



First innovative screens using stem cells to identify drugs for myotonic dystrophy, DM1 disease

Evry, March 16th, 2009 – Four research teams of I-STEM[†] have joined forces in a collaborative project that has just achieved a first pilot therapy-oriented screen of compounds and RNA interference aiming at reversing the altered phenotypes observed in human embryonic stem cells carrying the mutant gene for myotonic dystrophy type1. This assay inaugurates a series of R&D planned in 2009.

Human embryonic stem (hES) cells lines carrying the mutant gene responsible for diseases may replicate associated molecular defects associated and be used, therefore, to analyse pathological mechanisms and search for treatments. I-STEM teams have shown that hES cell lines carrying the mutant gene responsible for myotonic dystrophy type1 (DM1) –the most frequent myopathy in adult-present known cellular and molecular abnormalities. hES capacity of self-renewal and pluripotency provides an unlimited and highly versatile cell resource, relevant for large-scale analyses. In order to exploit fully these potentials of hES cell lines within the framework of its exploration of therapeutics for monogenic diseases, I-STEM has set up a screening department through a close partnership with the companies Velocity11, Discngine and Prestwick Chemical. I-STEM has installed at its site, in Evry-Genopole, a powerful automation platform using the innovative Velocity11 BioCel1800® technology, coupled to a specific data management system designed by Discngine. The Conseil Régional d'Ile-de-France and the Association Française contre les Myopathies (thanks to the French Telethon donations) co-funded this platform[‡]. The investments to build this facility assays have been developed in order to screen the "FDA approved" Prestwick Chemical library and a subset of the in house designed siRNA (small interferent RNA) library.

Using this screening platform, the I-STEM teams have looked for compounds and siRNA that would provoke the disruption of abnormal aggregation seen in the nucleus of human embryonic stem cells carrying the DM1 mutation. Several of the 1120 compounds and 50 siRNA assayed were identified as candidates.

I-STEM intends to perform five to ten similar screening campaigns per year on other genetic diseases, using its library of human stem cell lines carrying genetic mutations[§].

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[‡] Other main funders of I-STEM are INSERM, Genopole® and the Conseil Général de l'Essonne.

[§] Human ES cell lines are obtained, in particular, through collaborations with Pr Stéphane Viville (Centre DPI, Strasbourg) and Pr Karen Sermon (AZ-VUB, Brussels).

About I-STEM

The Institute for Stem Cells in the Treatment and Study of Monogenic Diseases— is a laboratory which has set out to explore the therapeutic potential of stem cells in the treatment of rare genetic diseases. Headed by Marc Peschanski (an INSERM Research Director), I-STEM has grown out of a collaboration between the French Muscular Dystrophy Association (AFM), the INSERM (the French National Institute for Health and Medical Research) and the University of Evry-Val d'Essonne (UEVE). It has been funded by Genopole and by several other institutions (the Conseil Régional d'Ile-de-France, the Conseil Général de l'Essonne, the French National Research Agency and the European Union) and is located at the heart of the Evry biopark. In early 2005, I-STEM was the first lab in France to be allowed to work on (imported) human embryonic stem cell lines. Then, in June 2006, it was authorized by the French Agency for Biomedicine to set up a library of mutated cell lines that can serve as models in the study of monogenic diseases. For more information: www.istem.eu

About Velocity11

Velocity11, an Agilent Technologies company, is a leading provider of innovative solutions for laboratory automation, including compound management, cell based assay, and genomics workflows. Our modular products operate on a common software platform and include automated liquid handlers and microplate processing instruments that work independently or are combined to form integrated systems. Our regional professionals work with you to deliver the ultimate automation experience. For more information, visit: www.velocity11.com or contact Dr Bill Bradbury, Primetek Solutions (Kingston, UK), tel. +44-208-546-0869, email: info@primetek-solutions.com

About Prestwick Chemical

Prestwick Chemical is a drug discovery contract research organization specialized in medicinal chemistry. It sells smart compound libraries for screening and offers research collaborations aimed at the discovery of new chemical entities. In the past years, Prestwick Chemical has discovered several drug candidates, the most advanced of which is currently in phase III clinical trial for cancer treatment. For more information, visit: www.prestwickchemical.com or contact Dr. Marie-Louise Jung, tel. +33 6 81 34 17 84, marielouise.jung@prestwickchemical.fr

About Discngine S.A.

Discngine is a consulting and solution provider specialized in Discovery scientific computing and robotics. Discngine helps pharmaceutical companies and biotechs by supporting Discovery technologies implementation like screening, sample tracking, chemo-informatics and scientific business intelligence. Discngine has a strong expertise on IT industry standards like Oracle, Accelrys, Spotfire, and molecular modeling tools as well as Beckman, Perkin-Elmer, Tecan or velocity11 in the automation domain. For more information, visit: www.discngine.com or contact Jean-Philippe Laval, tel. +33 6 14 12 54 66, jean.philippe.laval@discngine.com