



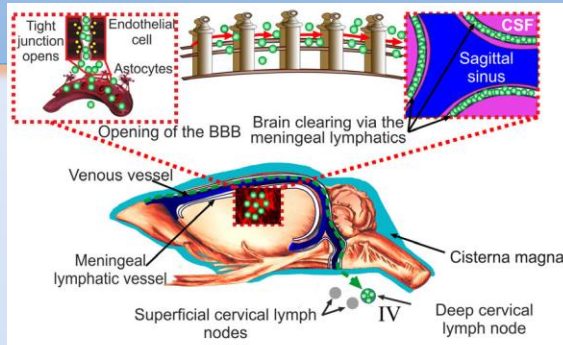
OPTIMIZATION OF PHOTODYNAMIC OPENING OF BLOOD-BRAIN BARRIER

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It is known that BBB is the natural restriction between the brain and the blood flow, that's why our main aim is to find a way to overcome this gatekeeper and use it for effective treatment of brain diseases. According to our previous researches, blood-brain barrier is the key to the brain clearance.

The recently rediscovered meningeal lymphatic system (MLS) opens new insight into pathways of brain clearing and drainage functions that play an important role in neurorehabilitation.

Here we demonstrate photostimulation (PS, 1268 nm) of clearing and drainage function of MLS in healthy male mice.



Methods

Assessment of BBB permeability

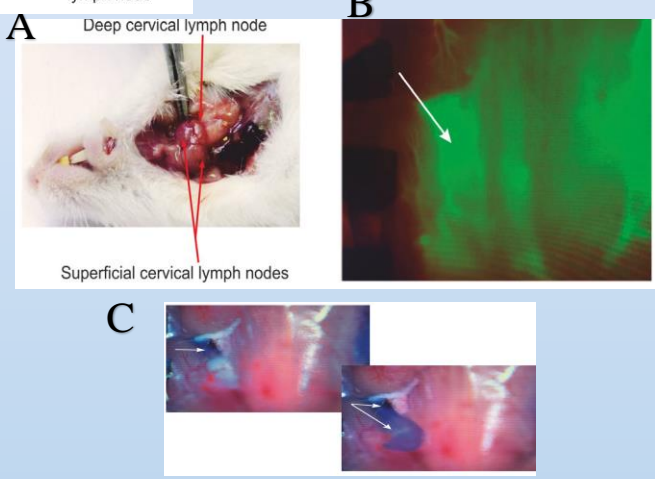
To analyze the BBB permeability in cortical region of the brain to high molecular weight molecules, we used two methods:

- A spectrofluorometric assay (SFA) of extravasation of the EB-albumin complex 68.5 kDa (EBAC).
- a confocal imaging of extravasation of TRITC-dextran 70 kDa (TRITCD).

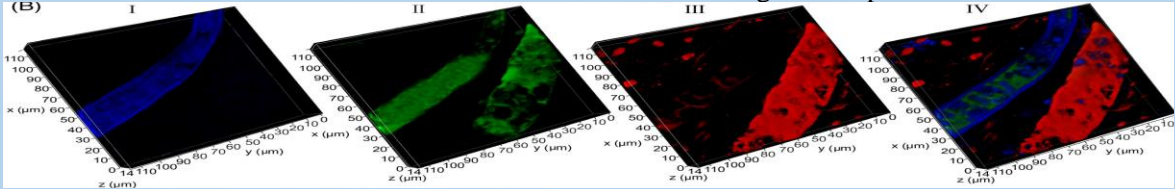
Analysis of clearing functions of MLS

For confocal analysis of MLVs, we used the protocol for the immunohistochemical (IHC) analysis with the marker LYVE1 (eBioscience, San Diego), for labeling of the cerebral vessels we used goat anti-mouse NG2 antibody (Abcam, Cambridge, UK).

Results



The clearance of FITCD via the lymphatic system: A – The anatomical position of dCLN; B – fluorescent imaging of FITCD accumulation in dCLN after its crossing of the opened BBB.



The confocal imaging of clearance of FITCD (green) via MLVs (blue): I-MLVs marked by Lyve-1, II-FITCD filled MLV and the cerebral vessel; III-the cerebral vessel marked by NG2, IV-the image merged from I-III.

Conclusion

In our preliminary data we demonstrate that MLVs are pathway of clearance of blood from the brain after intracranial hemorrhages in mice. The PS-stimulation of lymphatic drainage can be breakthrough technology for preventing and treatment of difficult to treat brain edema.

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