Creating Transgenic Chickens

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Origen Therapeutics Publishes in Nature a Robust and Versatile Method for Creating Transgenic Chickens

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Scientists from Origen Therapeutics have, for the first time, shown that they could introduce new genetic elements into the precursor cells that form chicken sperm and eggs, resulting in a versatile method for creating transgenic chickens. Such technology opens the door to the production of human sequence polyclonal antibodies and other therapeutic proteins at large scale in chicken eggs. (Early stage transgenic chicken embryos shown in photo). (Photo: Business Wire)

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Achievement Offers Potential for Large-Scale Production of Enhanced Protein Therapeutics in Eggs and the Development of Chickens with Enhanced Agronomic Traits

BURLINGAME, Calif.--(BUSINESS WIRE)--June 7, 2006--Origen Therapeutics announced today that it has succeeded in developing a robust and versatile technology for genetically modifying chickens that, for the first time, puts avian transgenics on a par with transgenic mice. The company made the announcement in conjunction with the publication of an article this week by Origen scientists and a collaborator from the University of California, Davis on its transgenic technology in the journal Nature. Using the new technology, Origen can, in principle, make any genetic modification desired to the chicken genome, including the insertion of genetic elements for the production of human therapeutics and the modification of the chicken immune system to produce novel human sequence polyclonal antibodies. Moreover, the new technology opens up the possibility of producing chickens with enhanced agronomic traits, including resistance to avian flu.

"This research breakthrough came when we turned our attention to primordial germ cells, the precursor cells to sperm and eggs," said Marie-Cecile van de Lavoir, senior scientist at Origen. "These cells -- which we are the first to successfully culture without changing their commitment -- proved to be the key to introducing genetic elements into...
the chicken genome. As a result, we can now take transgene designs that work well in model systems and breed flocks of birds depositing therapeutic proteins in their eggs. The use of primordial germ cells, the ease of producing small or large flocks of chickens, and the existing infrastructure for rearing chickens and processing eggs means that therapeutic proteins can now be produced efficiently and economically in the eggs of chickens.

Origen scientists first demonstrated the potential for the production of human protein therapeutics in chicken eggs in August 2005, when company scientists published in Nature Biotechnology the production of human sequence monoclonal antibodies having greatly enhanced cancer killing activity compared to antibodies produced via conventional methods.

"While that earlier research was done with chimeric chickens, it demonstrated the enormous opportunities that transgenic chickens hold as a therapeutics production system," said Robert Kay, Ph.D. Origen Therapeutics president and chief executive officer. "We believe a transgenic chicken system offers a number of advantages over either plant or other transgenic animal systems for protein production. Besides the ability to produce antibodies with enhanced cell killing properties, the time from antibody identification to production in eggs is a matter of months, the purification of proteins from eggs is relatively simple, and good manufacturing practices have long been established for vaccine production in chicken eggs. Moreover, the overall cost of facility and operations is a fraction of that associated with fermentation methods of manufacture. The ability to readily create transgenic chickens through this technology, and then to scale up production through conventional breeding further adds to the practicality of this technology for large-scale production of therapeutic proteins."

In the early embryo, only a few cells known as primordial germ cells (PGCs) become sperm or eggs in the adult animal. Previous attempts to culture PGCs from mice and humans produced embryonic germ cells that look and act like embryonic stem cells. The chicken is the first species from which PGCs can be isolated, cultured and genetically modified while retaining their commitment to the germ line. Additionally, under certain conditions, Origen scientists could induce the PGCs in vitro to differentiate into embryonic germ cells that contribute to somatic tissue.

"As well as the practical applications of this work, the ability to engineer PGCs and influence them to commit in cell culture to either the germline or the somatic lineages provides a very useful new tool for understanding some of the earliest and most fundamental events in developmental biology on a molecular level," said Robert J. Etches, Ph.D., D.Sc., vice president of research at Origen Therapeutics.

"This work addresses a major biomedical issue -- how to produce antibody-based medicines in an easy, cost-effective way," said Matthew E. Portnoy, Ph.D., of the National Institute of General Medical Sciences, which partially funded the research. "Beyond that, it will help researchers understand stem cell biology and development -- something that holds great value for all sorts of basic studies. This is exactly the kind of result we hope for through our Small Business Innovation Research Program."

The research published in Nature was supported by grants from Small Business Innovation Research Programs of the USDA and the National Institute of General Medical Sciences, of the National Institutes of
Health to Origen Therapeutics and by a USDA grant to Origen collaborator Mary Delaney, Ph.D. at the University of California, Davis.

Origen Therapeutics, headquartered in Burlingame, CA, is a privately held biotechnology company developing product opportunities from their emerging avian transgenic platform. The company’s mission is to become a leading developer and producer of complex recombinant protein therapeutics, including human polyclonal antibodies. By taking advantage of the speed and economy with which transgenic chickens can now be produced, Origen is working to establish significant corporate alliances with biotechnology and pharmaceutical companies for the commercialization of its technology.

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