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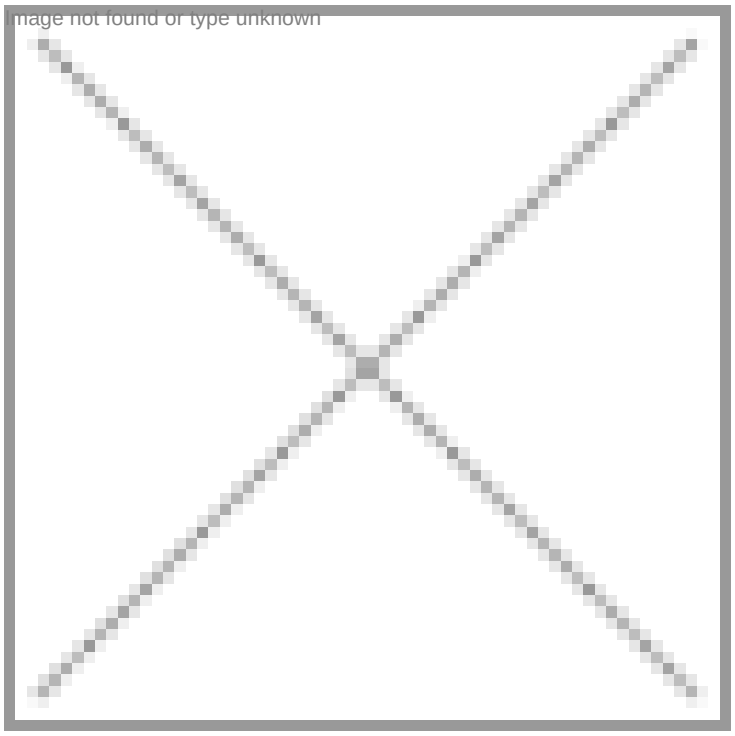

Indigenous rapid filarial diagnostic kit launched in India

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Filariasis conjures up images of elephantiasis in the minds of the patients and the tedious process of midnight blood sampling in the case of doctors. Now both of them will become history with the launch of a rapid, antibody-based diagnostic kit "Signal-MF" aimed at the early detection of filariasis.

Developed by Prof. P Kaliraj, Centre of Biotechnology, Anna University and his team in collaboration with Gujarat-based Span Diagnostics, this kit can be used to test blood samples anytime of the day and can detect the presence of infection in three minutes flat.

In earlier detection methods, for microscopic observation, the blood samples had to be taken at midnight when the microfilaria parasite becomes active, which is not only inconvenient but also laborious and time consuming, thus not practically feasible under field conditions. Another alternative were the imported test kits, but they can detect only Wuchereria bancrofti, one of the filarial parasites causing the disease, besides being expensive.

"The imported kits available in the market today are ELISA based and detect the antigenic protein. This detection methodology is not only expensive in terms of infrastructure required, but it also requires expertise and considerable time

(about 4-5 hours). Hence this is not suitable for mass surveillance in countries like India. Moreover, these kits are not able to detect the infection caused by Brugia malayi, another filarial parasite which is incidentally endemic in parts of India," said Prof P Kaliraj, lead scientist of the study.

Signal-MF is probably the world's first rapid antibody detection kit for simultaneous detection of Wuchereria bancrofti and Brugia malayi. Elaborating about the efficacy of the kit, Prof Kaliraj said, "The US-based Centre for Disease Control has carried out multicentric efficacy tests across five countries in different climatic conditions and the results revealed 90 percent sensitivity and 100 percent specificity."

"This test kit will enable the early detection of the infection even in the case of children (below 10 years of age) which was generally missed out by the other kit in the market currently," he added.

Launching the product on the occasion of the Foundation Day celebrations of the Department of Biotechnology in New Delhi, the Union minister for science and technology and earth sciences, Kapil Sibal said that such products would increase life expectancy and help achieve health for all. The technology transfer from Anna University, Chennai to Surat-based Span Diagnostics was facilitated by the Department of Biotechnology (DBT) for commercialization.

