

## 【Grant-in-Aid for Scientific Research (S)】

### Broad Section F



Title of Project : Identification of primer pheromones in mammals and elucidation of a neural basis for the pheromone action

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Research Project Number : 18H05267 Researcher Number : 00280925

Keyword : Pheromone, olfaction, receptor, neural circuit, reproduction

#### 【Purpose and Background of the Research】

Pheromones are categorized into two types; one that elicits specific behavior, calling a releaser pheromone, and another that causes physiological effects, calling a primer pheromone. Studies on a releaser pheromone have been much progressed at the level of molecule, receptor, and neural circuitry using insects and mice, whereas there are not many studies for mammals including human. In this study, we will identify primer pheromones in mice that induce synchronous estrus, accelerate puberty, or cause sexual suppression, and their receptors and neural circuits responsible for the effects. We will also look for primer pheromones in humans and identify a brain region involved in the physiology. The molecular and neural mechanisms underlying primer pheromone actions related to reproductive function will be revealed.

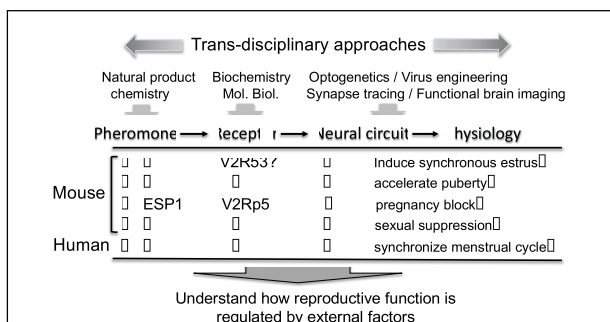


Figure Aims,

#### 【Research Methods】

Regarding mouse primer pheromones, we will develop an *in vivo* Ca<sup>2+</sup> imaging method using fiber photometry, purify active compound(s) from urine by HPLC, and determine the structure(s) based on GC-MS/LC-MS followed by chemical synthesis. We will reveal the receptors for the identified primer pheromone using a double in situ hybridization strategy from ~300 vomeronasal receptors. The neural circuitry underlying the pheromone action will be dissected by using virus technology and optogenetic and pharmacogenetic approaches. To identify human pheromones, we will use non-invasive functional brain imaging techniques and measure autonomic nervous functions and

endocrinological changes.

#### 【Expected Research Achievements and Scientific Significance】

Mouse primer pheromones identified during '80 by Novotony group have been denied in 2011 by Stowers group. The human dormitory effect reported by McClintock in 1971 has not been characterized at the level of molecule. The only primer pheromone in mammals so far is a goat male pheromone identified by Murata et al. in 2014. Thus, revealing primer pheromones, their receptors, and responsible neural circuits gives a high impact in the field. Moreover, this will be the first molecular study on human pheromone. The approach is transdisciplinary in the field of chemistry-biology; from natural product chemistry, receptor signaling biology, to brain science. In practical senses, the expected results will become valuable information that helps various problems in reproductive functions in human and mammals.

#### 【Publications Relevant to the Project】

• Hattori, T., Osakada, T., Masaoka, T., Oyama, R., Horio, N., Mogi, K., Nagasawa, M., Haga-Yamanaka, S., Touhara, K.\* and Kikusui, T.\* "Exocrine gland-secreting peptide 1 is a key chemosensory signal responsible for the Bruce effect in mice"

*Current Biology* 27, 3197-3201 (2017)

• Ishii, K., Osakada, T., Mori, H., Miyasaka, N., Yoshihara, Y., Miyamichi, K.\*, and Touhara, K.\* "A Labeled-Line Neural Circuit for Pheromone-Mediated Sexual Behaviors in Mice"

*Neuron* 95, 123-137 (2017)

【Term of Project】 FY2018-2022

【Budget Allocation】 147,600 Thousand Yen

#### 【Homepage Address and Other Contact Information】

<http://park.itc.u-tokyo.ac.jp/biological-chemistry/>