

HepaLife is Recognized by Frost and Sullivan for
Making Flu Vaccines Faster and Cheaper



“Partnering with clients to create innovative growth strategies”

Growing the flu virus in chicken eggs and then killing the virus is the process used to make virtually all of the influenza vaccines. While effective, this process takes some six to nine months to produce enough vaccine for the US market. The spread of avian influenza in Asia and elsewhere has sparked concern that this process may take too long in order to develop new vaccines and adequate quantities needed to deal with outbreaks of the disease. Researchers at the Michigan State University (MSU) Department of Animal Science in East Lansing may have found a way to make flu vaccines faster and at less cost by means of a cell line that may be able to grow human viruses instead of the traditional chicken egg process. HepaLife Technologies Inc. (OTCBB: HPLF), a biotechnology company specializing in cell-based technologies, has licensed the technology from MSU and plans to produce cell culture-based flu vaccine.

Paul Coussens, professor and director of the Center for Animal Functional Genomics, Department of Animal Sciences, at MSU, led a team researching new ways to produce vaccines to inoculate poultry against Marek's disease in a project supported by both USDA and the Michigan Agricultural Experiment Station (MAES). Marek's disease is one of the most common lymphoproliferative diseases of chickens causing huge losses to the poultry industry. "The MAES supports our research through payment of salaries for several key scientists, providing grants to fund disciplinary research and support graduate students," says Dr. Coussens, who noted that his group's initial cell line work was supported both through an MAES graduate student fellowship to Amin Abujoub, who conducted much of the early work, and through a USDA Animal Health Formula Funds Grant. As Dr. Coussens states, "Our laboratory has also been fortunate enough to be continuously supported by the USDA National Research Initiative Competitive Grants Program for almost 20 years. The cell line work that led to the discovery that these cells could grow influenza viruses well was, in part, funded through a USDA Small Business Innovation Research grant, led by Dr. David Reilly."

Adapting to Bioreactors

Dr. Coussens' team was originally searching for a continuous cell line: that is, one that will grow indefinitely in culture to generate low cost production methods and rapid detection systems for viruses of veterinary importance, including Marek's disease virus and Newcastle disease virus of poultry. "Once we succeeded in this, we tried other important viruses, such as avian, swine, equine, and human influenza strains. All of these grew very well in the cell line," explained the scientist, who described several hurdles that must be overcome to adapt the cell line for flu virus production. "The cells must be proven to be free of any exogenous or unwanted viruses, bacteria and fungi, but they have been previously sent out for select agents testing in 2000 and were proven clean, so we anticipate that will not be a concern," said Dr. Coussens. "The cells must then be shown to grow current human influenza vaccine strains efficiently. Finally, we will adapt the cells for growth in bioreactors and in serum-free media. This initial work will be conducted at MSU under a recently signed research contract with HepaLife and will make use of the new biosafety level 3 laboratory at the MSU Diagnostic Center for Population and Animal Health, under the direction of myself and Dr. Steve Bolin, an infectious disease expert."

Tom Herlace of the MSU Intellectual Property Office was initially contacted by Harmel Rayat, CEO of HepaLife, in East Lansing at the beginning of the year. "Once Mr. Rayat discovered the patents were available for licensing, we had a rather lengthy telephone discussion about the potential for growing influenza viruses and other pathogens in the cells. This led to a meeting in early June 2006 and the subsequent licensing agreement," recalled Dr. Coussens. The scientist outlined five ways the process would impact vaccine production:

- 1) **The cost of vaccine production:** The cell line is continuous, meaning that it will grow in culture essentially indefinitely. This is in contrast to current production systems that rely on embryonated chicken eggs where each egg can produce only a few doses of the vaccine. "We are working to adapt the cells to micro-carrier culture in bioreactors, further improving the cost savings in the production of vaccines," said Dr. Coussens.
- 2) **The cost of processing:** Growing vaccine viruses in cell culture, particularly in serum-free media (animal product-free) dramatically reduces downstream processing and purification, further reducing the costs and the necessary time to produce the vaccine.
- 3) **Response time:** Having an efficient cell-culture-based vaccine production system could dramatically reduce the time necessary to produce enough vaccine in the face of a high pathogenicity influenza outbreak.
- 4) **Diagnostics:** Currently, influenza diagnostics (particularly avian influenza) are based on the serial passage of test material through embryonated eggs, which is expensive and time consuming. Having a cell-culture-based method would reduce the detection time and the cost of analysis--critical factors in a large-scale surveillance program. A cell-culture-based system is easier to adapt to BSL-3 conditions and could be married with a polymerase chain reaction-based detection that could help type the virus in a relatively short time.
- 5) **Allergic reactions:** Since the vaccine is not produced in eggs, even those persons who are allergic to eggs and thus cannot receive flu vaccines, could be immunized with a cell-culture produced product. When asked about trends in flu vaccine development, Dr. Coussens replied, "The next generation of flu vaccines will almost certainly utilize reverse genetics to engineer vaccines that are more efficacious and protect against multiple strains of the virus within a single entity. Eventually, most flu vaccines will be produced in cell-culture-based systems. DNA-based vaccines are also a possibility, but further off."

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