

## **UK-Spanish Workshop - 'Stem Cells: from Bench to Bedside'**

**The Royal Society Meeting Rooms, Carlton Crescent, London, 24<sup>th</sup>-25<sup>th</sup> March 2009**

### **Introduction**

The proposal for this workshop came out of an earlier Spain-UK stem cell conference in 2007 organised by the UK and Spanish governments, which had identified 'stem cell banking' as an area for future collaboration between the two countries. In fact the original idea for these contacts came from an interaction between the Prime Ministers of Spain and the UK who agreed that the stem cell area was an area where their two countries should join forces. Sponsors for the meeting included the Foreign and Commonwealth Office (FCO), Instituto Salud Carlos III (ISCIII) and also the Department for Innovation, Universities and Skills (DIUS) from the UK.

The purpose of the meeting '*UK-Spanish Stem Cell Workshop' - From Bench to Bedside*' held in London 24-25 March 2009 was to bring the Spanish and UK stem cell banks together with representatives of other relevant stem cell activities to discuss critical scientific and technical issues for delivery of new stem cell technology to the clinics and to specifically consider what the UK and Spanish stem cell banks should be doing in coordination to promote this and assist the stem cell community. It was also intended that in addition to the contacts made between speakers at the workshop that UK-Spanish networking should be expanded by follow-up activities to be specified at the meeting. The delegate number was limited to enable good interactive discussion but delegates were selected to promote a balance of expertise and regional representation. Delegates were invited from academia and industry, both from adult and embryonic stem cell fields, social science and the European Commission. Some groups were also represented where existing Spanish-UK collaboration was already active to enable more informed discussion on developing such links.

At the first evening of the meeting, the coordinators for the Spanish and UK networking organisations, Prof. Javier García Sancho and Mr Ben Sykes respectively, presented on their national activities. Opportunities for these two national networks to be better coordinated were discussed and a direct link between websites was agreed as a starting point. Representatives of the London Regenerative Medicine Network (Prof. Chris Mason, LRMN) and the newly established Oxford Stem Cell Institute (Prof. Helen Mardon) were briefly outlined as examples of the diversity of stem cell/regenerative network that have developed in the UK; from a strong industry focus (LRMN) to a broader stem cell science and

translational research approach as in Oxford. Other UK regional stem cell network representatives joined the meeting and/or supplied information at the workshop.

The second day of the meeting was opened by Denise Holt, the UK's ambassador to Spain who was taking a special interest in this Spanish-UK collaboration and expressed a wish to be kept informed of developments. The meeting was organised in three sessions based on academic research, social and ethical issues, biobanking, clinical application and commercial exploitation.

### **Stem Cell Biology (Chair: Dr Pablo Menendez)**

Dr Ricardo Pardal spoke on carotid body stem cells and their potential clinical applicability, describing his work to produce neurosphere cultures for cell therapy against neurological disease. He also described his work using carotid bodies to define a new niche for adult neural precursors in which stem cells have a glial phenotype and are able to undergo physiologic neurogenesis to permit the adaptation of the organ.

Prof. Paul Fairchild used examples from detailed work on mouse ESCs to address the immunological barriers to regenerative medicine. Using ESC lines differing from recipient strains at defined genetic loci, he demonstrated that even minor histocompatibility antigens were sufficient to induce rejection of tissues differentiated from them, suggesting that banking alone could never overcome the immunological barriers. He also explained that whilst banks of iPS cells could in the future provide homozygous "super donor" cells, some of the immunological issues would remain to be solved.

Prof. Anna Veiga described the iPS cells platform developing in Barcelona, which is currently focused on Franconia anaemia but also addresses other inherited diseases such as neurofibromatosis, cystic fibrosis, muscular dystrophy and glycogen storage disease. She also showed data from work on mouse and human, adult spermatogonial cells to derive stem cell-derived cell lines and study the stem cell niche.

Dr Majlinda Lako described developments in our understanding and enhancement of differentiation of human embryonic stem cells. She presented work on hESC co-culture with stromal cell lines, being used to study the haematopoietic stem cell niche, and generation of iPS cells with similar properties to hESCs in terms of haematopoietic induction and generation of cardiomyocytes. Future plans included work on disease modelling where mouse models have proven unsuccessful.

