

Industry and SBE News

Averting an Epidemic — Novel Device Detects Avian Flu Virus in Less than Half an Hour

Avian influenza is now deeply entrenched in Asia, with sporadic human infections resulting from either direct contact with infected birds or limited human-to-human transmission. Globalization and seasonal avian migration patterns have resulted in the disease spreading rapidly to other parts of the world. With an early warning detection system in place, a potential avian flu epidemic can be averted.

Researchers at the Institute of Bioengineering and Nanotechnology (IBN), Institute of Molecular and Cell Biology (IMCB) and Genome Institute of Singapore (GIS) have successfully developed a lab-on-a-chip device that can be used to detect the highly pathogenic avian flu (H5N1) virus. According to project leader and lead author of the *Nature Medicine* (DOI: 10.1038/nm1634) publication, IBN research scientist Dr. Juergen Pippert, "With our device, medical or humanitarian aid workers would be able to detect the presence of the H5N1 virus directly from throat swab samples on-site in less than half an hour."

The device comprises a unique platform developed by IBN that uses magnetic force to manipulate individual droplets containing silica-coated magnetic particles. "The novelty of our method lies in the way that the droplet itself becomes a pump, valve, mixer, solid-phase extractor and real-time thermocycler. Complex biochem-

ical tasks can thus be processed in a fashion similar to that of a traditional biological laboratory on a miniature scale," explained Pippert. The all-in-one droplet-based device is superior to commercially available solutions as it integrates the entire workflow of viral RNA isolation, purification, preconcentration, and detection. Tests have shown that IBN's platform is as sensitive as, and around 10 times faster than available tests, yet it could potentially be 40 to 100 times cheaper. IBN has filed five patent applications on this novel device.

Cell-Free Protein Synthesis Comes of Age

"Can we disassemble a living organism and build a more productive biological system?" This critical question was posed by Dr. James Swartz, the Leland T. Edwards Professor of Engineering in the Dept. of Chemical Engineering and Dept. of Bioengineering at Stanford Univ., at the introduction of his presentation on cell-free protein synthesis (CFPS) at SBE's First International Conference on Accelerating Biopharmaceutical Development held this Spring. Compared with conventional *in vivo* (cellular) expression, CFPS systems offer several advantages, including the potential for higher productivity, parallel production and simplified purification. CFPS can significantly speed up product development time. According to Swartz, it can take from 7–10 months using Chinese hamster ovary (CHO) cells, while with CFPS, it would only take 10 weeks. However, even

Honoring a Bioengineering Pioneer — Dr. George Georgiou to Receive SBE's James E. Bailey Award

Dr. George Georgiou, the Cockrell Family Regents Chair in Engineering and Professor for the Dept. of Chemical Engineering at the University of Texas, Austin, is the recipient of the SBE's prestigious 2007 James E. Bailey Award (endowed by Cytos Biotechnology). The award is given in tribute of Professor Jay Bailey for his many pioneering contributions to biotechnology. It is presented to an individual who has had an important impact on bioengineering and whose achievements, have advanced this profession in any of its aspects.

Georgiou's research has had a profound impact on protein engineering and therapeutics (*CEP*, July 2007, p. 12). In particular, he has increased the fundamental understanding of protein biogenesis. His contributions to biotechnology include the invention of numerous, commercially important methods for



facilitating protein discovery and manufacturing. He is co-inventor of 34 patents, 19 of which have been licensed to pharmaceutical and biotechnology companies.

A member of the National Academy of Engineering, Georgiou has invented technologies for facilitating protein manufacturing (currently being used for the commercial production of several therapeutic proteins), for high throughput screening of biological molecules and for the efficient engineering of therapeutic antibodies. He is also co-inventor of Anthim (Elusys Therapeutics Inc.), the lead therapeutic antibody for protection against inhalation anthrax.

Georgiou will give his award lecture, "Engineering the Next Generation of Therapeutic Proteins," at AIChE's Annual meeting in Salt Lake City, UT, on Nov. 5. Visit www.aiche.org/annual to find out more.

with all of its advantages, CFPS is still often considered a bench-top novelty. Some of the obstacles that need to be overcome include: limitations in protein folding and assembly, particularly those with disulfide bonds; and a lack of scale-up technologies.

