

# "An in vivo humanized model for Alzheimer's disease from pluripotent stem cells"

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The generation of in vitro and in vivo models to study human corticogenesis is essential to address the molecular and cellular mechanisms involved in developmental and degenerative cortical diseases. We previously found that human pluripotent stem cells (PSC) can recapitulate major milestones of human corticogenesis in vitro. In addition, following the transplantation of human PSC-derived cortical cells into the mouse neonatal brain we observed a functional integration and establishment of specific axonal projections from the human neurons.

Several neurological diseases strike the integrity of the cerebral cortex including stroke, epilepsy and neurodegenerative diseases such as Alzheimer's disease (AD). When some of these diseases have been extensively studied, mostly they have been tackled using murine transgenic models that cannot completely recapitulate the etiology of the disease.

Here, we present a novel "in vivo humanized AD model" from human pluripotent stem cells. We transplanted PSC-derived human cortical neurons into the brain of transgenic AD mouse models to characterize early and late effects of amyloid pathology on human neurons. We found that human neurons exposed to the toxic amyloid-beta species in the transgenic mouse brain show very early signs of neurodegeneration, including aberrant accumulation of pre-synaptic neurotransmitter vesicles, and early neuronal loss. Signs of neuronal and axonal degeneration were also observed by EM analysis specifically in the human neurons. Interestingly, the human neurons located at amyloid-beta plaque sites were positive for pathological Tau tangle-like staining, a major hallmark of AD. A preliminary comparative RNA expression analysis at early stages between human neurons transplanted into wild-type and transgenic animals revealed some differentially expressed candidate genes that could shed new light on the biology of early stages of the disease.

In conclusion, the humanized model for AD can recapitulate major milestones of the AD human pathology in an in vivo context and could be instrumental for the study of early and late stages of the pathology, opening new venues for future research in the field. Overall, these data demonstrate that cortical neurons derived from human pluripotent stem cells represent an invaluable tool for the modeling of human cortical diseases, in particular adult onset, human specific neurological disorders, such as Alzheimer's disease.

[Full paper](#)



# Cell therapy today: Achievements, hopes and hype

## 9 – 12 September 2015 | Manchester, UK

### About the conference

Stem cell therapy has saved hundreds of thousands of lives since the establishment of bone marrow transplantation half a century ago but still faces significant hurdles for tissues other than blood and epithelia. Notwithstanding the many difficulties, clinical trials are ongoing that are providing critical information to refine protocols and implement tools aimed at achieving significant clinical efficacy.

At the same time, many poorly controlled or uncontrolled trials are also taking place, muddling the picture and often unjustifiably raising patient expectations and hopes.

Furthermore, the ethical implications of these therapies and their future impact on the economics of health provision are likely to be significant.

This EMBO Conference will focus on the clinical translation of stem cell based research, current trials, pre-clinical work as the foundation for future ones and the ethical and economical impact of these novel therapies.

Major experts in stem cell translational medicine, leading clinicians running these trials, as well as bioethicists and economists will

convene to discuss, learn and exchange views on this rapidly evolving and still partly controversial field.

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## Speakers

### Alessandro Aiuti

San Raffaele Telethon Institute for Gene Therapy,  
Italy

### Paolo Bianco

University of Rome, Italy

### Gillian Butler-Browne

UMPC-INSERM-Institut de Myologie, UMRS-S  
787, France

### Kenneth Chien

Karolinska Institute, Sweden

### Roger Barker

University of Cambridge, UK

### Juan Bueren

CIEMAT/CIBERER, Spain

### Marina Cavazzana

Necker Hospital for Sick Children, France

### Giulio Cossu

University of Manchester, UK

**Michele De Luca**

University of Modena and Reggio Emilia, Italy

**Stefanie Dimmeler**

University of Frankfurt, Germany

**Robin Franklin**

University of Cambridge, UK

**Bobby Gaspar**

University College London, UK

**Pamela Gehron Robey**

NIDCR, NIH, USA

**May Griffith**

Linköping University, Sweden

**John Harris**

University of Manchester, UK

**Frank Luyten**

University of Leuven, Belgium

**Peter Marinkovich**

Stanford University, USA

**Gianvito Martino**

San Raffaele Hospital, Italy

**Anne-Marie Moulin**

CNRS Unit SPHERE/Paris 7 University, France

**Luigi Naldini**

San Raffaele Telethon Institute for Gene Therapy, Italy

**David Napier**

University College London, UK

**Graziella Pellegrini**

University of Modena and Reggio Emilia, Italy

**Amedeo Santosuosso**

University of Pavia, Italy

**Kathryn Wood**

University of Oxford, UK

**Joseph Wu**

Stanford University, USA

# Programme

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## Day 1 – Wednesday, September 9, 2015

