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Purpose of Research

Most of the intranasal formulations for improved CNS delivery have not been put to practical use. This is primarily because the anatomical features of the human nasal mucosa have not been taken into consideration. The nasal mucosa consists of the olfactory epithelium and respiratory epithelium, each of which accounts for approximately 50% in rodents. In humans, on the other hand, the olfactory epithelium accounts for 2% and the respiratory epithelium for 98%. We created neuropeptides containing various functional sequences, seeking to develop the central delivery technology via the trigeminal nerve in the respiratory epithelium.

Summary of Research

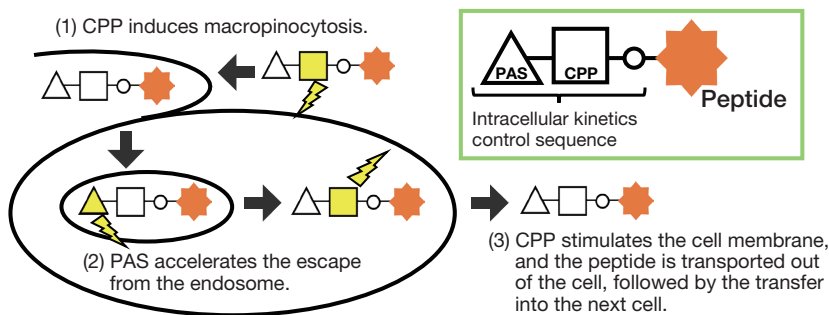


Fig. 1. Concept of derivatization

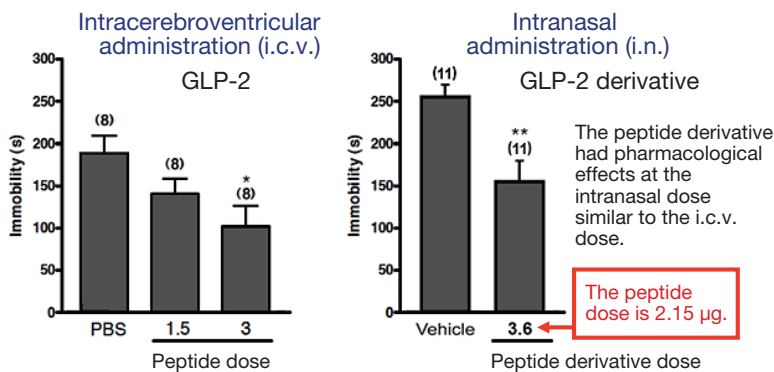


Fig. 2. Pharmacological effects by different administration routes

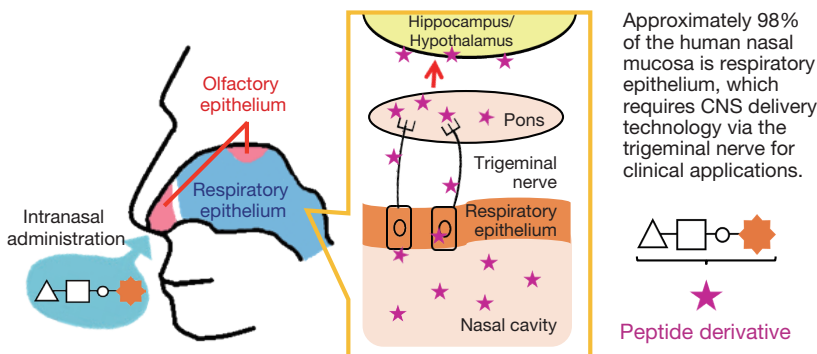


Fig. 3. Delivery route of peptide derivative to the CNS

Results

- Peptide derivatives are taken up by macropinocytosis and efficiently escape from endosomes.
- Peptide derivatives had CNS effects at the intranasal dose similar to the i.c.v. dose.
- The novel central delivery technology was used for intranasal administration to achieve CNS effects via the trigeminal nerve.
- The same results have been demonstrated with other peptides.

Points

- **Macropinocytosis that can take up 1-µm particles is expected to be applied to nucleic acids and antibody drugs as well as peptides and proteins.**
- **The central delivery technology of neuropeptides via the trigeminal nerve that is suitable for the human nasal mucosa is the first successful technology of its kind in the world.**

- Patent:
C. Yamashita et al., US2017/0253643
C. Yamashita et al., EP 3 190 129, 2017
- Applicants:
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