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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 感染症学　　氏名：Yannick MUNYEKU BAZITAMA
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学位論文題名
The title of the doctoral dissertation
Characterization of human tibrovirus envelope glycoproteins and its application for seroepidemiological studies
（ヒトティブロウイルス糖蛋白質の性状解析および血清疫学研究への応用）

Human tibroviruses are emerging rhabdoviruses discovered through metagenomic analyses of samples from healthy individuals or individuals with febrile illness or nodding seizures of unknown origin. They belong to the genus *Tibrovirus* in the family *Rhabdoviridae*. The genus *Tibrovirus* is called after Tibrogargan virus, the genus prototype virus and the first to be isolated. Several other tibroviruses have been detected or isolated mainly in animals or insects between 1981 and 1984. However, reports on novel tibrovirus infections in humans have been increasing in the last 15 years (Bas-Congo virus, Ekpoma virus 1, Ekpoma virus 2, and Mundri virus). Among these human-associated tibroviruses, Bas-Congo virus (BASV) was of great concern as it was associated with a small outbreak of fulminant hemorrhagic fever in 2009 in Mangala, the Democratic Republic of the Congo (DRC). Human tibroviruses are largely uncharacterized and little is known about their impact on human health.

In the first part of my PhD thesis, I characterized the envelope glycoprotein (G) of human tibroviruses, which likely play a critical role in viral pathogenicity. To gain insights into the interactions between these viruses and their potential hosts, I investigated primary and tertiary structures, antigenic differences, and cell tropism of human tibrovirus Gs. The results revealed that human tibrovirus Gs share some primary structures and display 14 conserved cysteine residues. Multiple glycosylation sites were found on G molecules. AlphaFold-predicted 3D structures of human tibrovirus Gs were overall similar and a little different from that of vesicular stomatitis Indiana virus (VSIV) G. I generated virus-like particles and used them for mouse antisera production. Using VSIV pseudotyped with Gs, I found that the antisera to respective tibroviruses showed limited cross-neutralizing reactivity. It was also found that BASV G showed the highest ability to utilize human C-type lectins and T-cell immunoglobulin mucin 1 as attachment factors for G-mediated entry into cells. The pseudotyped viruses infected a wide range of cell lines with a preferential tropism for human cell lines.

In the second part, I assessed human exposure to BASV and other tibroviruses in DRC. I used a pseudotype VSIV-based neutralization test to screen samples collected in Mangala in 2022 and two control sites (Matadi and Kinshasa) in 2021. Among the 267 individuals from

Mangala, the prevalence of BASV antibodies was 55.1% (147/267). BASV seropositivity odds significantly increased with age. Some occupational categories (e.g., farmer or public servant) were also associated with seropositivity. In contrast, only 5.6% (9/160) and 0.8% (1/124) of the samples from Matadi and Kinshasa, respectively, had neutralizing antibodies to BASV. Moreover, neutralizing antibodies to other tibroviruses, Ekpoma virus 1, Ekpoma virus 2, and Mundri virus, were detected in 31.5%, 94.0%, and 82.0% of Mangala samples; 8.8%, 38.8%, and 75.0% of Matadi samples, and 4.8%, 4.0%, and 26.6% of Kinshasa samples, respectively. These results suggest that human infection with tibroviruses could be common in the study areas and not associated with deadly hemorrhagic or debilitating syndromes. My doctoral research has provided fundamental information to understand biological properties and human exposure to tibroviruses.