14.00-19.00	Registration
17.30-17.50	Opening remarks
17.50-18.00	Keynote lecture presentation <a href="#">Giulio Cossu, Manchester, UK</a>
18.00-19.00	Keynote Lecture "Genetic engineering of hematopoietic stem cells for the treatment of inherited diseases and cancer" (sponsored by ReACT Community)

[Luigi Naldini, Milan, Italy](#)

19.00-22.30 Welcome Cocktail + Buffet Dinner (offered by e-Life)

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## Day 2 – Thursday, September 10, 2015

### Session 1, Hematopoietic Cells

Chair: [Michele De Luca, Modena, Italy](#)

- 09.00-09.30 Hematopoietic stem cell gene therapy for Wiskott Aldrich syndrome  
[Alessandro Aiuti, Milan, Italy](#)
- 09.30-10.00 Gene therapy of hemoglobinopathies : clinical results and future developments  
[Marina Cavazzana, Paris, France](#)
- 10.00-10.20 Effect of high glucose in Human Wharton's Jelly Mesenchymal Stem Cells (WJ-MS-C) promotes angiogenesis mediated by Netrin-1 in human umbilical vein endothelial cells (HUVEC).  
[Catalina Prieto, Santiago, Chile](#)
- 10.20-10.40 Preclinical experience and perspectives of a clinical trial using CD133 stem cells  
[Yvan Torrente, Milan, Italy](#)
- 10.40-11.10 COFFEE BREAK
- 11.10-11.40 Gene therapy for severe combined immunodeficiency  
[Claire Booth, London, UK](#)
- 11.40-12.10 Gene Therapy Approaches for Fanconi Anemia using Hematopoietic and Pluripotent Stem Cells  
[Juan Bueren, Madrid, Spain](#)
- 12.30-14.00 Lunch with "Meet the Expert" tables

**Session 2, Epithelia (sponsored by Holostem Therapie Avanzate)****Chair: [Enrique Amaya, Manchester, UK](#)**

14.00-14.30 YAP/TAZ-dependent depletion of epidermal stem cells in Junctional Epidermolysis Bullosa

[Michele De Luca, Modena, Italy](#)

14.30-15.00 Biomaterials as corneal regeneration templates in high risk transplantation cases

[May Griffith, Linköping, Sweden](#)

15.00-15.20 Epithelium Reconstruction of a Tissue Engineered Oesophagus Using Epithelial Stem/Progenitor Cells

[Paola Bonfanti, London, UK](#)

15.20-15.40 Mesoangioblasts - vessel associated progenitor cells- engraft epithelial tissues and express functional CFTR channel: prospects and promise for a cell therapy for Cystic Fibrosis

[Graziella Messina, Milan, Italy](#)

15.40-16.10 TEA BREAK

16.10-16.40 Gene therapy for recessive dystrophic epidermolysis bullosa

[Peter Marinkovich, Stanford, USA](#)

16.40-17.10 Hurdles in a successful example of limbal stem cell-based regenerative medicine

[Graziella Pellegrini, Modena, Italy](#)

**Special Session 1 (supported by EMBO Molecular Medicine)**

17.10-17.40 Scientific Publishing and Data Integrity

[Roberto Buccione, Heidelberg, Germany](#)

18.00-19.30 Poster Session

20.00- Dinner on own

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### Day 3 – Friday, September 11 2015

#### Session 3, Neuronal and Muscle Cells (sponsored by Duchenne Parent Project Italia)

Chair: [Roger Barker, Cambridge, UK](#)

- 09.00-09.30 Regenerating CNS myelin – from mechanisms to medicines  
[Robin Franklin, Cambridge, UK](#)
- 09.30-10.00 The role of neural stem cells in brain inflammation and regeneration  
[Gianvito Martino, Milan Italy](#)
- 10.00-10.30 Where are we with cell therapies for Parkinson's disease?  
[Roger Barker, Cambridge, UK](#)
- 10.30-10.50 Novel animal models reveal the impact of cyclosporine for cell therapy and neurorestoration in Parkinson's disease  
[Michael Decressac, Naples, Italy](#)
- 10.50-11.20 COFFEE BREAK
- 11.20-11.40 An in vivo humanized model for Alzheimer's disease from pluripotent stem cells  
[Ira Espuny, Leuven, Belgium](#)
- 11.40-12.10 Autologous myoblast cell therapy for oculopharyngeal muscular dystrophy (OPMD): a phase I/IIa clinical study with 24 patients now included  
[Gillian Butler-Browne, Paris, France](#)



