## Our Advancements in Cryo-Electron Microscopy Research and Development Over the Past Decade

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The resolution of single-particle analysis using cryo-electron microscopy was dramatically improved in 2013, ushering in a new era called the 'Resolution revolution.' Osaka University has been actively involved in improving the resolution of single-particle analysis through various technological developments on both hardware and software fronts even before this era. In 2009, we succeeded in obtaining the high-resolution structure of a small tetrahedral DNA origami of only 79 kDa. This result was the smallest molecule ever recorded before the "resolution revolution", and represented a breakthrough beyond the 100 kDa barrier, which was thought to be impossible at the time. On the other hand, hardware development has also been a major focus. Around 2010, we initiated a collaborative effort with JEOL Ltd. to develop a new cryo-electron microscope, resulting in the creation of the cryoARM200. Subsequently, cryoARM300, which is equipped with a cold field emission gun (cold-FEG) and operates at 300kV was produced. We achieved an impressive resolution of 1.54Å, marking the highest resolution in 2019.

We believe that "atomic resolution cryo-EM" proved that it was no longer exclusive to Titan Krios, giving users new options and accelerating the development of electron microscopy. In this workshop, we would also like to introduce the development of analytical techniques for samples that have been difficult to analyze.