New method for efficiently transporting antibodies across the blood-brain barrier reported

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Today the scientific journal *Neuron* published results on the Roche-designed Brain Shuttle technology that efficiently transfers investigational antibodies from the blood through the blood-brain barrier (BBB) into the brain in preclinical models. Roche Pharma Early Research and Development (pRED) scientists found that such enhanced transfer of antibodies through the BBB was associated with a marked improvement in amyloid reduction in the brain of a mouse model of Alzheimer's disease.

"Thanks to our sophisticated protein engineering we were able to design a system that exploits natural transport mechanisms to significantly increase the transfer of investigational antibodies into the brain in preclinical models," said Luca Santarelli, Head of Neuroscience, Ophthalmology and Rare Diseases at Roche pRED. "Using Roche's Brain Shuttle technology, the target engagement of investigational antibodies in the brain in a preclinical model was increased by over 50-fold compared to the parent antibody."

The BBB is a selective interface that restricts movement of molecules between the bloodstream and central nervous system. This barrier imposes a major challenge to the development of therapies for neurological diseases, in particular large molecules, due to the limited ability with which they can penetrate through the BBB. The study published in *Neuron* showed that the Roche Brain Shuttle acts by engaging the natural transferrin receptor (TfR) in a specific mode that triggers a process called receptor-mediated transcytosis to transport molecules into the brain.

"The efficacy of the Brain Shuttle technology in preclinical models suggests that this approach could deliver therapeutic molecules across the BBB. We will continue to investigate the potential of the Brain Shuttle technology to transport a variety of molecules such as growth factors, antibodies, peptides and oligonucleotides across the BBB," said Anirvan Ghosh, Head Neuroscience Discovery at Roche pRED.

"If we are able to clinically validate the preclinical results observed with the Brain Shuttle technology, it could lead us to a way to test investigational drugs in a variety of brain disorders," said Per-Ola Freskgard, the Preclinical Project Leader for this technology platform at Roche pRED.

More information: Niewoehner et al., Increased Brain Penetration and Potency of a Therapeutic Antibody Using a Monovalent Molecular Shuttle, *Neuron* (2014), dx.doi.org/10.1016/j.neuron.2013.10.061

Provided by Roche