Novel blood brain barrier model

Oxford academics have developed a fully defined protocol for generating brain microvascular endothelial cells from induced pluripotent stem cells.

The blood brain barrier (BBB) is primarily composed of brain microvascular endothelial cells (BMECs). These BMECs are connected by adherens and tight junctions resulting into high electrical resistance. They are functionally coupled with neurons, astrocytes, mural cells and extracellular matrix components to form so-called neurovascular units.

The BBB is of critical importance when designing and screening for potential therapeutics and many potential candidate drugs acting in the central nervous system will fail to provide their therapeutic effect if they are unable to cross the BBB in sufficient quantity. It is therefore crucial to study the BBB and transport mechanisms across it when developing new therapeutics. However, it is very difficult to do large scale drug screening to test if new molecules can cross the BBB using *in vivo* models, and hence there is a need for robust and accurate *in vitro* models.

Current barriers to success

Existing *in vitro* models have many drawbacks; they are difficult to reproduce, and often lack sufficient characteristics of a true BBB. The tight junctions between BMECs are often discontinuous in *in vitro* models and many models also show low trans-endothelial electrical resistance (TEER) measurements. Results from models using non-human mammalian cells often fail to translate to humans. Models that use human immortalised and primary cell lines poorly recapitulate normal physiology, have decreased barrier properties after removal from the brain microenvironment, and limited proliferative ability.

A model example

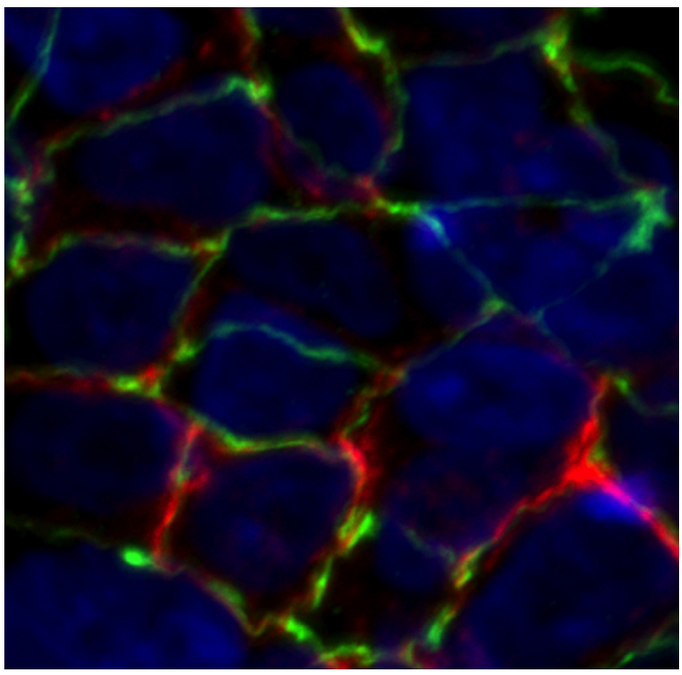
Oxford academics have developed a new protocol for generating BMECs from induced human pluripotent stem cells, for use in BBB models.

It offers many advantages over current methods:

- BMEC properties very similar to those *in vivo*
- Fully defined protocol
- High reproducibility with different IPSC lines
- Effective barrier formation – high TEER
- Cells can be used by themselves or co-cultured for a more representative *in vitro* BBB or neurovascular unit model

Commercialisation

The technology is subject to a patent application and is now available for license from Oxford University Innovation.



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