論文 / 著書情報
Article / Book Information

題目(和文)	新規鋤鼻受容体候補分子ancV1Rの機能解明
Title(English)	Functional analyses of a novel putative vomeronasal receptor ancV1R
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種別(和文)	論文要旨
Type(English)	Summary

（博士課程）
Doctoral Program

論 文 要 旨

THESIS SUMMARY

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学生氏名： Student's Name	近藤 宏	審査員主査： Chief Examiner	廣田 順二

要旨（英文 800 語程度）
Thesis Summary（approx.800 English Words ）

In many animal species, the perception of pheromones is crucial for regulating sexual and social behaviors. In terrestrial vertebrates, the vomeronasal organ (VNO) predominantly detects pheromones. Within the VNO, vomeronasal sensory neurons (VSNs) express vomeronasal receptors (V1Rs and V2Rs) that mediate pheromone detection. Generally, *V1R* genes exhibit significant variation in number and repertoire among species.

Recently, an exceptionally conserved *V1R* gene, referred to as "*ancient V1R* (*ancV1R*)", was identified. This gene is shared across bony vertebrates, ranging from the basal lineage of ray-finned fishes to mammals. *AncV1R* remains intact in all species with functional VNOs but becomes pseudogenized in species with degenerated VNOs. Notably, *ancV1R* is expressed in the majority of VSNs and co-expressed with canonical *V1R*s and *V2R*s. This expression pattern is distinct from canonical *V1R*s, which exhibit a punctate expression pattern known as the "one neuron-one receptor" role. The robust evolutionary conservation and unique expression profile suggest that ancV1R plays a fundamental role in VNO-mediated pheromone detection.

To elucidate the function of ancV1R, I conducted phenotypic analyses of ancV1R-deficient mice. Since pheromone detection by the VNO is essential for gender discrimination and sexual receptivity in female mice, first, I analyzed the sexual behaviors of ancV1R-deficent female mice. Behavioral analyses revealed that ancV1R-deficient females exhibited increased rejective responses toward male sexual behavior and ancV1R-deficient females displayed no preference for male urine over female urine. These findings suggest that ancV1R is essential for normal sexual behaviors of females and attraction to male urinary pheromones.

Next, I examined physiological responses of the VNO to male pheromones. Female mice were exposed to male urine or male individuals, and activated VSNs in the VNO were visualized through the induction of immediate early gene expression or ribosomal protein phosphorylation. VSNs activated by male pheromones were detected in ancV1R-deficient females, indicating ancV1R is not absolutely essential for VSN activation. However, the number of activated VSNs was significantly reduced in ancV1R-deficient females. I further assessed the VNO responses following exposure to other pheromone sources and molecules, such as male bedding, pups and a sexual enhancing pheromone ESP1, and β-estradiol 3-sulfate, and found that the number of activated VSNs was decreased in ancV1R-deficient females. These results suggest that ancV1R enhances VNO responses to various pheromonal stimuli.

To understand how attenuated male pheromone signals in peripheral neurons are processed in higher brain regions, I analyzed neural activation from secondary to higher-order neurons in the vomeronasal system. In ancV1R-deficient females exposed to male urine, there was a significant reduction in activated cells in the accessory olfactory bulb and medial amygdala, likely reflecting decreased input from the VNO in ancV1R-defecient females. On the other hand, in ancV1R-deficient females exposed to males, the number of activated cells in the medial amygdala and posteromedial cortical amygdala was significantly higher in ancV1R-deficient females. This increased activation may be attributed to non-vomeronasal input and/or associated with the expression of rejection behaviors. Furthermore, upon contact with males, ancV1R-deficient females exhibited increased neural activity in the lateral septum, a stress-associated brain region, along with elevated stress hormone levels. Such effects were not observed in females exposed solely to male urine, suggesting that male sexual behaviors but not vomeronasal inputs acts as a stressor for ancV1R-deficient females.

Overall, my findings suggest that ancV1R facilitate VNO response to pheromone stimuli. The loss of ancV1R diminishes the sensory input from the VNO, leading to a lack of preference for male urinary pheromones. Moreover, ancV1R-deficient females fail to recognize males as potential mates, and thus male approaches and mounting behavior trigger sexual rejection and stress responses in ancV1R-deficient females.

備考 ： 論文要旨は、和文 2000 字と英文 300 語を 1 部ずつ提出するか、もしくは英文 800 語を 1 部提出してください。
Note : Thesis Summary should be submitted in either a copy of 2000 Japanese Characters and 300 Words (English) or 1copy of 800 Words (English).

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