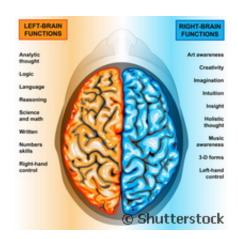


Breaking through the blood-brain barrier

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To mark the European Month of the Brain, we look at one EU-funded project that has focussed efforts on drug delivery across the so-called blood-brain barrier. The blood-brain barrier (BBB), while preforming a key protective function, is now recognised as the major obstacle in the treatment of most neurological disorders. It hinders the delivery of many potentially important therapeutic and diagnostic substances to the central nervous system (CNS).

Previous approaches to improving <u>drug delivery</u> have primarily been aimed at 'highjacking' the transcellular transport machinery that is dedicated to the selective transport of specific molecules across the BBB. These approaches have had limited success, especially with regard to drugs comprising large molecules.

Central to the problem are the cerebrovascular cell-to-cell junctions, which essentially decide what can pass through and what cannot pass through the BBB. Until recently, lack of knowledge of the molecular composition and functioning of these junctions has hampered the development of safe strategies for drug delivery.

Members of the JUSTBRAIN project ('Blood-Brain

Barrier Junctions as Targets for Paracellular Drug Delivery to the Brain'), with EUR 3 million in FP7 funding and coordinated by Professor Dr. Britta Engelhardt of the University of Bern, have accumulated crucial knowledge on the structure and function of BBB cell-to-cell junctions. They have identified cellular signals controlling the expression of individual junctional proteins and have begun to develop approaches to the opening or closing of BBB junctions.

Using in vitro and in vivo BBB models and animal models of neurological disorders, where BBB opening may be therapeutic, JUSTBRAIN has worked to identify an entire novel platform of drugable molecular targets that could be used to bypass the BBB. By these means, JUSTBRAIN expects to improve efficient delivery of large molecules into the CNS and thus to expand the diagnostic and therapeutic possibilities for neurological disorders.

There is a lack of therapies for most of these disorders, ranging from rare but fatal diseases such as primary brain tumours to major public health concerns such as brain metastases, multiple sclerosis, stroke or Alzheimer's disease. The delivery of effective diagnostic or therapeutic compounds into the brain remains a major challenge for medical science.

Current estimates show only 2 % of small-molecule drugs and even lower amounts of large-molecule drugs crossing the BBB, dramatically impeding the development of pharmacotherapies and immunotherapies in brain diseases.

By helping us to better understand the mechanisms involved in the delivery of drugs across the BBB, the JUSTBRAIN project is making a major contribution in this urgent field of study.

More information: JUSTBRAIN www.justbrain-fp7.eu/
University of Bern
www.zib.unibe.ch/content/index eng.html



Provided by CORDIS

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