The kit uses the anti-filarial antibody detection method, which is considered to be the most sensitive and accurate way of diagnosis of filariasis. The detection process provides evidence of the ongoing exposure to filarial infection long before the development of microfilaria, where detectable level of antigen is low due to slow growing nature of the disease. Even the WHO policy for global surveillance, monitoring and elimination of the disease recommends the antibody kit for the field application to monitor the exposure to disease in children and travelers.

The diagnostic kit has passed through the stability testing as per European Pharmacopoeia and has also undergone both national and global surveillance studies, therefore recommended for use in India and other countries.

Signal-MF has been developed as a part of the Filarial Genome Project of the World Health Organization, in which the Centre for Biotechnology, Anna University was involved in the process of sequencing the Brugia malayi genome.

As the post genomic approach, Kaliraj's team had identified more than 20 targets of diagnostic and prophylactic importance from the cDNA libraries of Brugia malayi and Wuchereria bancrofti, the filaria causing parasitic worms.

When asked about the challenges encountered during the development of the kit, Prof Kaliraj reminisced, "Filariasis being one of the neglected diseases, there are very few funding agencies which came forward to support the commercialization of the lead developed. We faced this problem after we had completed the sequencing efforts and had identified the candidate molecules. It was then that Span Diagnostics come forward and P Desai, chairman, Span Diagnostics, being a research oriented person, supported us. My earlier research experience in the industry also held me in good stead and the technology business incubator at the Anna University facilitated in taking the lead molecule forward."

Upbeat about the recent commercial launch of the kit, he added, "A positive fallout of the our experience has been that realizing the challenges involved in the "bench to market route". The DBT has sanctioned a Rs 4.2-crore grant to develop a "Productization Platform" at the Anna University. Once developed, its facilities can be availed by any scientist in the country to take their leads forward."

Sharing his views about the pricing of the product, he said, "Currently the price of the kit has been pegged at Rs 40 which can further come down once the demand for the kit picks up."

"Beyond India, the kit has a market in South East Asia and some African countries where the disease is endemic. The initiatives and the required efforts to take the kit beyond India shall be taken by Span Diagnostics in the near future," he said.

Dr Kaliraj's laboratory has also successfully developed a multiple antigen vaccine against the disease. Their filarial vaccine initiative had started about 10 years back and recently the research team has found 80 percent positive results in animal models with their vaccine. The Phase I clinical trials of the vaccine are likely to start soon after procuring the required approvals from the regulatory authorities. This project is being supported by the DBT and the Indian Council of Medical Research (ICMR). Prof Kaliraj is hopeful that if all goes well, in about two years time the vaccine will be in the market.

Currently, human lymphatic filariasis affects more than 1.2 billion of the global population and is endemic in tropical regions of Asia, Africa, Central and South America. Significantly over one third of the endemic population is in India. The most common symptom of lymphatic filariasis is elephantiasis that involves thickening of the skin and underlying tissues. Elephantiasis is caused when the parasites lodge in the lymphatic system and it affects mainly lower extremities of the body.

Rolly Dureha

Molecular scale nanoscissor developed

Researchers in Japan have developed a pair of molecular-scale scissors that open and close in response to light. The tiny scissors are the first example of a molecular machine capable of mechanically manipulating molecules by using light, the scientists say.

The scissors measure just three nanometers in length, small enough to deliver drugs into cells or manipulate genes and other biological molecules, said principal investigator Takuzo Aida,, professor of chemistry and biotechnology at the University of Tokyo.

"Chemists and biochemists may also use the scissors to precisely control the activity of proteins," Aida says. He presented details of the new technique today at the 233rd national meeting of the American Chemical society, the world's largest scientific society.

Scientists have long been looking for ways to develop molecular-scale tools that operate in response to specific stimuli, such as sound or light. Biologists, in particular, are enthusiastic about development of such techniques because it would provide them with a simple way to manipulate genes and other molecules.