But, these issues are quickly being resolved. Advances made at Stanford and Fundamental Applied Biology, Inc. (FAB), of which Swartz is the chair and founder, are helping CFPS to realize its potential to becoming a viable manufacturing platform. FAB has developed a proprietary biosynthetic Cell-Free Protein Synthesis (Cell-Free) that activates protein expression from combined transcription and translation reactions without the need for living cells.

The company was awarded a \$500,000 Small Business Technology Transfer (STTR) Phase II grant from the National Science Foundation to develop a cell-free process to produce insulin-like growth factor I (IGF-1), which contains three disulfide bonds and can not be readily expressed in a soluble form in *E. coli*. Prior Phase I work showed production of IGF-1 in very high yields (*i.e.*, 800 µg/L) by a careful control of the environmental conditions and the catalysts that were used. These results show that not only the cell-free production of IGF-1 is technically feasible, but also that cell-free technology may be an important method for the production of any disulfide-containing protein that is difficult to produce in bacterial systems. The Phase II project focuses on quality control (*i.e.*, product characterization and optimization), reaction scale-up, and cost reduction.

Genetically Engineering Microorganisms into Pharmaceutical Factories

Using microorganisms, such as *E. coli*, to efficiently and inexpensively produce novel pharmaceutical compounds, as well as high-value chemicals, is one step closer to becoming a reality thanks to research being conducted by scientists at the University at Buffalo (UB). "Ultimately, we want to be able to take a designed *E. coli* off of the shelf and drop into it the enzymes that constitute a particular biosynthetic pathway in order to make the product we want," says Mattheos Koffas, assistant professor of chemical and biological engineering in the School of Engineering and Applied Sciences and leader of the UB team.

The UB approach to synthetic chemistry addresses some of the challenges in conventional industrial production of specialty chemicals. "Through the use of specially adapted bacteria, specialized enzymes and natural feedstocks, microbial biosynthesis reduces or eliminates the need for petrochemical sources, elevated temperatures,

Upcoming 2008 SBE Events

1st International Conference on Stem Cell Engineering, Jan. 20–23, 2008, Coronado Island, CA

This conference emphasizes how basic and applied efforts in stem cell biology and engineering can combine to aid in the development of stem cell therapeutics and bioprocesses. Topics will emphasize how quantitative approaches can yield an increased understanding of the biological mechanisms that underlie these stem cell fate choices, technologies to study stem cell function, and the development of bioprocesses to culture stem cells for commercial applications.

4th International Conference on Bioengineering and Nanotechnology, July 22–24, 2008, Dublin, Ireland

Leading international bioengineering and nanotechnology experts will share the latest research advancements at the interface of science, engineering, and medicine.

Conference topics include:

- Drug delivery systems and devices
- Protein and gene delivery systems
- Cell and tissue engineering
- Artificial organs and implants
- Medical and biological devices
- Biocatalysis, organocatalysis and nanobiotechnology
- Nanoparticle sequestration in biomolecules

For more information, go to www.aiche.org/sbe/events.

toxic heavy metal catalysts, extremes of acidity and dangerous solvents," Koffas said. Also, the natural enzymes can facilitate chemical reactions that are difficult to accomplish through conventional chemistry, such as chiral synthesis, glycosylations and targeted hydroxylations.

Koffas' lab recently achieved the functional expression in *E. coli* of P450 monooxygenases, enzymes that are used widely in nature, but are not readily expressed in industrially important microorganisms. "P450 is important in the synthesis of natural products," said Koffas. "For example, both Taxol, the breast cancer drug that is currently produced from plant cultures, and artemisinin, the anti-malaria drug, have P450 enzymes in their biosynthetic pathways." Koffas' lab has introduced ways to modify both the P450 monooxygenase enzymes and the host cell, thereby improving their yield of flavonoids.

In work published in *Applied and Environmental Microbiology* in June, Koffas and his colleagues produced about 400 mg of flavonoids per liter of cell culture, far above the next highest yield of about 20 mg/L produced by other microbial synthesis efforts. "We have done this by increasing the amount of precursor available and re-engineering the native microbial metabolism," he explained, adding that they have taken different approaches to identifying the pathways that lead to the biosynthesis of precursors for desired compounds.