Dr José Cibelli, working both in the USA and Spain, had carried out a study using transcriptome analysis comparing the profiles of hESCs and iPS cells using H9 as a representative hESC line. This analysis together with teratoma and epigenetic data indicated to him that there was great similarity between hESC and iPS cells. However, he emphasised that new developments and a great deal of “non-sexy” experimentation were needed to establish a safe but expedient route to the clinic for iPS cells. Dr Cibelli felt that this could only be achieved by a well coordinated network of stem cell scientists.

Prof. Peter Coffey, working with the Centre for Stem Cell Biology in Sheffield, had identified that certain hESC lines had the capability to produce retinal pigmented epithelial cells which, if placed under the damaged retina on a polyester patch, appeared to have the potential to effect repair and regain vision. Prof. Coffey had achieved high purity RPE cells from both hESC and iPS cells. He was progressing now to establish a clinical trial for the cost-effective repair of macular degeneration in the elderly and had plans for large animal studies in the near future.

Prof. Anthony Hollander described the ground-breaking translational research in tissue engineering as a result of which a Spanish patient’s life had been saved by replacement of part of her trachea with decellularised donor tissue seeded with derivatives of her own bone marrow cultured *in vitro*. The outcome had been enabled through a European Commission research project and was a direct collaboration between the University of Bristol and a surgical unit in Barcelona.

### **Ethics and Social Science (Chair: Dr Javier Arias-Diaz)**

Prof. Carlos Alonso-Bedate revisited the key arguments surrounding the use of the human embryo for research. He stated that the debate had been led by discussion on the promises of hESC research, the rights of the unborn and their mothers, and public opinion. He said that we need to be alert to the fact that this can lead to scientific issues being lost in the debate. He also indicated that iPS cells do not necessarily resolve all of the ethical dilemmas and we should consider that pluripotency resides in the regulatory biochemical pathways and networks and is not unique to a particular cell.

Prof. Andrew Webster discussed some of the key ethical and regulatory factors in “trans-institutional banking” which would be of direct relevance to any plans to achieve greater coordination between the UK and Spain. Prof Webster believed that there is a need for iteration between researchers and the

banks on issues of characterisation, quality control and quality assurance. Regulation in this area would require long term attention on issues such as consistency in bioprocessing and standardisation. He went on to say that this would require coordination between banks and translational scale-up centres to deliver this difficult and tedious task which would not necessarily attract the attention of researchers interested in basic science.

Dr Joanna Namorado explored the key issues to be considered in EU calls for proposals and their ethics review for stem cell researchers across Europe. She envisaged an important role for bio banks in developing best practice, disseminating reliable information and protocols.

### **Bio-Banking (Chair: Dr Pablo Menendez)**

Dr Carlos Simón presented the project from his laboratory to enable hESC derivation from single blastomere whilst maintaining the viability of the original embryo. He also described work at the Valencia Stem Cell Bank to establish and characterise hESC lines and methods to sustain their undifferentiated state.

Dr Glyn Stacey described the international remit of the UK Stem Cell Bank as a provider of quality controlled and ethically sourced human stem cell lines for research and the development of therapy. He also explained the careful way in which the Bank operated to avoid commercial and scientific conflicts of interest, thus enabling it to act as an independent broker in the stem cell field.

### **Case Studies from the Stem Cell 'Biotech' Industry (Chair: Dr Glyn Stacey)**

Dr. Jorge Alemany outlined five clinical cell therapy products, established by Cellerix. He identified the key challenges for delivery of cell therapy as regulation, the logistics of delivery of cell culture treatments with short shelf-lives and public perception of the ethical issues. In addition he highlighted the problems of financing new high risk products and the importance of recognising the differences between the protection of intellectual property for cell therapies compared to small molecule medicines. Finally, he also outlined the significant issues to be addressed in sourcing appropriate raw materials for manufacturing and implementing the manufacture of cell-based therapies under GMP.

