NRC Institute for Biological Sciences (NRC-IBS)

Business Opportunity:

Vector Technology to Deliver Neurotherapeutics across the Blood Brain Barrier

The Business Opportunity:

The blood-brain barrier (BBB) prevents the access of a majority of small molecular weight therapeutics and virtually all biologics to the brain. NRC-IBS developed a platform technology to enhance the delivery of existing neurotherapeutics into the brain and to develop new blood-brain barrier-permeable biopharmaceuticals.

The Technology

The NRC-IBS technology exploits a process known as receptor-mediated transcytosis (RMT) across the BBB, which is amenable for delivery of both small molecular-weight therapeutics and biologics, including peptides, antibodies and RNA.

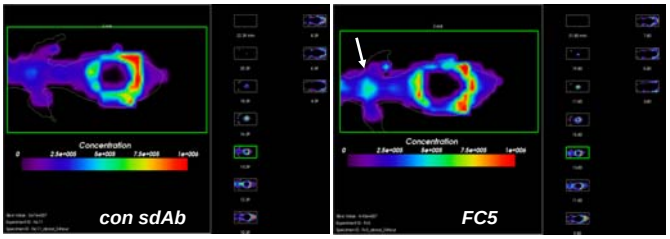
In contrast to the competing RMT BBB-delivery technologies which utilize transferrin receptor, insulin receptor or LRP1/2 receptor(s) expressed at the BBB to 'carry' molecules into the brain, NRC-IBS technology utilizes a novel, recently discovered receptor, involved in BBB RMT. Unlike other receptors listed above, which are highly expressed in peripheral organs and therefore lack selectivity, receptor exploited by NRC-IBS technology platform is highly enriched in the blood-brain barrier and up-regulated in specific brain diseases, which could enable selective brain targeting of drugs.

The NRC-IBS BBB-delivery technology platform is based on single-domain antibodies selected to bind to the novel receptor, internalize into the BBB cells and transmigrate across the BBB into the brain

Single-domain antibodies are small (13 kD), stable, and could be easily engineered for improved performance.

NRC-IBS BBB delivery single-domain antibody has been demonstrated in animal models to:

- Deliver imaging contrast agents across the intact BBB
- Deliver therapeutic peptides across the intact BBB
- Deliver nanoparticles carrying therapeutics across the intact BBB
- Deliver pharmacologically efficacious doses of neuro-peptides across the intact BBB
- Deliver cancer-targeting drugs across brain-tumor barrier



Brain delivery (arrow) of the optical contrast agent coupled to the BBB-transmigrating sdAb, FC5, but not with the control sdAb in live animal imaging.

Patent Position

- Patent applications are pending. NRC IBS cases 11085, 11750 and 11865.

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Select Publications

- Muruganandam et al., *Selection of phage-displayed llama single-domain antibodies that transmigrate human blood-brain barrier endothelium. FASEB J* 16:240-242
- Abulrob A et al., *The blood-brain barrier transmigrating single domain antibody: mechanisms of transport and antigenic epitopes in human brain endothelial cells.* J Neurochem. 95:1201-1214.

The Market

The therapeutic market for neurodegenerative diseases is vast and requires the capacity for the compound to cross the BBB and reach the target in the brain. An effective system to transport the therapeutic agents, in particular emerging biologics, into the brain will have a broad market potential.

Technology Transfer Possibilities

- BBB-transmigrating single-domain antibodies are available for non-exclusive licensing for specific application.
- Co-development of new neurotherapeutics incorporating BBB-transmigrating single-domain antibody technology is possible through collaborative agreements.

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