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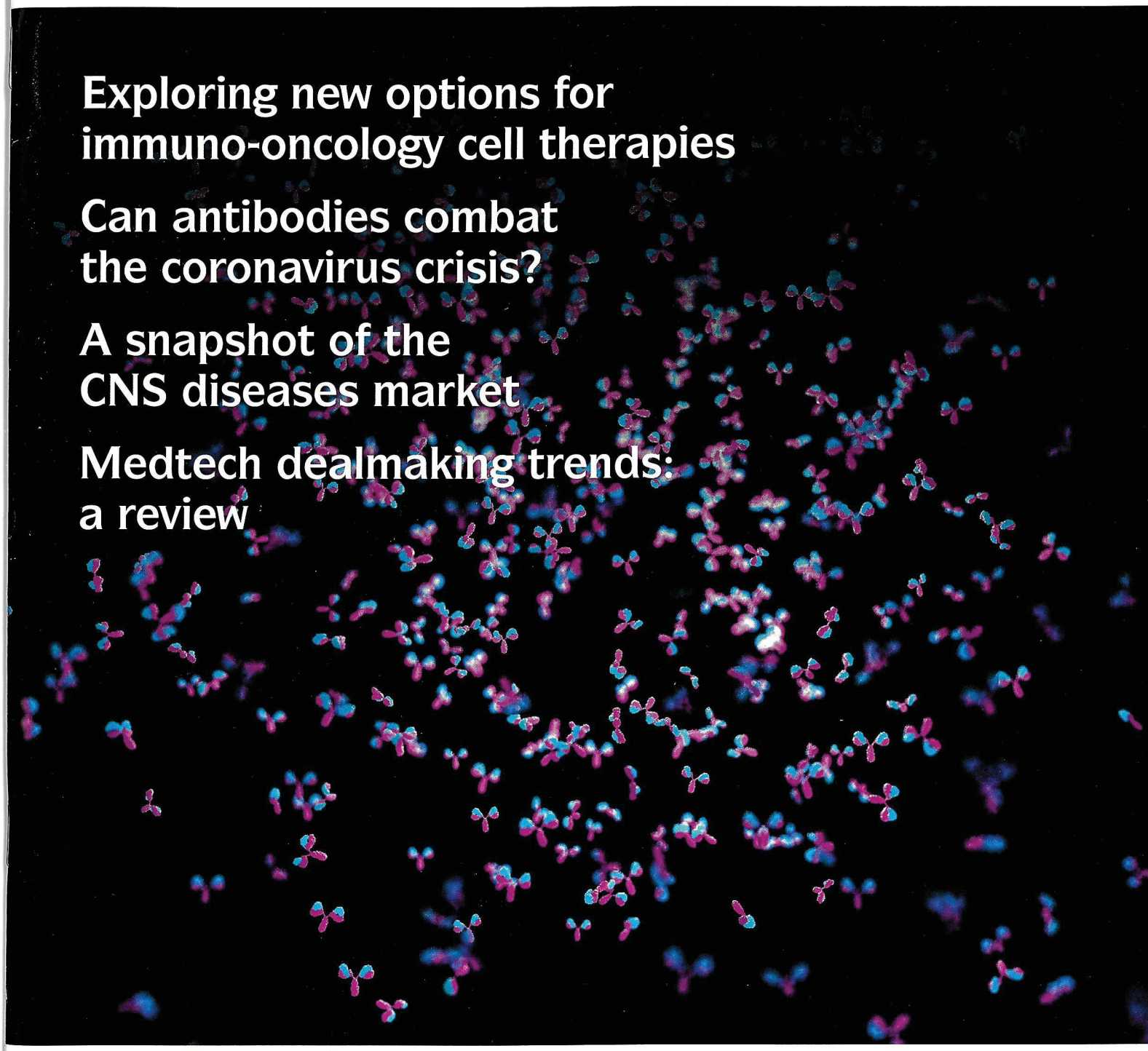

Exploring new options for immuno-oncology cell therapies

Can antibodies combat the coronavirus crisis?

A snapshot of the CNS diseases market

Medtech dealmaking trends: a review

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Vect-Horus
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VECT-HORUS
BREAKING BARRIERS

Customized vectors for targeted drug delivery

Vect-Horus' versatile drug targeting technology uses receptor-mediated transport to deliver drugs or imaging agents to the brain and cancer tissues.

The delivery of therapeutics to target areas continues to be a challenge for drug developers. Getting drugs to their site of action is crucial to increase their efficacy and reduce toxicity. In the case of drugs developed for central nervous system (CNS) conditions such as Alzheimer disease and Parkinson disease, getting through the blood–brain barrier (BBB) is a major hurdle.

The endothelial cells of blood vessel walls that constitute the BBB protect the brain from toxic molecules, viral and bacterial infections, but also restrict the ability of molecules with therapeutic potential to transfer from the blood into the CNS.

"It is estimated that 98% of drugs don't reach the brain," said Jamal Temsamani, Director of Drug Development at Vect-Horus. This results in low clinical efficacy and safety concerns owing to the need for high dosage, as well as high attrition rates for CNS drug developers.

