STEM CELLS FOR SAFER MEDICINES: A PREDICTIVE TOXICOLOGY CONSORTIUM

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THE OPPORTUNITY TO IMPROVE PHARMACEUTICAL RESEARCH AND DEVELOPMENT

The pharmaceutical industry is facing many challenges, not least the substantial loss of revenue as a consequence of a number of products coming off patent. We are witnessing escalating drug development costs combined with reduced numbers of products gaining regulatory approval and hence introduction into clinical practice. Too many drugs fail in development and a significant proportion (around 25 per cent) of drug attrition is due to toxicity issues. It is recognised therefore that improved drug screening models are urgently needed for the identification of potential toxicity, which should result in an increased success rate as 'flawed' candidate drugs are eliminated early.

Stem Cells for Safer Medicines, SC4SM, is a public-private partnership that was founded as a direct recommendation of the UK Stem Cell Initiative (Sir John Pattison Report, 2005) to develop predictive toxicology tools from human embryonic stem cell (hESC) lines. The partnership capitalises upon the emerging strength of stem cell science in the UK, with its strong ethical and governance framework combined with the enabling environment, both politically and socially, to generate and validate novel *in vitro* models that can be used to predict risk for many of the potential adverse effects of new drugs and chemicals.

AIMS AND OBJECTIVES OF THE CONSORTIUM

To address the challenges in the development of new medicines, we need to generate and validate more innovative, preferably cellular (in vitro), tools. One way is the development of models for toxicity testing that are reliable, high throughput and above all, predictive of risk for man.

The aim of the SC4SM partnership is to produce optimised methods for the preparation of particular cell types (initially, the liver as the major organ affected by drug toxicity) from hESC lines with well-defined and 'fit for purpose' functionality. Differentiated cell types derived from hESCs offer significant benefits in terms of unlimited supply, the opportunity for standardisation and potentially improved predictiveness. Following scale-up and manufacture, the derived liver cells would then be incorporated into high throughput toxicity screening platforms and subjected to comprehensive validation and benchmarking against current existing cellular models. A successful outcome would be confirmation of the reliability and utility of the stem cell model to identify those compounds with potential risk of toxicity for man. In this case, it would be anticipated that pharmaceutical companies would integrate the new stem cell model into the range of screening procedures that are required to test the efficacy and safety of new medicines.

OPERATING MODEL FOR THE PARTNERSHIP

SC4SM, as one of the earliest public-private partnerships (PPPs) focused on generating predictive toxicology tools, was a pioneering model in how pre-competitive collaborations between companies, government and academia could be used to drive innovation in a technically challenging area such as hESCs. This collaboration reflects wider changes in the industry which are now increasingly entering into pre-competitive PPPs (eg the Innovative Medicines Initiative in the EU) to tackle major challenges where collaboration allows both the knowledge and the risk to be shared.

SC4SM operates as a not-for-profit company with its ethical policies and a strong governance framework agreed upfront. Operating as a pre-competitive consortium of industrial members and public sector partners, the company's funds support a range of academic collaborators. Currently, SC4SM industrial members include AstraZeneca, GSK, Roche and UCB, and in addition to providing funds, the companies make a major contribution to the project through scientific input and availability of their expertise, data and other resources, for example technology platforms. Recognition of the importance in improving predictive tools was demonstrated by public funding being made available by a number of government agencies including the Medical Research Council, Biotechnology and Biological Sciences Research Council, and the Department of Health and Technology Strategy Board.

The research programme is being conducted through academic collaborations with the universities of Bath, Liverpool and Manchester and is project-managed directly by SC4SM. A Scientific Advisory Board (SAB) provides external peer review and overall scientific guidance and includes a range of relevant academic experts plus representatives from the industrial partners. An Executive Board is responsible for overall corporate governance and approves scientific strategy and direction.

BENEFITS AND CHALLENGES

The formation of SC4SM as a public-private partnership facilitates collaboration between cutting-edge academic science in the UK and the vitally important research-based pharmaceutical industry. The opportunity for risk, cost and pre-competitive data sharing is a clear benefit for the industrial members and at the same time, access to company R&D know-how and experience is of great value to support the activities of the network of academic collaborators who are working in a highly competitive and challenging scientific environment.

Through these combined resources, a successful pilot phase project has been completed (with IP generated and a patent filed) and a three-year research programme is currently underway.