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〈講　　演〉

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ヒット化合物から開発化合物まで
――止痒薬の開発を例として――

長瀬　博*

Design and Synthesis of κ-Opioid Receptor Agonist, TRK-820

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Abstract

A new type of κ-agonist, TRK-820, was designed and synthesized on the basis of message-address concept and accessory theory. A unique structural feature of TRK-820, which is different from other prototypical κ-opioid receptor agonists, is existence of the 4,5-epoxymorphinan structure with a tyrosine–glycine moiety for endogenous opioid peptides such as dynorphin. TRK-820 exhibited high potency and high κ-selectivity in *in vitro* assay. In the mouse acetic acid-induced writhing model and mouse tail flick model of antinociception, TRK-820 was 85–140 times more potent than morphine and 85–350 times more potent than U-50488H. This novel κ-agonist showed neither preference nor aversion in Conditioned Place Preference test, which means this compound has no dependence and psychotomimetic effect. This compound was found to have antipruritic effect and is now on clinical study (phase 3) for patients with uremic pruritus.

Key words: opioid, TRK-820, κ-agonist, antipruritus, no dependence.