Pyramidal Neurons Derived from Human Pluripotent Stem Cells Integrate Efficiently into Mouse Brain Circuits In Vivo

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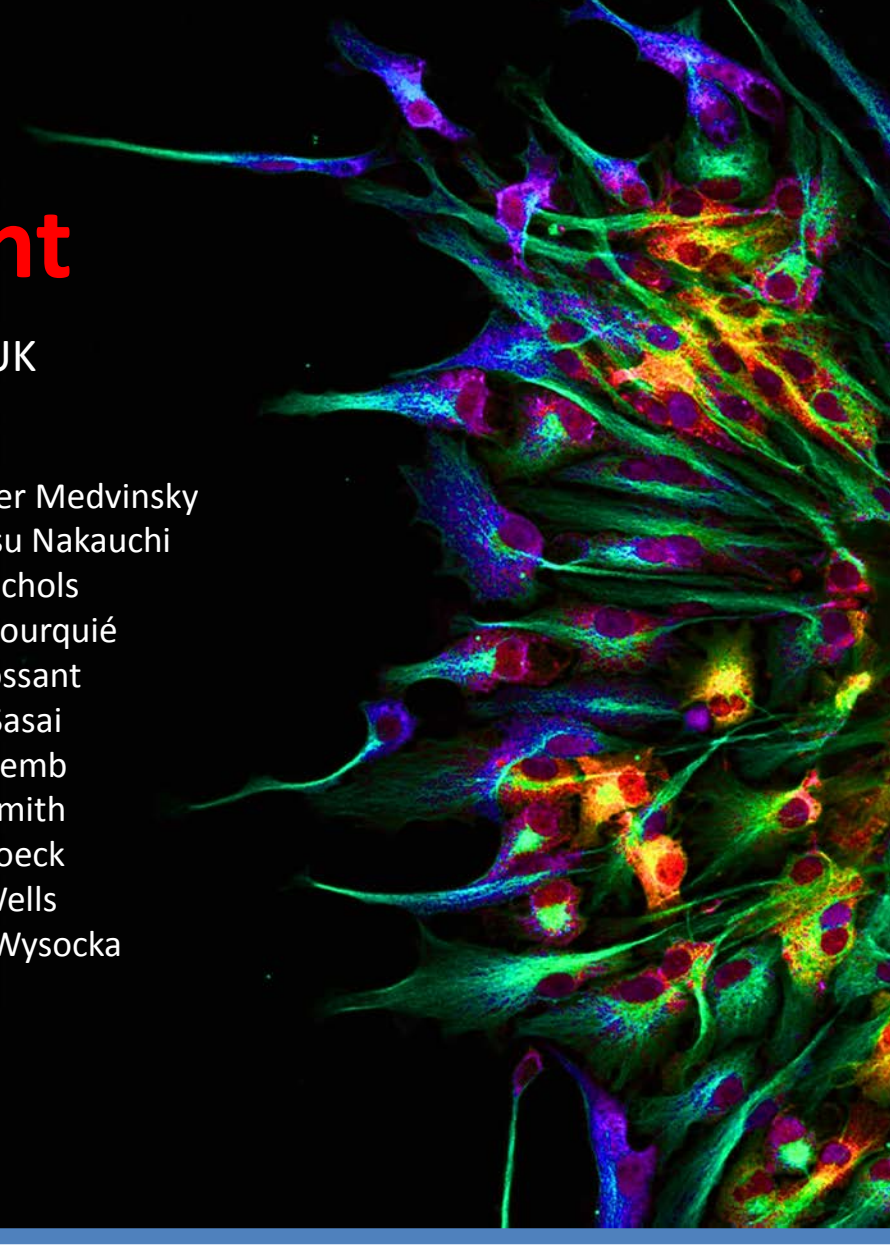
The generation of *in vitro* and *in vivo* models to study human cortical development is essential to address the molecular and cellular mechanisms involved in brain evolution as well as to elucidate major pathways affected in developmental and degenerative cortical diseases. Here we found that human embryonic (ESC) and induced pluripotent (iPSC) stem cells, cultured without added morphogens, recapitulate corticogenesis *in vitro* leading to the sequential generation of functional pyramidal neurons of all six layers identities. Following transplantation into the mouse neonatal brain, human ESC-derived cortical neurons integrated robustly and established specific axonal projections corresponding to native cortical neurons of diverse cortical layers and areas. Neuronal differentiation and connectivity complexified progressively over several months *in vivo,* culminating with the development of elaborate dendritic patterns, the presence of dendritic spines, and the establishment of reciprocal synapses with the host in a time dependent fashion highly reminiscent of the human species. Our data demonstrate that human cortical neurons generated *in vitro* from ESC/iPSC can develop complex hodological properties characteristic of the cerebral cortex *in vivo*, thereby offering unprecedented opportunities for the modelling of human cortex diseases, and brain repair.

Please, state why this workshop is useful for you:

My present research is focused on the modeling of human cortical development and the mechanisms altered in some of the diseases affecting the development or the aging cerebral cortex. My future career and work progress could profit from the study of different systems in vitro aiming to reproduce cortical organogenesis, as well as the study of the epigenetic programs determining fate determination in the embryo.

