

***inCerebro*TM In Vitro Brain Penetration Studies**

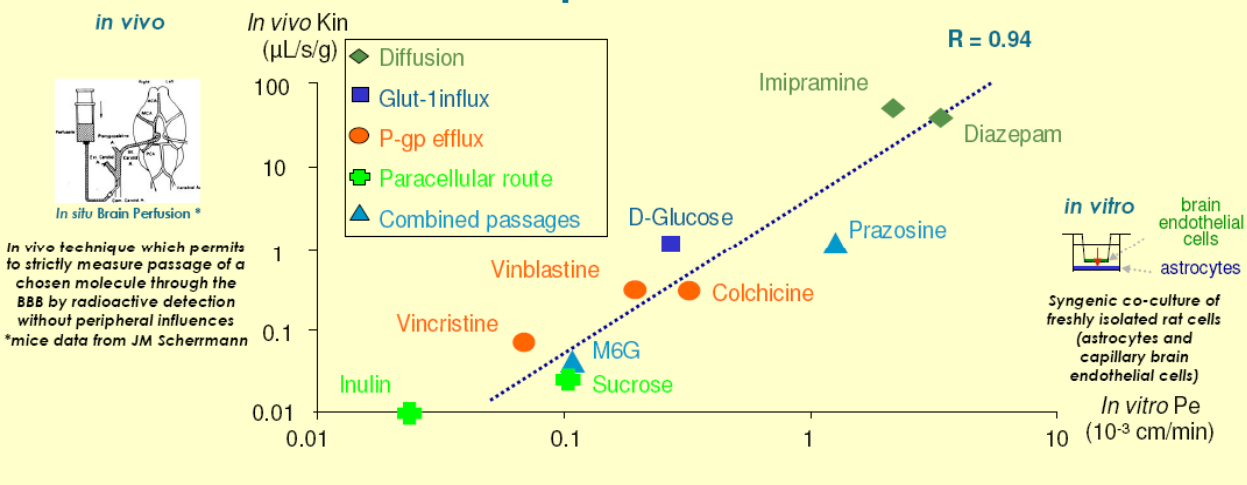
For CNS-targeted therapeutic compounds, penetration into the brain through the blood-brain barrier (BBB) is of utmost importance. Until recently, the toolkit for researchers has been limited to poorly performing *in vitro* systems, and/or *in vivo* studies relying on whole brain compound concentrations, surrogate measures such as cerebrospinal fluid (CSF) or technically demanding techniques such as quantitative microdialysis. The need for a suitable *in vitro* tool for quickly and reliably assessing the BBB penetrability of compounds has remained largely unmet.

The *inCerebro*TM Rat Brain Endothelial Cell Permeability Assay (RBEC) provides an ideal solution for an *in vitro* test system designed to characterize the BBB penetrability of compounds, which is well correlated to *in vivo* results.

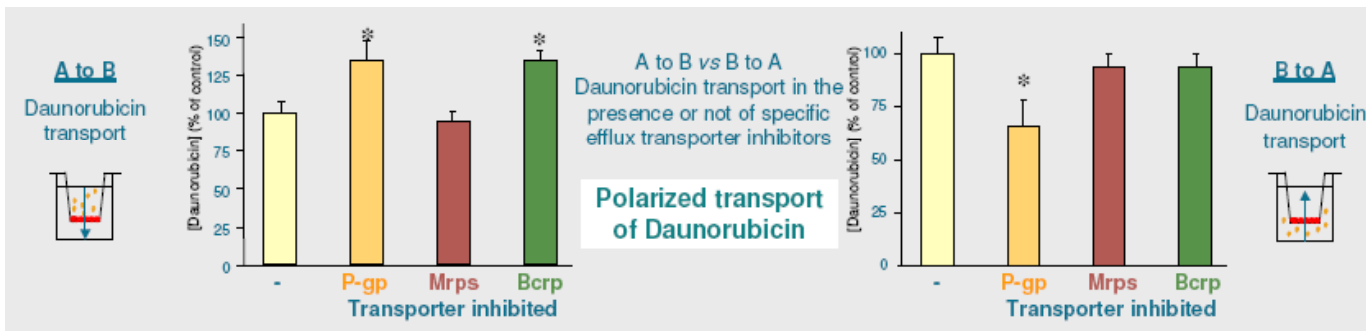
Highlights of the *inCerebro*TM RBEC Assay Include:

- ❖ Syngenic co-culture of freshly isolated primary rat brain endothelial cells and astrocytes, which forms tight-junctions and shows polarized transporter expression
- ❖ Cells are seeded on trans-well inserts at a defined cellular density for permeability assays and assays are performed within 11 days from isolation to avoid dedifferentiation
- ❖ Test articles are assayed in parallel without cells to account for non-specific binding, and TEER and Fluorescein controls are used to ensure the integrity of the membrane
- ❖ Permeability studies show good correlation with *in vivo* results, and experiments with specific transporter inhibitors can be done to characterize transporter interactions
- ❖ Permeability coefficients and clearance values are determined, which can be used in the *inCerebro*TM Physiologically Based Pharmacokinetic Model (PBPK), to yield a Brain/Blood concentration time course simulation

Predictive pharmacokinetics



Strong correlation between *in vitro* and *in vivo* permeabilities, independent of the passage mechanisms



In Vivo Confirmation

NoAb BioDiscoveries offers several *in vivo* rodent models to further characterize the brain disposition of compounds. These include Brain Perfusion, Whole Brain Collection PK studies, Serial CSF and Plasma Collection PK studies and Quantitative Microdialysis.

For more information please contact us at:

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