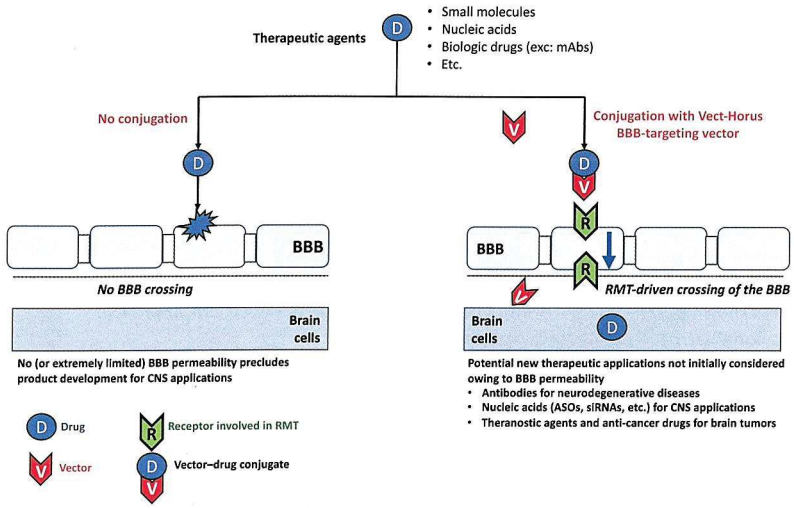

Fig. 1 | Vect-Horus conjugates therapeutic drugs and imaging agents to vectors targeting blood–brain barrier (BBB) receptors for receptor-mediated transcytosis (RMT). ASO, antisense oligonucleotide; CNS, central nervous system; mAB, monoclonal antibody; siRNA, short interfering RNA.

BBB-targeted drug-conjugated vectors

To address this problem, Vect-Horus, a biotechnology company founded in 2005 as a spin-off from the Institute for Neurophysiopathology at Aix Marseille University, directed by Michel Khrestchatisky and co-founded with Alexandre Tokay, CEO, is developing drug-conjugated vectors that bind to BBB receptors with high-affinity, triggering transport into and across cells (Fig. 1).

"We are developing peptide and nanobody vectors that bind to well-defined receptors expressed by cells lining the BBB that facilitate the entry of essential nutrients such as transferrin, insulin or cholesterol particles," explained Temsamani. Vect-Horus has demonstrated how small peptides that target the low-density lipoprotein (LDL) receptor can be coupled with drugs and transported across the BBB[1].

More recently, the company has been working on antibody fragments consisting of a single variable domain on heavy chain (VHH) antibodies (nanobodies) that target the transferrin receptor, which is responsible for the transport of iron into the brain, as another type of vector to deliver drugs to the CNS.

Both LDL and transferrin receptors can induce receptor-mediated transcytosis (RMT), a process involved in the transport of ligands from the blood to brain tissue.

"RMT is believed to be the most effective and safest physiological pathway for the transport of endogenous substances into or across cells," said Temsamani. Vect-Horus has already established proof-of-concept of its technology in animal models by conjugating different types of molecules (small molecules, short interfering RNAs (siRNAs), peptides and large biomolecules) to its vectors.

Because some of these receptors are also highly expressed in certain cancers, Vect-Horus is exploring the use of its vectors to deliver drugs and imaging agents to tumors.

In collaboration with RadioMedix, a US-based radiopharmaceutical company, the company is co-developing a theranostic agent for an especially aggressive form of brain cancer, glioblastoma. The agent comprises a peptide vector that targets the LDL receptor coupled to a radionuclide-chelating agent for imaging or radiotherapy. "Following successful in vitro and in vivo studies in animals, we are expecting to start phase 1 clinical trials next year and to expand the use of our technology for other cancer indications," Temsamani explained.

Introducing VECTrans

Vect-Horus' unique technology platform, VECTrans, is dedicated to the discovery and optimization of innovative drug delivery vectors and is available for pharmaceutical and biotech companies looking for efficient ways to transport their drug or imaging agent to target tissues.

"At Vect-Horus we develop each vector–payload complex on a case-by-case basis, so drugs are coupled to the most appropriate vector," said Temsamani. Unlike competitors that focus on one type of vector or one type of receptor, VECTrans offers unmatched flexibility. The vectors target well-defined human and mouse receptors without interfering with natural ligand binding, to aid clinical translation. Furthermore, they can be coupled via chemical conjugation or genetic engineering to drugs and imaging agents that range from small organic molecules, peptides and nucleic acids to therapeutic proteins and antibodies. "The highly versatile nature of our vectors means they can be used for a wide range of therapeutics and for the treatment of different disease indications," Temsamani added.

Vect-Horus operates a hybrid or mixed business model that relies on: the development of an internal pipeline of products that combine its vectors with molecules, with the aim of out-licensing them to pharmaceutical or biotech companies following preclinical or early clinical studies; and establishing R&D collaborations with industrial partners to target their drugs to the brain and other organs.

To date, Vect-Horus has set up 10 collaborative programs with companies developing CNS drugs, cancer drugs and theranostic agents and is seeking to establish further strategic partnerships to improve the delivery of therapeutic or imaging candidates for indications with strong unmet medical needs.

1. Molino, Y. et al. Use of LDL receptor-targeting peptide vectors for in vitro and in vivo cargo transport across the blood-brain barrier. *FASEB J.* **31**, 1807–1827 doi:10.1096/fj.201600827R (2017).

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