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令和３年度研究助成（参加費助成）研究成果報告書

2022 年　01　月　05　日

公益財団法人遺伝学普及会 代表理事　殿

貴財団より助成のありました研究の成果を下記のとおり報告します。

氏名　Mallarapu Lalitha Devi　印

出席学会等名称

開 催 場 所　Neuroscience 2021 (Virtual)

開 催 期 間　2021 年　11 月　08 日　～　2021　年　11 月　11 日

研 究 成 果 の 概 要

Recently, I attended the **Neuroscience 2021** international conference (Virtual) which is also the 50th Annual meeting of **"Society for Neuroscience"**- the world's largest organization of scientists and clinicians devoted to understanding the brain and the nervous system. I was very fortunate to attend this meeting by availing the **funding from "公益財団法人 遺伝学普及会" Association for Propagation of the Knowledge of Genetics"**. I am thankful for providing such an opportunity for international exposure.

Neuroscience 2021 held in a virtual format because of the COVID-19 pandemic. My work was presented in the form of a poster. Nearly 9,500 neuroscientists from across the world attended this meeting, which featured, 22 lectures, 54 symposia and 999 poster sessions. This meeting was excellent way to meet others who are working in the same field as me to exchange the ideas and to gain a better view of my doctoral study.

In my doctoral research I am looking into **"how genetic polymorphisms influence maternal behavior**" in mice and cause behavioral differences among individuals. My research primarily focused on the identification of Estrogen Receptor α (ERα) gene polymorphisms between wild and laboratory mouse strains. ERα is a hormonal receptor gene which is important for maternal behavior. We generated a mice model using CRISPR/Cas9 gene editing technique and found out that ERα polymorphic mice shows abnormal maternal behavior. In my current analysis, I'm more interested in what is the neural mechanism for change in the maternal behavior.

During the meeting's poster session, I was assigned in a group of 10 speakers who are working on the topic of parental behavior. It was quite interesting to observe their research content and approach which they choose to address their research question. I spoke with **few foreign researchers** who are working on **deciphering the neural mechanism of maternal behavior**. I received few helpful recommendations, as well as insight into how to make my research work more interesting. Finally, I would like to thank **"公益財団法人 遺伝学普及会"** for giving me this wonderful opportunity.

Title: Effect of ERα polymorphisms in maternal behavior of mouse

Abstract:

Induction of maternal behavior in mammals relies on changes at the level of the genome. However, the ability to characterize a specific behavioral phenotype to a naturally occurring genetic change i.e. polymorphism is considered to be a rare phenomenon. Maternal responsiveness is thought to be mediated by several hormonal and neuronal changes, yet the effect of underlying polymorphisms on the extent of bonding cannot be foreseen. One of the well-studied protein for its role in determining maternal- infant bonding is Estrogen receptor α (ERα), encoded by gene estrogen receptor 1 (*Esr1*). The expression of ERα in hypothalamic medial preoptic area (MPOA) and the adjacent ventral bed nucleus of stria terminalis (vBNST) plays an essential role in controlling maternal behavior. Mice are extensively used model animals to study regulation and function of ERα *in-vivo*. In our study we identified that mice from different genetic background, laboratory strain C57BL/6J (B6) and wild derived mouse strain MSM/Ms (MSM) differs in *Esr1* gene structure. We found an insertion polymorphism, (insertion "A") in exonic region of B6 genome when compared to MSM. To analyze the role of the insertion "A", we developed an $Esr1^{\Delta A}$ mice in which the "A" sequence was deleted in B6 mice through CRISPR/Cas9-mediated genome editing. We report here that (i); $Esr1^{\Delta A}$ heterozygous mice showed reduced pup survival in the breeding. (ii); Maternal behavior analysis showed that $Esr1^{\Delta A}$ heterozygous mice were reluctant to retrieve pups (took more time) when compared to the wild type control. (iii); $Esr1^{\Delta A}$ heterozygous mice showed higher mRNA and lower protein expression, indicating the effect of polymorphism on regulation of translation. (iv); Reduced ERα and cFOS (immediate early gene) expression in the MPOA of $Esr1^{\Delta A}$ heterozygous mice after maternal behavior. Altogether, our study provides a glance of how a *Esr1* genetic polymorphism has affected the brain and maternal behavior within mice species. In future studies, we would like to understand how the abnormal maternal behavior was occurred in the $Esr1^{\Delta A}$ heterozygous mice and what are pathways involved.