12.10-12.40 Rebuilding the Heart via Paracrine Factor modRNA and Human Ventricular Progenitor Cell- Based Tissue Engineering  
[Kenneth Chien, Stockholm, Sweden](#)

12.40-14.15 Lunch with "Meet the Expert" tables

#### **Session 4, Bone cells**

**Chair: [Susan Kimber, Manchester, UK](#)**

14.15-14.45 Skeletal stem cells in biology and medicine  
[Paolo Bianco, Rome, Italy](#)

14.45-15.15 Regenerative Medicine & Tissue Engineering: Clinical Translation of Cell based Products for Skeletal Repair  
[Frank Luyten, Leuven, Belgium](#)

15.15-15.35 Developing scaffold free constructs for bone and cartilage tissue engineering through optimization of culture conditions for human periosteum-derived cells  
[Luis Mendes, Leuven, Belgium](#)

15.35-16.05 TEA BREAK

16.05-16.25 In vivo reprogramming to pluripotency enhances regeneration and functional rehabilitation of injured skeletal muscle  
[Irene de Lazaro, London, UK](#)

16.25-16.55 Development of bone marrow stromal cells as a cell therapy  
[Pamela Gehron Robey, Bethesda, USA](#)

16.55-17.15 Cartilage Repair Using Human Embryonic Stem Cell-derived Chondroprogenitors  
[Aixin Cheng, Manchester, UK](#)

#### **Special Session 2**

- 17.15-17.20 Keynote lecture presentation  
[Robin Franklin, Cambridge, UK](#)
- 17.20-18.20 Keynote Lecture: Stem cells - controlling the immune response  
[Kathryn Wood, Oxford, UK](#)
- 20.00- Conference Dinner
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## Day 4 – Saturday, September 12 2015

### Session 5, Ethics, Economics and Law

Chair: [David Napier, London, UK](#)

- 09.00-09.30 Stem Cells, Epigenetics, AI and our Future Worlds  
[John Harris, Manchester, UK](#)
- 09.30-10.00 Stem Cells, Regenerative Medicine, and Public Trust  
[David Napier, London, UK](#)
- 10.00-10.30 Stem cells, the dialectic of the possible and the real.  
Ethics on the move  
[Anne-Marie Moulin, Paris, France](#)
- 10.30-11.00 COFFEE BREAK
- 11.00-11.30 The best protection of individual rights and public good:  
scientific correctness  
[Amedeo Santosuosso, Pavia, Italy](#)
- 11.30-12.30 Round table: The challenges of Cell Therapy (Chair:  
David Napier)
- 12.30-14.00 Lunch

### Session 6, Cardiac and other cells

Chair: [Giulio Cossu, Manchester, UK](#)

- 14.00-14.30 Regulatory RNAs and Cardiovascular Regeneration  
[Stefanie Dimmeler, Frankfurt, Germany](#)
- 14.30-15.00 Cell therapy for muscular dystrophies: lessons learned and the road to efficacy  
[Giulio Cossu, Manchester, UK](#)
- 15.00-15.20 The importance of Epigenetics in stemness and differentiation  
[Ariane Chavgier, London, UK](#)
- 15.20-15.40 Mesenchymal stem cells overexpressing IL-13 decrease lesion size and demyelination after spinal cord injury  
[Dearvhaile Dooley, Hasselt, Belgium](#)
- 15.40-16.10 TEA BREAK
- 16.10-16.30 Human Artificial Chromosome-Mediated Genetic Correction of Human Dystrophic Skeletal Muscle Progenitors for the Autologous Cell Therapy of Duchenne Muscular Dystrophy  
[F. Saverio Tedesco, London, UK](#)
- 16.30-16.50 Cardiac stem cells cultured from aged donors with ischemic cardiomyopathy have an impaired regenerative capacity  
[Ghazaleh Rafatian, Ottawa, Canada](#)
- 16.50-17.20 iPSCs for Cardiac Disease Modeling and Drug Discovery”  
[Joseph Wu, Stanford, USA](#)
- 17.20-17.35 Concluding remarks and prizes (offered by e-Life)

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## Registration

### REGISTRATION DEADLINE

July 31, 2015

## ABSTRACT SUBMISSION DEADLINE

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## PAYMENT DEADLINE

July 31, 2015

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STUDENTS/POST DOC	ACADEMIC	INDUSTRY
€250	€430	€600

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Registration Fee includes:

- Coffee/Tea breaks, lunches, welcome cocktail and conference dinner

## PAYMENT

Please proceed with payment by clicking [here](#), after completion of the online registration procedure. Please note that successful payment is required to complete your registration and secure your place.

