Title of Project : Identification of Bull Pheromone and its Application to the Improvement of Fertility

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【Purpose and Background of the Research】

Improvement of the fertility is one of the biggest concerns for Japan and other developed countries over the world.   Fertility rate has been decreasing for many years despite of the advancement of the science.   The loss caused by the decreased fertility is around 100 billion Japanese Yen.

The current study aims to utilize the bull pheromone as a means to improve the fertility by stimulating reproductive axis.   The 'male effect' was found decades ago in sheep and goats and the existence of a pheromone has been suggested by many experiments.   In cows, the presence of bulls has also been suggested to improve the fertility. The release of gonadotropin-releasing hormone (GnRH)/gonadotropin, therefore, would be kept at a normal level by bull pheromone in cows.   The absence of bull pheromone in a farm with the modern animal reproduction would cause a feeble estrus or reproductive disorders.

The present research focus on the isolation and identification of the bull pheromone to improve the fertility in milking and beef cows (Figure 1).
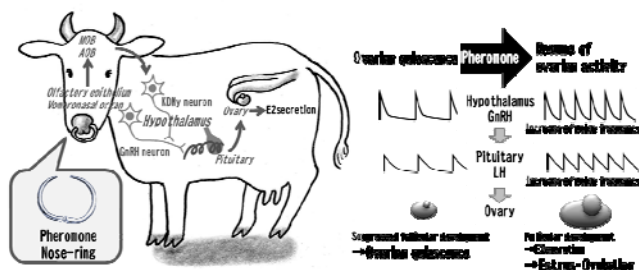

Figure 1 Conceptual illustration   Left, pheromone released from the nose-ring is sensed by pheromone receptors to stimulate hypothalamic KNDy neurons and then GnRH/LH release resulting in ovarian estrogen secretion.   Right, GnRH pulses are slowed-down in anaestrous cows and estrogen secretion is suppressed at a low level.   The exposure to pheromones enhances the pulse frequency to stimulate estrogen secretion and then estrus and ovulation.

【Research Methods】

Our first attempt is to get bioassay systems to detect the pheromonal activity in bull samples. We will establish an immortalized bull vomeronasal cells and/or cell lines expressing every pheromone receptors in order to detect the pheromone activity in bull samples.   In addition, we will take another way to identify pheromone activity with gonadotropin pulses and hypothalamic multiple unit activity of KNDy neurons.

Collaborations with the National Livestock Breeding Center and Gifu Prefectural Livestock Research Institute are appreciated to collect hair samples from bulls.

【Expected Research Achievements and Scientific Significance】

The bull pheromone will be the second primer pheromone following the male goat pheromone. It would be of great scientific interests how these specific pheromones interact with each vomeronasal pheromone receptors.

From the application point of view, the development of pheromone preparation would be a novel method to improve the fertility of milking and beef cows.

【Publications Relevant to the Project】

· Maeda, K.I., Ohkura, S., Uenoyama, Y., Wakabayashi, Y., Oka, Y., Tsukamura, H., Okamura, H. (2010) Neurobiological mechanisms underlying GnRH pulse generation by the hypothalamus. *Brain Research* 1364:103-115.
· Murata K., Tamogami S., Itou M., Ohkubo Y., Wakabayashi Y., Watanabe H., Okamura H., Takeuchi Y., Mori Y. (2014) Identification of an olfactory signal molecule that activates the central regulator of reproduction in goats. *Current Biology* 24: 681-686.

【Term of Project】 FY2015-2019

【Budget Allocation】 144,200 Thousand Yen

【Homepage Address and Other Contact Information】
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