Dr. Johan Hyllner presented the impressive portfolio of 150 academic collaborations established by Cellartis based on their in-house hESC lines and supported by the European Commission. Cellartis had recently established a UK scale-up facility in Dundee, and Dr Hyllner saw the establishment of quality assurance in bioprocessing systems as vital to progress. The in-house hESC lines of Cellartis are used by the company to derive products such as cardiac and hepatic cells as well as mesenchymal progenitors for the life science community (both industry and academia).

### **Conclusions and Forward Plan (Dr Glyn Stacey)**

Before the conclusion of the meeting, the MRC and ISCIII representatives, Dr Rob Buckle and Dr Peter Klatt respectively, presented a draft plan to develop a funding programme in which each of the research funding bodies would look to support applications to instigate Spanish-UK collaborations on translational research.

A number of issues had been raised in relation to specific interactions between the Spanish and UK banks and these were summarised as follows:

Consider what characterisation the banks need to recommend for clinical grade cell lines particularly with respect to immunological factors.

Ethical comparisons based drawing on the comparison between Spain and the UK in the Bioethics presentations.

What practical initiatives could be developed by the Spanish and UK banks to facilitate exchange of cell lines between the two countries.

What intellectual property issues should the banks be aware of and how could they respond to facilitate the development of products.

Dr Stacey and Dr Menendez would coordinate a response on these to take forward.

Dr Stacey also proposed a forward plan for wider dissemination of the meeting output and ongoing promotion of interactions between Spanish and UK stem cell researchers, clinicians and companies.

*Forward Plan:*

- Circulate a summary report from the workshop and make this available through the national network representatives to their respective stem cell communities.
- Create a direct link between the Spanish and UK network websites.
- Establish a webpage on the UKNSCN website where Spanish and UK scientists can post their contacts information and begin a match making process for new potential collaborators.
- The Spanish and UK stem cell banks would plan a follow up visit to begin closer coordination of their activities.

**Workshop Speakers/Delegates and Their Affiliations**

Dr Jorge Alemany, Cellenix, Spain

Prof. Carlos Alonso-Bedate, Centro de Biología Molecular, CSIC, Spain

Dr Javier Arias-Diaz, Instituto Salud Carlos III, Spain

Ms Sara Cebrian, British Embassy, Madrid, Spain

Dr Concepcion Martin Arribas, Instituto Salud Carlos III, Spain

Dr Natividad Cuende, Andalusian Advanced Therapies Initiative, Spain

Dr Rob Buckle, MRC, UK

Prof. Martin Burchall, University College of London, UK (apologies)

Dr José Cibelli, Celular Reprogramming Laboratory, Michigan State University, USA

Prof. Peter Coffey, Ocular Biology and Therapeutics, University College of London, UK

Dr Catriona Crombie, MRC, UK

Prof. Paul Fairchild, Dunn School of Pathology, Oxford University, UK

Ms Ana Fernandez, British Embassy, Madrid, Spain

Prof. Javier García-Sancho. IBGM, Universidad de Valladolid, Spain. Spanish Cell Therapy Network.

Prof. Anthony Hollander - Cellular and Molecular Medicine Sciences Department. University of Bristol, UK

Dr Johan Hyllner, Cellartis AB, UK

Dr MajLinda Lako, NESCI and Institute of Human Genetics. Newcastle Upon Tyne, UK

Dr Joanna Namorado, European Commission, Brussels.

Dr Ricardo Pardal. Instituto de Biomedicina de Sevilla (IBIS), Spain

Dr Marilyn Robertson, Scottish Stem Cell Network, Scotland, UK

Dr Carlos Simón, Fundación Valenciana de Investigaciones Biomédicas, Valencia, Spain

Mr Mark Sinclair, British Embassy, Paris, France

Dr G Stacey, UK Stem Cell Bank, HPA-NIBSC, UK

Mr Ben Sykes, UK National Stem Cell Network (UKNSCN), UK

Dr Anna Veiga, Banco de Líneas Celulares, Centro de Medicina Regenerativa de Barcelona, Spain

Prof. Andrew Webster, Director SATSU, Department of Sociology, University of York

Dr Javier Arias, Instituto de Salud Carlos III, Spain