

## 論文の内容の要旨

### 論文題目 **Morphogenesis of Influenza Virus Particle**

(インフルエンザウイルスの粒子形成機構)

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Influenza A virus, a member of the *Orthomyxoviridae*, is an enveloped virus with an eight-segmented, negative-sense, single-stranded RNA genome. When influenza virions are observed by using negative-staining electron microscopy, they often appear as spherical, elliptical, filamentous, or sometimes irregular shapes, which is referred to as pleomorphism. Inside the virion, each viral genomic RNA segment forms a ribonucleoprotein complex (RNP) together with viral nucleoproteins and the heterotrimeric RNA-dependent RNA polymerase complex. Recent electron microscopic studies have shown that eight RNPs are arranged in a specific array, with seven RNPs surrounding a central one, and are selectively packaged into the virion, underneath its budding tip. Extensive research on the polymorphic outer features of virions and on the RNP architecture inside the virions has been conducted; however, the morphogenesis of influenza virions is not yet fully understood.

By using various electron microscopic techniques, I have studied the interior and exterior morphologies of influenza virions. In Chapter I, to clarify the native morphology of the influenza virion, I attempted to determine whether the irregular-shaped influenza virions form naturally and which viral components are important for virion integrity. I found that the irregular-shaped virions are, in fact, artifacts caused mainly by ultracentrifugation and that the native morphology of the influenza virion is actually spherical, elliptical, or filamentous. I was also able to show that the cytoplasmic tail of the M2 ion channel protein is essential for virion integrity. In Chapter II, I analyzed the orientation of the viral RNPs inside the virion to elucidate the morphogenesis and genome packaging mechanisms of influenza virus. I found that the RNPs are oriented differently inside the virion, suggesting the presence of a complicated genome packaging mechanism. Together, these data contribute to our understanding of influenza viral morphogenesis.