"It is known, for example, that near-infrared light can reach deep parts of the body," said Kazushi Kinbara, associate professor of chemistry and biotechnology at the University of Tokyo and co-investigator of the study. "Thus, by using a multi-photon excitation technique, the scissors can be manipulated in the body for medicinal applications such as gene delivery."

The scissors-like molecular machine uses a photo-responsive chemical group that extends or folds when light of different wavelengths falls upon it.

Just like "real" scissors, the molecular scissors consist of a pivot, blades and handles. The pivot part of the scissors is a double-decker structure made of chiral ferrocene, with a spherical iron (II) atom sandwiched between two carbon plates. The three-piece unit creates a shaft that allows the scissors to rotate and swivel.

Driving the motion are two handles strapped with photo-responsive molecules called azobenzene, which not only has the ability to absorb light, but comes in two isomeric forms: a long-form and short-form. Upon exposure to UV light, the long-form of azobenzene is converted into the short-form. Exposure to visible light transforms the short-form into the long-form.

When UV and visible light are used interchangeably, the length of the azobenzene decreases and increases, which drives the handles in an open-close motion. The movement activates the pivot, followed by an opening-closing motion of the blades.

Attached to the scissors' blades are organometallic units called "zinc porphyrin." When the zinc atom in the zinc porphyrin binds with a nitrogen-containing molecule, such as DNA, the zinc and nitrogen act like magnets, securing a firm grip on the molecule.

"As the blades open and close, the guest molecules remain attached to the zinc porphyrin, and as a result, they are twisted back and forth," Kinbara said.

In a recent study, the scientists demonstrated how the light-driven scissors could be used to grasp and twist molecules. The group is now working to develop a larger scissors system that can be manipulated remotely. Practical applications still remain five to 10 years away, the scientists said.

Small molecule to act as cancer therapeutic

A small molecule derived from the spacer domain of the tumor-suppressor gene Rb2/p130 has demonstrated the ability to inhibit tumor growth in vivo and could be developed into an anti-cancer therapeutic, according to researchers at Temple University's Sbarro Institute for Cancer Research and Molecular Medicine.

The researchers reported their findings, "A small molecule based on the pRb2/p130 spacer domain leads to inhibition of cdk2 activity, cell cycle arrest and tumor growth reduction in vivo," in the March 22 issue of the journal Oncogene. Rb2/p130 was discovered in the early 1990s by Antonio Giordano, director of the Sbarro Institute and the Center for Biotechnology in

Temple's College of Science and Technology, who headed the study.

The researchers discovered that within Rb2/p130's spacer domain-a sequence of 212 amino acids located in the pocket or middle section of the gene-was a small portion that resembled an amino-acidic sequence contained in the protein p21, which acts as a cdk (cyclin dependent kinase) inhibitor. Cdks play a critical role in cell cycle regulation.

"What we tested was the ability of the Rb2/p130 spacer region to inhibit the kinase activity of cdk2, which is the same kinase p21 inhibits," said Giordano, one of the study's lead authors. "And to our surprise, it happened." The researchers then set about trying to reduce the spacer domain's 212 amino acids down to the smallest sequence that would still produce the same functionality as p21, explained Giordano.

"We thought we could narrow down the spacer region that contains the protein-like motif to a small portion that could be delivered as a small molecule or peptide," Giordano said.

They discovered a 39 amino-acid-long sequence, which they named Spa310. The molecule that was synthetically produced in the laboratory was introduced into mice that had been injected with tumor cells.

"Tumor growth was inhibited and the tumors began to reduce in size until they disappeared," Giordano said.

Giordano said because of the intrinsic nature of the compound, it can be easily reproduced as a biological drug in large quantities and does not require potentially dangerous means of delivery like viruses, as do most gene therapies; therefore Spa310 has a good chance to succeed as an anti-cancer therapy. For these reasons, he believes it may be easier to get approval for clinical trials.

"Fifteen years after discovering Rb2/p130, our research and hard work has led us to the discovery of this small molecule, which is a step forward in cancer research and a big step toward a cancer treatment," he said.