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学位論文内容の要旨
Abstract of the dissertation

博士の専攻分野の名称：博士（獣医学）

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学位論文題名
The title of the doctoral dissertation

The role of mouse 2', 5'-oligoadenylate synthetase 1 paralogs
(マウス 2', 5'-オリゴアデニル酸合成酵素 1 パラログの役割)

The interferon-induced oligoadenylate synthetase (OAS) family is one of the most important immune response proteins to the viral infection. The OAS protein binds dsRNA and is activated to produce 2',5'-oligoadenylates, which lead to the activation of latent form of RNase L, resulting in degradation of cellular and viral RNA and inhibition of viral replication. In mice, the *Oas* gene family locates on chromosome 5. The mouse *Oas* gene locus undergoes a recent series of duplication event, leading to the presence of eight paralogs of *Oas1* genes (*Oas1a* through *Oas1h*) that forms *Oas* gene cluster with the *Oas2*, *Oas3* and two *OasL* (*OasL1* and *OasL2*) genes. Previous studies demonstrated that the mouse *Oas1b* gene conferred resistance to the flavivirus infection in mice; however, the antiviral activity of other mouse *Oas1* gene family is still unknown. Therefore, in the present study, we have evaluated the mouse *Oas1* paralogs regarding the enzymatic activity and antiviral activity against the two neurotropic flaviviruses, West Nile virus and tick-borne encephalitis virus. The mouse *Oas1* genes were cloned from C57BL/6J (B6) as well as the *Oas1b* derived from feral mouse strain, MSM. The obtained results demonstrated that only *Oas1a* and *Oas1g* showed enzymatic activity. Although MSM-derived *Oas1b* showed antiviral activity to both viruses, all B6-derived OAS paralogs did not show antiviral activity. These results suggest that *Oas1a* and *Oas1g* play a role in potentiating viral RNA-induced interferon response in the cell, whereas the *Oas1b*

works as a specific anti-flavivirus factor unless it is mutated. However, the role of other paralogs is unknown and should wait for further investigation.