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学 位 論 文 題 名

Study of the Relationship between Antiviral and Enzymatic Activities in the Chicken Oligoadenylate Synthetase

（ニワトリオリゴアデニレート合成酵素の酵素活性と抗ウイルス活性の関係に関する研究）

学位論文内容の要旨

West Nile encephalitis is an infection of the brain caused by the West Nile virus (WNV). Previous studies in mice identified the Oas1b gene as a determining factor for resistance to WNV infection. In addition, it has been suggested that human OAS1 and OAS-L are associated with WNV resistance and susceptibility. WNV is maintained in nature through a complex life cycle involving wild birds and mosquitoes. Birds are not only susceptible to the WNV, but also act as hosts, thus, participating in the spread of the disease. It has previously been reported that chicken OAS-L has the oligoadenylate synthetase activity. However, until now the antiviral activity of chicken OAS-L (ChOAS-A) has not been determined.

Therefore, in the Chapter I of this Ph.D thesis study, the putative

antiviral activity of chicken OAS-L was investigated by ectopically expressing this enzyme in mammalian cell and then infecting these cells with WNV replicon. It has demonstrated that ChOAS-L has an antiviral activity against the WNV.

In the Chapter II of this Ph.D thesis, the relationship between enzymatic and antiviral activities was investigated by generating 8 mutations either using the site-directed mutagenesis or standard PCR protocol. The wild type as well as the mutated proteins was ectopically expressed in the repBHK-21 cells, stably expressing the repWNV/SEAP. The results revealed that all mutant proteins showed no enzymatic activity except for ChOAS-B and UbL2 del. However, all mutated proteins showed antiviral activity to inhibit the replication of the repWNV/SEAP replicon. These results suggest that the ChOAS-L expresses the antiviral activity in a manner independent of the RNase L. Moreover, the enzymatic activity is shown to be independent of the antiviral function. However, the complete deletion of the UbL domains resulted in a loss of the enzymatic function, which may be due to the instability of the ChOAS-L.

学位論文審査の要旨

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The thesis consist of 80 pages written in English and 8 Figures, 3 tables and 66 references are included.

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Therefore, we acknowledge that Mr. Tag El-Din Hassan Hassan Tag El-Din is qualified to be granted the Degree of Doctor of Philosophy in Agriculture from Hokkaido University.