From Stem Cells to Human Development

21-24 September 2014 | Wotton House, Surrey, UK



Workshop topics

Pluripotency
In vitro organogenesis
Epigenetics of cell fate
Ectoderm derivatives
Endoderm derivatives
Mesoderm derivatives
Ethics of stem cell research

Confirmed speakers

Clare Blackburn
Benoit Bruneau
Elaine Dzierzak
Susan Fisher
Göram Hermerén
Danwei Huangfu
Insoo Hyun
Gordon Keller
Jürgen Knoblich
Arnold Kriegstein
Rick Livesey
Alexander Medvinsky
Hiromitsu Nakauchi
Jenny Nichols
Olivier Pourquié
Janet Rossant
Yoshiki Sasai
Henrik Semb
Austin Smith
Hans Snoeck
James Wells
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Provisional programme

Sunday 23 September 2018

11:00	**Registration opens**
12:30	**Lunch**
14:00	**Welcome**
14:15	**Antoon Moorman – Academic Medical Centre, The Netherlands** A 3D atlas of human development
14:45	**Alain Chédotal – Institut de la Vision, France** Tridimensional analysis of human embryogenesis
15:15	**Short talk selected from abstracts**
15:30	**Short talk selected from abstracts**
15:45	**Coffee**
16:15	**Janet Rossant – The Hospital for Sick Children, Canada** How closely do human and mouse pluripotent stem cell states reflect normal development?
16:45	**Short talk selected from abstracts**
17:00	**Ali Brivanlou – The Rockefeller University, USA** Self-organisation of spatial patterns in human embryos
17:30	**Alfonso Martinez Arias – University of Cambridge, UK** The self-organisation of the mammalian embryo: an *in vitro* approach
18:00	**Pre-dinner drinks and poster viewing**
19:30	**Dinner**

Monday 24 September 2018

07:00	**Breakfast**
09:00	**Kathrin Plath – University of California, Los Angeles, USA** Epigenetic regulation in early human development
09:30	**Short talk selected from abstracts**
09:45	**Short talk selected from abstracts**
10:00	**Alex Meissner – Max Plank Institute for Molecular Genetics, Germany** Epigenetic regulation in early human development
10:30	**Coffee**
11:00	**Mitinori Saitou – Kyoto University, Japan** Mechanism and *in vitro* reconstitution of human germ cell development

11:30	**Short talk selected from abstracts**
11:45	**Prisca Liberali* – Friedrich Miescher Institute for Biomedical Research, Switzerland** Self-organization and symmetry breaking in intestinal organoids development
12:15	**Aryeh Warmflash* – Rice University, USA** Micropatterned systems to study human self-organized developmental patterning
12:45	**Lunch**
14:00	**Matthias Lutolf – Ecole polytechnique fédérale de Lausanne, Switzerland** Engineering stem cell self-organisation
14:30	**Tracy Grikscheit – Children's Hospital Los Angeles, USA** Tissue engineering components of the gastrointestinal tract: from stem cells to organ development
15:00	**Fiona Watt – King's College London, UK** Studying cell transition states in mammalian epidermis
15:30	**Coffee**
16:00	**Christopher Walsh – Harvard Medical School, USA** Somatic mutation and cell lineage and the human brain
16:30	**Alex Pollen* – University of California, San Francisco, USA** Evolution and development of human radial glia
17:00	**Short talk selected from abstracts**
17:15	**Arturo Alvarez-Buylla – University of California, San Francisco, USA** Origin and self renewal of adult neural stem cells
17:45	**Poster session 1 and pre-dinner drinks**
19:45	**Dinner**

Tuesday 25 September 2018

07:00	**Breakfast**
09:00	**Melissa Little – Murdoch Children's Research Institute, Australia** Recreating human kidney tissue
09:30	**Christine Seidman – Harvard Medical School, USA** Steps and missteps in building a human heart
10:00	**Short talk selected from abstracts**
10:15	**Olivier Pourquié – Harvard Medical School/Brigham and Women's Hospital, USA** The human segmentation clock
10:45	**Coffee**

11:15	**Discussion session: Ethical issues relating to human embryo and stem cell research** **Chair: Robin Lovell-Badge – The Francis Crick Institute, UK**
12:45	**Lunch**
14:00	**Free time**
15:45	**Coffee**
16:15	**Neil Hanley – University of Manchester, UK** Integrated strategies to deconstruct human organogenesis
16:45	**Jason Spence – University of Michigan, USA** Interrogating endoderm lineage organ development using organoids and embryos
17:15	**Emma Rawlins – The Gurdon Institute, UK** Cell-cell interactions in normal human lung development
17:45	**Poster session 2 and pre-dinner drinks**
19:45	**Dinner**

Wednesday 26 September 2018

07:00	**Breakfast**
09:00	**Silvia Cappello – Max Planck Institute of Psychiatry, Germany** Dissecting molecular and cellular mechanisms of human migrating neurons
09:30	**Short talk selected from abstracts**
09:45	**Short talk selected from abstracts**
10:00	**Paola Arlotta – Harvard Medical School, USA** Understanding brain development: from the embryo to human brain organoids
10:30	**Coffee**
11:00	**Malin Parmar – Lund University, Sweden** Generation of authentic and subtype-specific neurons for effective brain repair
11:30	**James Wells – Cincinnati Children's Hospital Medical Center, USA** Human pluripotent stem cell-derived gastro-intestinal organoids: from organogenesis to personalised medicine
12:00	**John Dick – University Health Network, Canada** Backtracking human leukaemia evolution to a stem cell origin
12:30	**Closing remarks**
12:45	**Lunch & depart**

*These speakers are supported by The Company of Biologists' early career researcher programme.