Sights set on the next generation of shuttle peptides to target the brain

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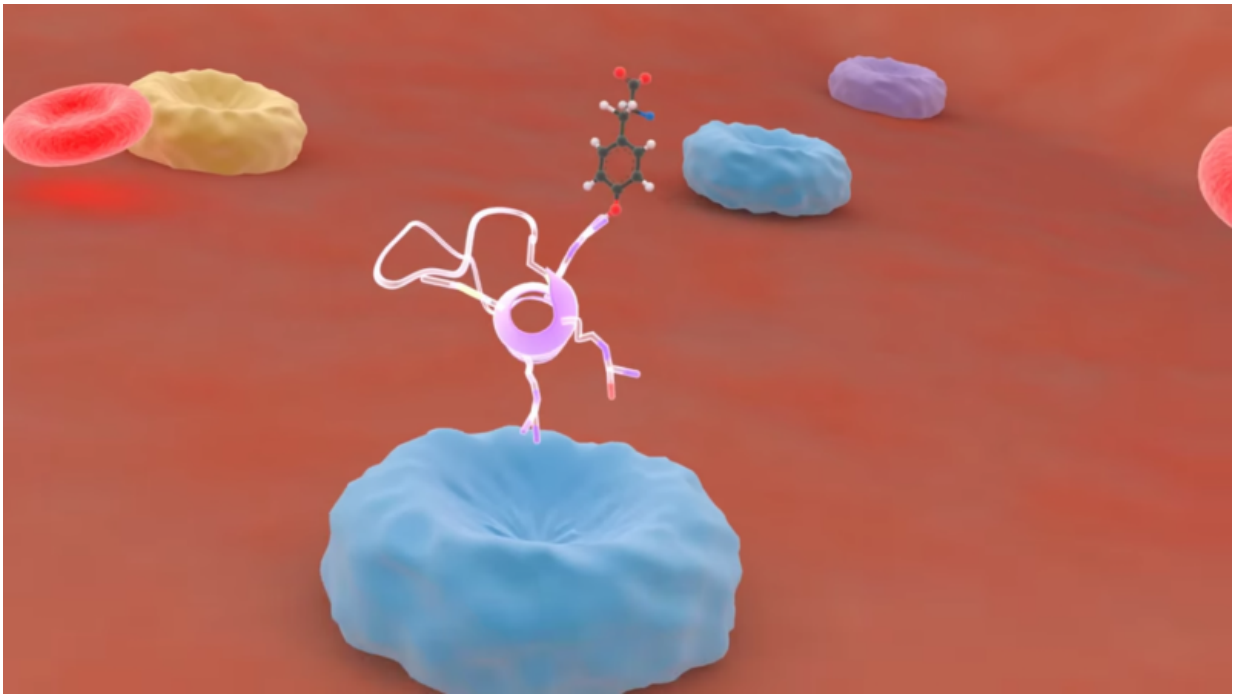

Shuttle peptides are molecules that have the capacity to transport drugs across the blood-brain barrier and thus treat diseases affecting the central nervous system. Credit: Institute for Research in Biomedicine-IRB

IRB Barcelona scientists Benjamí Oller, Macarena Sánchez, Ernest Giralt, and Meritxell Teixidó, all from the Peptides and Proteins Lab of the Chemistry and Molecular Pharmacology Programme, have written a review on the emerging field of shuttle peptides—molecules that have

the capacity to transport drugs across the blood-brain barrier and thus treat diseases affecting the central nervous system. The article will be featured on the cover of September's issue of *Chemical Society Reviews*.

Ten years ago, IRB Barcelona group leader Ernest Giralt started work on peptide shuttles to overcome the blood-brain barrier— a line of research that Dr. Meritxell Teixidó is now in charge of. In this regard, they are one of the few expert groups worldwide in this field, which brings together chemistry, pharmacy and biomedicine. In this period, researchers at IRB Barcelona have published 15 scientific articles and hold 4 patents, thus contributing to the development of the field and becoming an international reference on this topic.

Objective: the brain

The article highlights that the administration of drugs to the brain is one of the main challenges of drug development, given the significant number of patients with neurological diseases and the low efficiency of the treatments currently available. Although the barrier that protects the brain—known as the blood-brain barrier (BBB)—limits the capacity of drugs—many with great potential—to reach their target, molecular peptide vectors, known as BBB shuttles, are emerging as a promising tool to overcome this obstacle.

In recent years, transporters based on peptides—small proteins—are attracting attention in the field due to their low production cost, small effect on immune system response, and chemical versatility compared with traditional antibodies and other larger proteins.

The review article presents the BBB as a formidable obstacle but at the same time a great opportunity for the administration of drugs to the brain. The review provides an introduction to the concept of peptide shuttles and makes reference to the most important ones, paying special

mention to two peptides that have reached clinical assays.

It then goes on to explain thee examples of shuttles that highlight the main advances in relation to several types of cargo that they can transport, and some basic features to be viable as drugs, such as protease-resistance, which allows long life in blood. The researchers finally describe current trends and challenges to tackle to achieve the next generation of shuttle peptides.

More information: Benjamí Oller-Salvia et al. Blood–brain barrier shuttle peptides: an emerging paradigm for brain delivery, *Chem. Soc. Rev.* (2016). DOI: 10.1039/C6CS00076B

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