MEMORIA DE LA ACTIVIDAD DEL BANCO NACIONAL DE LÍNEAS CELULARES DE 2018

En la Subdirección de Terapia Celular y Medicina Regenerativa reside la Dirección, así como la Presidencia y Secretaría de la Comisión Técnica del Banco Nacional de Líneas Celulares. Se trata de un biobanco en red, con nodos en Granada, Barcelona y Valencia, que pone a disposición de la comunidad científica todas las líneas de células troncales derivadas en nuestro país.

Reuniones celebradas

Se celebraron dos reuniones presenciales el 25 de junio de 2018 y el 13 de diciembre de 2018, presididas por Dª Emilia Sánchez Chamorro.

Miembros de la Comisión Técnica del BNLC.

Modificaciones en 2018. Durante 2018 se incorporaron como miembros de la Comisión Técnica Dª Helena Mira, Dª Angeles Vicente, D. Joaquín Sarrión, D. Cristóbal Belda Iniesta en sustitución de Dº Pablo Menéndez Luján, Dª Yolanda Gómez Sánchez, Dº Augusto Silva y Dª Belen Bornstein respectivamente.

Relación de las líneas depositadas en 2018

Durante el año 2018 se han depositado en el BNLC 30 líneas pluripotentes inducidas (iPS). Estas líneas han sido desarrolladas en los siguientes Centros de Investigación: 8 en el Instituto Cajal del CSIC, 6 en el Instituto de Bioingeniería de Cataluña (IBEC), 4 en la Universidad Pompeu Fabra, 4 en la Fundación del Instituto de Microcirugía Ocular (IMO), 3 en el centro GENYO, 2 en el Centro de Investigación Príncipe Felipe (CIPF), 1 en el Instituto de Investigación Sanitaria de Santiago de Compostela (IDIS), 1 en el Centro de Diagnóstico de Enfermedades Moleculares de la Universidad Autónoma de Madrid (CEDEM) y 1 en el Instituto de Investigaciones Biomédicas Alberto Sols (IIBM).

Líneas solicitadas

Durante el año 2018 se han solicitado y aprobado la cesión de 18 líneas celulares (7 embrionarias, 11 iPS) para 8 proyectos (4 de ellos de centros extranjeros) desarrollados por 8 investigadores.
Líneas embrionarias: se solicitaron las líneas PBMC2-iPS4F8 – RBM15-MKL1, AND-1, AND-2, AND-3 (2), HVR-1, ES[4] para 7 proyectos de investigación.

Líneas iPS: se solicitaron las líneas MSUH-001, 3PNF_FiPSsv_PM_2, 3PNF_SiPSsv_MM_11, 5PNF_TDiPSsv_PM_6, 5PNF_TDiPSsv_MM_4, [CRTRd]FiPS3819-4F-2, CRTRd]FiPS3067-4F-9, iCas9-FL-BCL-iPSC (2), CBiPS1sv-4F-5 y CBiPS1sv-4F-40 para 11 proyectos de investigación.

Actividad de los nodos

Actividad del nodo de Barcelona

The research activities that took place during 2018 at the CMRB's Stem Cell Bank (BLC) arepresented below. We first list the BLC's activities regarding registration, banking, and generation of human pluripotent stem cell lines. Then, we briefly summarize the overall research activities that were completed and resulted in manuscripts published during 2018, with references given to the relevant publications.

BLC_1. Banking and registration of hPSC lines

GENERATED AND BANKED		
Line name	**Project name**	**PI**
OCD FiPS1-Ep6F-16	Genetic and epigenetic mechanism in the refractory obsessive compulsive disorder: developmen and validation of a celular line through reprogramation.	Raul Alelú (Canis Majoris. Madrid)
OCD FiPS2-Ep6F-10		
BST PBiPS1-Sv4F-1	Hematopoietic regeneration from pluripotent stem cells.	Núria Nogués (BST. Barcelona)
BST PBiPS2-Sv4F-6		
NF STiPS 25-Sv4F-10	Reprogramming Vestibular Schwanoma cells: generation of patient-specific NF2(+/-) and (-/-) induced pluripotent stem cells (iPSC)	Eduard Serra (IGTP. Barcelona)
NF STiPS 245-Sv4F-6		
NF STiPS 245-Sv4F-12		
NF STiPS 267-Sv4F-4		
CT PBiPS 1-Sv4F-1	Modelling Cardiotoxicity in paediatric Cancer patients tReated with anthracyclines: a miRNA	Pilar Sepúlveda

