経鼻投与における JAL-TA9 の脳内輸送

Delivery of JAL-TA9 to the brain by nasal application

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We have reported on two Catalytides (Catalytic peptides), JAL-TA9 (YKGSGFRMI) and ANA-TA9 (SKGQAYRMI). Both peptides belong to the Tob/BTG family proteins and cleave Aβ42 [1, 2]. Although Catalytides must be delivered to the brain parenchyma to treat Alzheimer's disease, the blood-brain barrier (BBB) limits their entry into the brain from the systemic circulation. Thus, we evaluated the direct route of ANA-TA9 from the nasal cavity to the brain to bypass the BBB [3]. In this study, we present our findings on JAL-TA9. Animal studies using rats and mice clarified that the plasma clearance of JAL-TA9 was more rapid than its in vitro degradation in plasma, whole blood, and cerebrospinal fluid (CSF). After nasal administration of JAL-TA9, brain concentrations were significantly higher than after intraperitoneal administration, despite much lower plasma concentration. This observation strongly suggests direct delivery of JAL-TA9 to the brain from the nasal cavity. Similar findings were observed for its transport to CSF after nasal and intravenous administration. The concentration of JAL-TA9 in the olfactory bulb peaked at 5 min, while those in the frontal brain peaked at 30 min and in the occipital brain at 60 min. In conclusion, JAL-TA9 was efficiently delivered to the brain by nasal application compared to other routes.

[1] Hatakawa *et al.*, *Heliyon*, **5**, e02454 (2019)

[2] Hatakawa *et al.*, *Alzheimers Dement. (N Y)*, **7**, e12146 (2021)

[3] Hatakawa *et al., Pharmaceutics,* **13,** 1673 (2021).