

## Glacios 2 Cryo-TEM and Smart EPU Software streamline Cryo-EM for drug design with higher throughput

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### Background incl. aims

Cryo-EM has significantly impacted the field of structural biology due to its capabilities to resolve the three-dimensional structure of proteins, protein complexes and other biological macromolecules at high or even atomic resolution. However, acquiring high-quality data still largely depends on the expertise of the microscope operator. This limits the speed of adoption as researchers must invest considerable time into understanding microscopy and the technicalities of the workflow. Here, we show how the Thermo Scientific™ Glacios 2™ cryo transmission electron microscope (Cryo-TEM) with low-energy-spread Cold Field Emission Gun (E-CFEG) and combined with Thermo Scientific™ Smart EPU Software enables users of all expertise levels to acquire high-quality cryo-EM data.

### Methods

In collaboration with the Greber lab (Institute for Cancer Research), several high-resolution structures of the 85 kDa Human CDK-activating kinase (CAK) were determined. CAK is a master regulator of cell growth and division and is a promising target for cancer therapeutics.

### Results

Structures of CAK were rapidly determined in free and nucleotide-bound states as well as in complex with 14 inhibitors(1). In addition to achieving high-resolution structures from large datasets, ~4 Å and ~3 Å-resolution structures of ligand-bound complexes were determined using from only 1 hour and 4 hours of data collection respectively. Furthermore, in combination with an E-CFEG we have been able to generate a 1.5 Å reconstruction of Apoferritin; the highest resolution 200 kV structure to date.

### Conclusion

These results show the use of cryo-EM to enable structure-based drug design.

### Keywords:

Cryo-EM; Cold FEG; automation; throughput

### Reference:

1. Cushing, V.I., Koh, A.F., Feng, J. et al. High-resolution cryo-EM of the human CDK-activating kinase for structure-based drug design. *Nat Commun* 15, 2265 (2024).  
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**Graphic:**



**Keywords:**

cryo-EM, cryo-ET, micro-ED, community, training