	approach. CARDIOCARE	(La Fe. Valencia)
CPVT FiPS 51-Ep6F-1 CPVT FiPS 54-Ep6F-6 CPVT FiPS 55-Ep6F-8	Study of the genetic and molecular bases of hereditary cardiac arrhythmias (ACH-IPS RESEARCH)	Elisabet Selga Ramon Brugada (IDIBGI. Girona)
IN CHARACTERIZATION		
BS FiPS 64-Ep6F-1 BS FiPS 65-Ep6F-9 BS FiPS 66-Ep6F-4	Study of the genetic and molecular bases of hereditary cardiac arrhythmias (ACH-IPS RESEARCH)	Elisabet Selga Ramon Brugada (IDIBGI. Girona)
REGISTERED		
[SWB]FiPS 159-R4F-4 [SWB]FiPS 344-R4F-2 [DUPSW]FiPS501-R4F-2 [DUPSW]FiPS701-R4F-6	Generation of pluripotent induced cells for reprogramming of individual fibroblasts with alterations the number of copies of the region Q11.23 (7DUP/Autism and Williams syndrome)	Roser Corominas (UPF. Barcelona)
REGISTRATION IN PROCESS		
OCD FiPS1-Ep6F-16 OCD FiPS2-Ep6F-10	Genetic and epigenetic mechanism in the refractory obsessive compulsive disorder: developmen and validation of a celular line through reprogramation.	Raul Alelú
BST PBiPS1-Sv4F-1 BST PBiPS2-Sv4F-6	BST PBiPS1-Sv4F-1 BST PBiPS2-Sv4F-6	Hematopoietic regeneration from pluripotent stem cells.

Lines cession

Investigator	Centre	Lines	Date
Zameel Cader's	University of Oxford	iCas9-FL-BCP-hiPSC	26.3.2018
Clifford Woolf	FM Kirby Neurobiology Center. Boston Children's Hospital	iCas9-FL-BCP-hiPSC	2.5.2018
Cris Eguizabal	Centro Vasco de Transfusión y Tejidos Humanos	ES[10]	21.08.18
Nuria Montserrat	IBEC	CBiPS sv-4F-5	14.09.18
		CBiPS sv-4F-40	
Josep Canals	UB. Creatio	ES[4]	19.08.18
Chandresh Gajera	Stanford University	[CRTRd]FiPS3819-4F-2	25.9.18
		[CRTRd]FiPS3067-4F-9	
		FiPS Ctrl1-R4F-4	
		FiPS Ctrl2-R4F-5	

Banking

iPSC line	Centro	IP
iPSC-HDFs-clone 30	Josep Carreras Leukaemia Research Institute y Universidad Pablo de Olavide (CABD)	P.Menéndez (Fundació Carreras. Barcelona)

6PNF SiPSrv-PM-2	Institut de Recerca Germans Trias i Pujol(IGTP)	E. Serra (IGTP. Barcelona)
7PNF SiPSrv-PM-12		
3PNF FiPSsv-PM-2		
3PNF FiPSsv-MM-11		
5PNF TDiPSsv-MM-4		
5PNF TDiPSsv-PM-6		

BLC_2. Participation in collaborative initiatives for hPSC generation/banking

Project: Allogeneic iPSCs from homozygous SCU units for high prevalence haplotypes (IPS-PANIA)

In collaboration with Banc de Sang i Teixits (BST) (PI: Dr. Sergi Querol)

The use of the patient's own cells for the generation of iPSC and the subsequent differentiation to a certain cell type for his treatment, ensures immunological compatibility and minimizes the risk of rejection. However, the time and cost needed for the creation of clinical-grade patient-specific cells is very high. An alternative would be the creation of an iPSC bank that would collect diverse HLA haplotypes to ensure the maximum possible coverage of the population and minimize immunological rejection. The cord blood units banked in the cord blood banks are good candidates as a source of original cells, as the reprogramming methodology using these cells is well known and stablished, and they are already HLA typed in the banks.

The aim of this project is the generation of 7 iPSC lines from umbilical cord blood homozygous for the most frequent haplotypes and their banking in GMP (Good Manufacturing Practices) conditions. These 7 iPSC lines will represent the prototype of a bank of clinical-grade lines to be used to treat a significant percentage of the population.

The first phase of the project is to search the most frequent homozygous HLA cord blood units among the 5 cord blood banks of the PNSCU (Plan Nacional de Sangre de Cordón Umbilical), and contact with donors.

The iPSC generation and characterization from the selected units will take place at the CMRB. The reprogramming will be performed in xeno-free conditions and using GMP products. Finally, the obtained iPSC lines will be expanded and banked in clinical-grade conditions at the BST (Master

Cell Bank, MCB). A Working Cell Bank will be created from one vial of each line of the MCB, and will be made available to the researchers or clinicians who request them.

BLC_3. Optimization of hPSC generation/banking

More fundamental research activities have also been carried out by the CMRB's BLC during 2018 to optimize the overall conditions leading to hESC derivation and/or hiPSC generation.

Within the optimization of the hiPSC generation methodologies, new original cell types has been included as mononuclear cells from peripheral blood using Sendai virus and now is a fully implemented in the protocols of the BLC.

Derivation of fibroblasts from a skin biopsy has been also optimized in the absence of feeders, using synthetic matrices (matrigel, laminin, etc.). It will be necessary for the use of the resulting iPSC in a future clinical translation.

New PCRs were set up to proof absence of exogenous reprogramming factors in induced Pluripotent Stem Cells (iPSCs) generated by nucleofection of somatic cells with episomal plasmids. To proof absence of copies of reprogramming plasmids in iPSC lines, copy number PCRs were done by extraction of gDNA and performing of PCRs usingsybr green/Lightcycler, including standard curve done with the pCXLE plasmid. To proof absence of expression of plasmid derived factors, mRNA from iPSCs is extracted, cDNA is synthesized and a qRT-PCR is performed (sybr green/Lightcycler).