased tests. Second, by evaluating the performance and stability of all commercialized tests to help guide procurement by the public sector. Third, by developing new reagents that address



*A rapid diagnostic test showing positive result for malaria in a blood sample*

geographic variability in malaria antigens and that show the thermostability needed in tropical climates. Lastly, we will chart a technical and business plan towards the development and distribution of superior assays.

There are currently several projects in the malaria portfolio at FIND. These are 1) a bank of reference materials and laboratory evaluation of existing RDTs; 2) clinical evaluation of high-performance RDTs; 3) development of a reference molecular test for field use (LAMP for malaria); 4) positive control wells; 5) novel and thermostable RDT; and 6) a business and technical plan for improved RDTs. ■

<sup>1</sup> FIND is working closely on their malaria program with WHO, which also contributes staff to the management of the program. Dr. David Bell, working in the Western Pacific Regional Office of WHO, is a key member of the team. FIND expects to complete the team shortly once the Head of the Malaria Diagnostics Program joins the foundation.

## FIND welcomes Global Health Fellows

On 20 June 2007, a delegation of fourteen Global Health Fellows (GHF) from various academic institutions visited the FIND offices to learn more about the work of the foundation through a special presentation delivered by FIND's Senior Policy & Implementation Officer, Dr. Vinand Nantulya.



Dr. Vinand Nantulya addressing students in the GHF program during their visit to FIND

Duke University's Sanford Institute of Public Policy, in partnership with the WHO's Globalization, Trade and Health Program, organizes a series of site visits for its GHF and selected WHO staff. For the Geneva course on

*Health Policy in a Globalizing World*, FIND was invited to present the challenges and aims of the foundation as a public-private partnership, particularly its activities pertaining to the development of new tuberculosis (TB) diagnostics for developing countries.

Speaking on behalf of the students, Joy Rankin, Senior Coordinator of the Duke University Program on Global Policy and Governance, Geneva, said she found the visit to FIND was "insightful, interesting and educational".

Dr. Anthony So, who is Director of the Terry Sanford Institute's Program on Global Health and Technology Access and the Course Director for the Global Health Fellows Program said, "Hearing Dr. Nantulya draw so seamlessly from his field and policy experience in presenting the challenges that FIND is tackling was particularly special for the students." ■

For more information on the Global Health Fellows program, please visit: <http://www.pubpol.duke.edu/graduate/mpp/geneva/documents/GHFBrochure110206.pdf>

## Senator Mary Henry honors FIND with a visit

Following Dr. Vinand Nantulya's testimony given before the Irish Joint Committee on Foreign Affairs in March 2007, Ireland's Senator Mary Henry visited the FIND office on 21 June 2007 to discuss and explore how the government of Ireland could support FIND's work.

In Ireland, Dr Nantulya had the opportunity to further describe FIND's activities and objectives. In addition to discussing the value of diagnostics as the first step in the treatment of neglected diseases, he also explained how the lack of effective and low-cost diagnostics for

combating infectious diseases in the developing world was an impediment to the rational use of drugs and efficient disease control.

Senator Henry, who was accompanied by her husband and FIND's consultant in the UK, Susan Dykes, met with FIND's Chief Executive Officer and Senior Policy & Implementation Officer, Drs. Giorgio Roscigno and Nantulya, respectively.

A meeting to further explore funding opportunities with Irish Aid is scheduled for 6 August 2007. ■

## Experts gather in Riga for IUATLD's 4th European Congress

Some 800 experts and health professionals from Eastern and other parts of Europe attended the 4th Congress of the International Union Against Tuberculosis and Lung Disease, Europe Region, which took part in Riga, Latvia,

from 27-30 June 2007. During the four-day event, FIND was an active participant, holding two symposia and a booth. ■

The full article is available on the FIND website at [http://www.finddiagnostics.org/news/events/iuatld\\_riga\\_conf2007.shtml](http://www.finddiagnostics.org/news/events/iuatld_riga_conf2007.shtml)

## FIND's Team

**Chief Executive Officer:** Giorgio Roscigno

**Project Manager and Regulatory Affairs:** Eric Adam

**Scientific Assistant for Malaria Diagnostics:** Audrey Albertini

**Project Manager:** Sylvain Bieler

**Medical Officer:** Catharina Boehme

**Accounting Manager:** Louisa Chaubert

**Administrative Assistant to CEO:** Diana Choa

**Chief Financial Officer:** Herbert Clemens

**Human Resources Manager:** Jacques Debayle

**Communications Officer:** Beatrice Gordis

**Senior Medical Officer:** Evan Lee

**Logistics Assistant Officer:** Mike Mahiga

**Senior Technology Officer:** Gerd Michel

**Senior Policy and Implementation Officer:** Vinand Nantulya

**Head of HAT Diagnostics Programme:** Joseph Ndung'u

**Head of Product Evaluation and Demonstration:** Richard O'Brien

**Head of TB Laboratory Support:** C.N. Paramasivan

**Chief Scientific Officer:** Mark Perkins

**Human Resources Officer:** Laurence Perret

**Senior Medical Officer, QA & Regulatory Affairs:** Bärbel Porstmann

**Communications and Advocacy Coordinator:** Jewel Thomas

**TB Scientific Team Administrator:** Julie Vercruysse

**HAT Scientific Team Administrator:** Hanna Yirga

### Consultants

**Scientific Officer:** Heidi Albert

**Health Scientist:** Heather Alexander

**Medical Diagnostic Technologies & IP:** Julian Gordon

**Project Management:** Ralf Linke

**Technology and Business Development:** Ranald Sutherland

**Events Coordinator:** Alessandra Varga

*The newsletter is published in English on a quarterly basis.*

**Editor:** Vinand Nantulya

**Editorial assistants:** Jewel Thomas and Beatrice Gordis

**Contributions:** FIND staff and consultants

**Layout:** Latitudesign, Nyon, Switzerland

### FIND

Foundation for Innovative New Diagnostics  
71, av. Louis Casai, PO Box 93  
CH-1216 Cointrin, Geneva, Switzerland  
Tel: +41 (22) 710 05 90  
Fax: +41 (22) 710 05 99

[www.finddiagnostics.org](http://www.finddiagnostics.org)

To receive a free copy of the FIND newsletter, please send an e-mail to: [info@finddiagnostics.org](mailto:info@finddiagnostics.org)

© 2007 Foundation for Innovative New Diagnostics. All rights reserved.