

Final Project Report Stem Cell Network

The DPUK Stem Cell Network formed an outstanding network of leading scientists involved in modelling neurodegenerative disease in human induced pluripotent stem cells. The work proved to be highly productive, as evidenced in three ways:

1. Publications produced, as listed above.

2. Cellular reprogramming

Chandran (Edinburgh) has completed reprogramming and generation of induced pluripotent stem cells for 24 carefully selected members of the 1936 Lothian Birth Cohort of control individuals. Individuals for iPSC generation were chosen as average agers (n=8, blue), unhealthy agers (n=8, red) and healthy agers (n=8, green). See Figure 1.

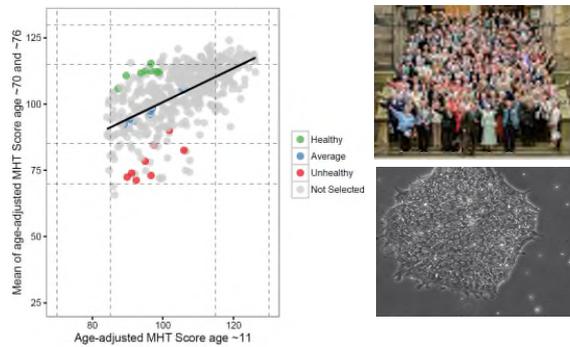


Figure 1: Average, healthy and unhealthy agers selected from the 1936 LBC Birth Cohort selected for iPSC generation

Working with Wade-Martins, Cader (Oxford) has completed reprogramming and generation of iPSC lines from 20 members of the MRC Deep and Frequent Pilot Cohort. All lines are reprogrammed and QC checked. Oxford commenced differentiation and phenotyping of lines in 2018.

!	No. !patients!!	Lines!available!	Source!
Sporadic!AD!	!	!	!
PSEN1!mutants!	7!	3!lines!each!	StemBANCC!
APP!mutants!	2!	3!lines!each!	StemBANCC!
MAPT!mutants!	2!	3!lines!each!	StemBANCC!
!	!	!	!
Sporadic!AD!	!	!	!
ApoE4/E4!	3!	3!lines!each!	StemBANCC!
ApoE4!het!	4!	3!lines!each!	StemBANCC!
Deep!and!Frequent!	20!	1!line!each!	StemBANCC/Oxford!
!	!	!	!
Ageing!!	!	!	!
LBC!1936!	24!	3!lines!each!	Edinburgh!
!	!	!	!
Familial!PD!	!	!	!
PINK1!	5!	15!	StemBANCC/Oxford!
PARKIN!	3!	10!	StemBANCC/Oxford!
GBA!	9!	29!	StemBANCC/Oxford!
LRRK2!	10!	22!	StemBANCC/Oxford!
SNCA!	5!	14!	StemBANCC/Oxford!
!	!	!	!
Sporadic!PD!	!	!	!
Pure!	14!	20!	StemBANCC/Oxford!
Rapid!dementia!	4!	8!	StemBANCC/Oxford!
Rapid!dyskinesia!	3!	3!	StemBANCC/Oxford!
Impulse!control!disorder!	4!	8!	StemBANCC/Oxford!
!	!	!	!
Aged!controls!	9!	26!	StemBANCC/Oxford!

The DPUK Stem Cell Network is building a set of iPSC lines available for our work, most notably in AD, PD and normal ageing cohorts, many of which were generated by Cowley. The list will develop through partnership activity, but here we show the current list (left), as requested by the Oversight Panel.

StemBANCC: EU IMI Consortium led by Oxford.

3. Networking activity

MRC Stem Cell Partnership Workshops

The DPUK Stem Cell Network thrived based on an excellent level of interaction between the seven PIs across the six Centres. We held regular monthly PI teleconferences and six-monthly face-to-face PI meetings. Of special note was the inaugural DPUK Stem Cell Network Spring School, held in April 2017 in Edinburgh. Sixty-five scientists attended and 22 were invited to speak, with an emphasis and priority for Early Career Researchers. There were extensive opportunities for networking, discussions and sharing of expertise and developing new collaborations.

The 2nd annual DPUK Dementia Stem Cell Network workshop brought together 93 delegates from all partner universities. The two-day workshop consisted of 21 talks split into seven diverse sessions ranging from genetics to transcriptomics and from iPSC models of neurodegeneration to synaptic activity and the blood brain barrier. The highlights of day one were the fascinating lysosomal angle of neurodegeneration brought to light by some very interesting talks; in particular, those of Emyr Lloyd-Evans and Helene Plun Favreau. Another highlight was the amazing images presented to us by Ravi Solanki during his talk on the neuronal-glia interactions in cortical organoids. Day one culminated in a poster event which showcased work from nine of our researchers and provided an opportunity for them to not only communicate their research but to also network and build future collaborations within our partnership. Day two was equally as impressive as day one, with a wide range of research on show. The Synaptic activity in iPSC neuronal models was particularly impressive, with an engaging talk by Francesco Tamagini.



Dissemination and communication

The Stem Cell Network has taken the comments of the Oversight Board on the dissemination and communication of its resources and activities very seriously. It has worked very closely with Beatrice Shelley, DPUK Communications Officer, to establish a presence on the DPUK web-site and highlight the work going on in the 7 principal laboratories. These details, accessible in the “For Researchers” tab then “Our Research Communities” provides information on the labs (see UK-wide expertise) and the Technology resources that could be exploited collaboratively. Finally, a section on iPSC resources for researchers provides the opportunity for researchers to formally request over 100 stem cell lines derived from healthy and diseased individuals. This resource focused section is complemented by two detailed reports in the “Our impact” section of the web-site. These reports titled, “Uncovering the potential on the shelves of drug libraries” and “iPSCs: a shared resource” provide more details about the exciting research frontiers being tackled by the group.

The group held regular communications with the DPUK Comms Team to provide additional material for the web-site and annual reports.