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## **NEO100**

Intracarotid injection of mannitol has been applied for decades to support brain entry of therapeutics that otherwise do not effectively cross the blood-brain barrier (BBB). However, the elaborate and highrisk nature of this procedure has kept its use restricted to well-equipped medical centers. Wang et al. are developing a more straightforward approach to safely open the BBB, based on the intraarterial (IA) injection of NEO100, a highly purified version of the natural monoterpene perillyl alcohol.

In vitro barrier permeability with NEO100 was evaluated by transepithelial/transendothelial electrical resistance (TEER) and antibody diffusion assays. Its mechanism of action was studied by western blot, microarray analysis, and electron microscopy. In mouse models, we performed ultrasound-guided intracardiac administration of NEO100, followed by intravenous application of Evan's blue, methotrexate, checkpoint-inhibitory antibodies, or chimeric antigen receptor (CAR-T) cells.

NEO100 opened the BBB in a reversible and non-toxic fashion in vitro and in vivo. It enabled greatly increased brain entry of all tested therapeutics and was well tolerated by animals. Mechanistic studies revealed effects of NEO100 on different BBB transport pathways, along with translocation of tight junction proteins from the membrane to the cytoplasm in brain endothelial cells.

They envisioned that this procedure can be translated to patients in the form of transfemoral arterial catheterization and cannulation to the cerebral arteries, which represents a low-risk procedure commonly used in a variety of clinical settings. Combined with NEO100, it is expected to provide a safe, widely available approach to enhance brain entry of any therapeutic <sup>1)</sup>.

Wang W, Marín-Ramos NI, He H, et al. NEO100 enables brain delivery of blood-brain barrier-impermeable therapeutics [published online ahead of print, 2020 Sep 2]. Neuro Oncol. 2020;noaa206. doi:10.1093/neuonc/noaa206

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