

学位論文発表会

Title: Mechanisms by which Bacterial and Viral Pathogens cause Ovarian dysfunction

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Infections of bacterial and viral origin are notable causes of diseases of the female reproductive system and infertility in both animal and human populations. The presence of receptors for bacteria and viruses allows for internalization in the host cell and an accompanying inflammatory response from the host when detected by toll-like receptors. TLR7/8 agonist, Resiquimod (R848) is an immune modifier and Lipopolysaccharide (LPS) is an endotoxin released by gram-negative bacteria, and they can pass through the protective physical barriers and tight junctions of the basement membrane of the ovary. In this study we elucidated the mechanism by which ovarian dysfunction occur as a result of bacterial and RNA virus infections. In bacterial infection, follicle development occurs normally morphologically, but LPS/endotoxins cause an abnormal demethylation of DNA in granulosa cells of the ovary leading to a failure in the ovulation process. Furthermore, it was revealed that RNA virus infection induces follicle development and ovulation, but the fertility of the ovulated eggs was significantly reduced. Interestingly, RNA virus infection induced early lutea phase in follicles and this may explain the reduction in fertilization ability of the eggs ovulated. Together, these results establish that ovulation failure and other fertility disorders, which had been unknown until now, may be caused by infection. In addition, these findings are expected to contribute to improving the reproductive performance of livestock and technological innovation of infertility treatment.

感染症は、家畜の繁殖成績を低下させ、ヒトの不妊の原因になりますが、その詳しいメカニズムはわかっていません。本論文では、細菌感染と RNA ウイルス感染により卵巣機能が低下する仕組みについて解明を試み、細菌感染では卵胞発育は形態的には正常に起こるが、顆粒膜細胞の DNA の脱メチル化異常が引き起こされ、細胞の機能的変化が生じないため排卵不全となることを突き止めました。さらに、RNA ウイルス感染では、卵胞発育と排卵は誘起されるが、排卵された卵の受精能力が著しく低下していることを明らかとしました。この原因として、卵胞内の早期黄体化が関与している可能性も示されました。上記の結果は、これまでは原因不明とされてきた排卵不全や受精障害が感染により引き起こされていることを明らかとしたもので、家畜の繁殖成績の向上と不妊治療の技術革新への貢献が期待されます。

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本講演は、大学院セミナーの単位になります。