In addition to the substantially discounted registration rate for PhD students and Post-Docs, a number of travel bursaries will be made available to PhD students. Please manifest your interest after registration by contacting the meeting administrator at [janet.adnams@manchester.ac.uk](mailto:janet.adnams@manchester.ac.uk).

## SELECTION CRITERIA FOR ORAL PRESENTATIONS

The selection of speakers from the submitted abstracts will be based on scientific excellence and conceptual advance with preference for translational/pre-clinical work and cell therapy trials. However, we will give priority to oral presentations given by early stage researchers (post-docs) rather than PIs.

# Organizers

Giulio Cossu

University of Manchester, UK

Roberto Buccione

EMBO Molecular Medicine, Germany

Michele De Luca

University of Modena and Reggio Emilia, Italy

# Contact

Giulio Cossu

Email: [giulio.cossu@manchester.ac.uk](mailto:giulio.cossu@manchester.ac.uk)

# Venue

**Manchester Conference Centre,**

Weston Building, Sackville Street,

Manchester M13BB, UK

[website](#)



## HOW TO GET TO THE VENUE

### RAIL

#### FROM PICCADILLY STATION ON FOOT:

Head for the escalators to the left of the concourse. Follow the signs for Fairfield Road/ 'Taxis'.

Cross Fairfield Street to

the Bulls Head pub. To the left of the pub is Granby Row. Walk to the end of Granby Row and turn left onto Sackville

Street. Walk 250 yards and the Manchester Conference Centre will be on the right.

#### OXFORD ROAD STATION:

At the bottom of the station approach turn right onto Oxford Street. After 180 yards, cross Oxford Street and turn left

onto Charles Street. After 350 yards (at Retro Bar) turn right and the Manchester Conference Centre is on the right.

#### VICTORIA STATION:

Take the MetroLink Tram to Piccadilly Rail Station. Exit to the street at platform level following the signs for Fairfield

Road/ 'Taxis'. Cross Fairfield Street to the Bulls Head pub. To the left of the pub is Granby Row.

Walk to the end of

Granby Row and turn left onto Sackville Street. Walk 250 yards and the Manchester Conference Centre will be on the

right.

#### FROM THE NORTH VIA M6 M61:

Follow STRETFORD signs onto M60. Leave at Junction 12 and join M602 SALFORD. At end of Motorway, follow A57

MANCHESTER sign (Regent Road) for approx. 1 mile. Proceed under railway bridge, continuing onto A57M

(Mancunian Way). Continue on A57M and take 2nd exit. Immediately fork right on slip road onto Sackville Street,

following UNIVERSITY sign. Turn left at the Retro Bar onto Charles Street for the NCP CAR PARK.

FROM YORKSHIRE VIA M62/M60:

Leave at Junction 17 signed CITY CENTRE, and follow A56 towards Manchester for 4 miles (Bury New Road, becoming

Great Ducie St.) Enter city under railway bridges and keep straight ahead, still on A56, onto Deansgate. In 1/2 mile,

turn left at traffic lights (signed UNIVERSITIES) onto John Dalton Street and continue straight ahead at next lights

onto Princess Street. In 1/2 mile, pass under railway bridge and immediately turn left at lights onto Charles Street.

The NCP CAR PARK is on left.

FROM DERBYSHIRE VIA A6:

Follow A6 signs towards Manchester City Centre until reaching the flyover junction with A57M.

Continue on A6 and in

200 yards pass under railway bridge and turn left at traffic lights onto Fairfield Street. Pass Sackville Gardens on your

right, and turn left at traffic lights onto Sackville Street. Pass under railway bridge and turn right onto Charles Street.

for the NCP CAR PARK.

FROM THE SOUTH VIA M6 / NORTH WALES & CHESTER VIA M56:

Leave M6 at Exit 19 and follow A556 MANCHESTER for 4 miles. Join M56 MANCHESTER at roundabout and follow to

end of M56 and continue straight onto A5103 MANCHESTER for 4 miles. At roundabout take 3rd exit following A57M

SHEFFIELD to next roundabout. Here take 2nd exit up ramp to join A57M. Keep in nearside lane for 200 yards, and

leave 1st exit signed UNIVERSITY. Immediately fork right on slip road, following UNIVERSITY

sign. Turn left at the

Retro Bar onto Charles Street for the NCP CAR PARK.

FROM MERSEYSIDE VIA M62:

Leave at Exit 12 and join M602 MANCHESTER. At end of Motorway, follow A57 MANCHESTER sign (Regent Road) for

approx. 1 mile. Proceed under railway bridge, continuing onto A57M (Mancunian Way). Continue on A57M and take

2nd exit. Immediately fork right on slip road onto Sackville Street, following UNIVERSITY sign.

Turn left at the Retro

## ACCOMMODATION

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