New molecule sneaks medicines across the blood/brain barrier

October 30 2014

Delivering life-saving drugs across the blood-brain barrier (BBB) might become a little easier thanks to a new report published in the November 2014 issue of *The FASEB Journal*. In the report, scientists describe an antibody, called "FC5," is one-tenth the size of a traditional antibody and able to cross the BBB. Moreover, FC5 uses the same pathways as nutrients that the brain needs to survive, allowing it to "smuggle" larger antibodies across the barrier. Like a Lego building block, FC5 connects into many types of antibody designs, helping them reach their disease targets in the brain. This research could lead the way for the development of new therapies to fight a wide range of brain diseases, such as Alzheimer's, Parkinson's, cancer, epilepsy, genetic brain diseases, neurodegenerative disease, chronic neuropathic pain, and other conditions.

"Neurological diseases are often devastating for both the affected person and their families. Current treatments are unsatisfactory and have many side effects, and the development of precise, new medicines has so far been unsuccessful because it is difficult or impossible to deliver enough medicine into the brain," said Danica B. Stanimirovic, Ph.D., a researcher involved in the work from the Human Health Therapeutics Portfolio at the National Research Council of Canada in Ottawa, Ontario. "With the technology developed in this collaborative work, we hope to open up opportunities for many promising treatments, including antibodies, against neurological diseases to be evaluated in clinical trials and eventually become available to patients."

To make their discovery, Stanimirovic and colleagues attached FC5 to a larger molecule in different configurations and then tested it in cell models and in rats to determine if it was transporting the larger molecules across the BBB. They also incorporated a peptide (a small protein) into the larger molecule being transported by FC5. This peptide was a pain-fighting molecule that cannot enter the brain by itself through the bloodstream. This FC5-peptide combination was injected into the bloodstream and the pain-fighting peptide crossed the BBB to reach the brain.

"The blood-brain barrier is such a robust security system that it should make today's computer programmers and engineers envious," said Gerald Weissmann, M.D., Editor-in-Chief of *The FASEB Journal*. "Unfortunately for us, this security system might be a little too good in the sense that it makes it extremely difficult to deliver drugs to the brain. This report may finally offer the key to unlocking a wide range of therapies that could dramatically improve millions of lives."

More information: Graham K. Farrington, Nadia Caram-Salas, Arsalan S. Haqqani, Eric Brunette, John Eldredge, Blake Pepinsky, Giovanna Antognetti, Ewa Baumann, Wen Ding, Ellen Garber, Susan Jiang, Christie Delaney, Eve Boileau, William P. Sisk, and Danica B. Stanimirovic. A novel platform for engineering blood-brain barrier-crossing bispecific biologics. *FASEB J.* November 2014 28:4764-4778; DOI: 10.1096/fj.14-253369

Provided by Federation of American Societies for Experimental Biology