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Media Release – For Immediate Distribution

Nature Scientific Reports Article Touts Versatility, Promise of 3D Human Liver Microtissues for Drug Development

Liver spheroids display longer culture lifetime, liver-like functionality, and increased sensitivity for detection of hepatotoxic drugs.

Schlieren, Switzerland – June 16, 2016 Research published by the Karolinska Institute and collaborators as part of the European Community Innovative Medicine Initiative project (MIP-DILI) offers further, independent verification of the utility and promise of 3D liver microtissues for studying liver function, liver diseases and long-term drug-induced liver injury (DILI). The research was published last month in *Nature Scientific Reports*, an open-access journal.

The paper demonstrates the extended *in vitro* lifetime and organotypic characteristics of primary human hepatocytes (PHH) when cultured in a scaffold-free 3D configuration, displaying viability and liver-like functionality for up to five weeks in culture. Proteomic analysis revealed that inter-individual variability was retained between spheroids generated from different individual hepatocyte donors. The study also used the prolonged *in vitro* lifespan of 3D cultured hepatocytes to perform chronic exposure testing of known DILI-inducing drugs, and found they could predict toxicity at clinically-relevant doses. In addition, the spheroid model system proofed to be suitable for studying liver diseases such as cholestasis and steatosis.

Commenting on the publication, Dr. Jens M. Kelm, Chief Scientific Officer and co-founder of InSphero AG says the paper, "Reinforces to the scientific community the benefits of 3D liver microtissues for the purpose of safety assessment during drug development. 3D liver models show enhanced culture lifetime in comparison to standard 2D cultured hepatocytes. This allows for long-term, repeat dose exposure studies, and enhances the sensitivity and predictive power of the model."

InSphero uses its patent-pending 3D Select™ Process to enable industrial-scale production of 3D liver microtissues for *in vitro* liver research and DILI testing conducted by the world's largest pharmaceutical and chemical companies. Dr. Kelm notes that InSphero has performed similar proteomic and genomic characterization of its 3D InSight™ Human Liver Microtissues grown over 28 days in culture, results presented at the EuroTox Annual Meeting in 2015. InSphero's 3D Select™ Process yields liver microtissues with consistent morphology and viability by ensuring only the healthiest cells incorporate into tissues, a critical difference from conventional methods. "Cryopreserved hepatocytes contain large numbers of necrotic and functionally compromised cells. This percentage varies greatly between donor lots and vendors, making it challenging to make uniform microtissues in the numbers needed for industrial-scale testing. Through our 3D Select™ Process, we remove these compromised cells prior to the aggregation step, making microtissue formation more reliable, while improving morphology and viability. This translates to a more robust, mechanistically accurate *in vitro* model that enables testing standardization across multiple sites, and across the industry as a whole."

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For more information about InSphero 3D InSight™ Human Liver Microtissues, and the 3D Select™ Process, visit www.insphero.com.

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About InSphero

InSphero provides superior biological relevance to *in vitro* testing with its easy-to-use solutions for production, culture and assessment of more organotypic 3D cell culture models. The company's patented technologies include the 3D Select™ Process (pending) and scaffold-free 3D cell culture plates that enable large-scale, reproducible production of a broad range of assay-ready 3D InSight™ Microtissues derived from liver, pancreas, tumor, heart, brain and skin. These models and contract research services utilizing them help to identify promising drugs and toxic liabilities with greater predictivity at early development stages, enabling better pre-clinical decision making, saving development cost, and shortening time to market. InSphero technologies drive significant findings in peer-reviewed journals, through collaborative projects such as EU-ToxRisk and HeCaToS, and have gained validation in the world's largest government institutions and pharmaceutical, chemical and cosmetics companies. This 3D know-how is also being applied in the diagnostics field to aid development of personalized chemotherapeutic strategies for the treatment of cancer.

Founded in 2009, the privately held company is headquartered in Schlieren, Switzerland with subsidiaries in the United States (Brunswick, ME) and Waldshut, Germany. It has been recognized for its scientific and commercial achievements with a number of national and international awards.

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