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Researchers develop novel cell line for screening of brain drugs

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Researchers from the Department of Pharmacy at the University of Copenhagen have developed a cell line, which may be used to investigate new drugs and help predict whether they are able to enter the brain.

The brain is protected by the so-called blood-brain barrier, a practically impermeable wall in the brain's blood vessels. This dense wall contains lots of proteins, which act as efflux pumps for numerous drug compounds. The research group modelled these two functions of the blood-brain barrier by genetically inserting the human efflux pump, P-glycoprotein, in a cell line with an almost impermeable barrier.

The new cell line can help other scientists and as well as the pharmaceutical industry when they investigate whether or not newly developed drug compounds can enter the brain as well as tumor tissue where the pump normally acts to keep drugs out. Long-term, these findings can also supporting the development of improved treatments for brain diseases such as Alzheimer's disease, Parkinson's disease and brain cancer.

The research has recently been published in the renowned pharmaceutical journal *Molecular Pharmaceutics*.

Different degrees of interaction

This new study combines an already existing approach where efflux

proteins are inserted in cell lines with culture protocols where only cells with high amounts of efflux pump proteins survive. The capability of these cells to form a tight barrier means that the cell line resembles the blood-brain barrier in terms of low permeability and high pump activity.

"We have developed a tool with the ability to distinguish between different degrees of interaction thus making the cell line valuable for drug discovery and drug development research, but also for simply investigating how P-glycoprotein works," says Group Leader Birger Brodin, Section of Pharmaceutical Design and Drug Delivery, Department of Pharmacy at University of Copenhagen.

"Think of the P-glycoprotein as a bouncer in a nightclub. The bouncer will recognize all unwanted guests and kick them out before they even enter the nightclub, or the brain in this case", adds Birger Brodin. "But if we can test which types of guests the bouncer will let into the club, before expensive and demanding experiments are performed in animals and humans, research can be performed faster and cheaper."

Potential benefits

This research will afford scientists in both academia and the medical industry a new tool for investigating drug uptake in brain tissue and tumors where P-gp is expressed. The cell line is developed in collaboration with Bioneer:FARMA, a business unit of Bioneer A/S. The research group believes that it holds great potential for applied use.

"This new cell line can be used in the selection of new drug compounds. Simple lab experiments using this cell line can indicate if new candidates are able to reach the target tissues or if they are being kept away by the multidrug resistance pump. Our hope is that other scientists will use the cell line and that the pharmaceutical industry will employ the cell line as a tool for screening studies of new drug candidates," Brodin concludes.

Provided by University of Copenhagen