What is the Blood-Brain-Barrier, what is its function and how does the Blood-Brain-Barrier affect the treatment of brain tumours?

The brain is a very unique organ with a specialized barrier that selectively restricts the movement of substances from the blood into the brain. This barrier is comprised of the endothelial cells that form the lining of blood vessel capillaries and astrocytes which come in contact with the blood vessels.

In contrast to organs where the endothelial cells are loosely arranged, brain endothelial cells have a very tightly arranged conformation which forms the physical basis of the Blood-Brain-Barrier (BBB). This barrier limits the movements of certain substances from the blood into the brain while allowing others. The BBB restricts molecules that are either large, highly charged or have low lipid solubility.

In some instances substances that do not meet the above criteria such as glucose can still be transported into the brain by specialized proteins. There are also specialized proteins such as the multidrug resistant (MDR) proteins which would actively pump some drugs out of the brain after crossing the BBB.

In terms of function, the BBB serves a very protective role by selectively excluding potentially harmful chemicals as well as maintaining a stable environment conducive for brain function. However, the BBB integrity can be comprised in certain conditions such as exposure to toxic substances, severe hypertension, brain injury, brain infections or tumours which can result in swelling and impairment of brain function.
The BBB clearly presents a significant challenge in the treatment of brain tumours with chemotherapy. Most systemically administered chemotherapy agents do not readily cross the BBB because of the physical restrictions of the BBB. The MDR protein further limits availability of chemotherapy within the brain.

Hence strategies to temporally disrupt the Blood-Brain-Barrier either by physical or chemical mechanism have been investigated as a means to improve delivery of chemotherapy into the brain. In addition, blocking the MDR protein with drugs such as verapamil is one strategy to increase the amount of chemotherapy delivered into the brain.

Most recently, there has been a focus on nanotechnology - whereby particle clusters at the atomic scale can be engineered to deliver drugs across the BBB by mechanism designed to overcome the physical and chemical restrictions of the BBB. The preliminary results of this new technology appear promising and could have significant implications for both the diagnosis and treatment of brain tumours.

A special thank you to Dr. James Rutka for taking the time to answer this important question. Dr. Rutka is a Professor for the Department of Laboratory Medicine and Pathobiology and Chairman of Division of Neurosurgery for the University of Toronto and Co-director of the Labatt Brain Tumour Research Centre at the Hospital for Sick Kids.

Dr. Rutka was awarded a 2009 Research Grant from Brain Tumour Foundation of Canada for his project entitled “Characterization of nanoparticle delivery across the blood brain barrier.” Dr. Rutka also volunteers for Brain Tumour Foundation of Canada as a member of our Professional Advisory Group.