

Segmentation of a cryo-electron tomogram. Proteasomes tethering to the nuclear pore complex (purple). Courtesy of Dr. Ben Engel, Dept. of Mol. Struct. Biology, MPI for Biochemistry, Martinsried, Germany

Brain Research: Correlation of sample morphology and gene expression

INVESTIGATION OF MOLECULES WITHIN THEIR SUBCELLULAR CONTEXT

To fully investigate complex biological mechanisms, life science researchers require reliable structural information of molecules within their subcellular context. To achieve this, the target molecules and their cellular environment need to be accurately resolved at subnanometer resolution.

Leica Microsystems and Thermo Fisher Scientific have collaborated to create the first fully integrated Cryo Electron Tomography workflow that responds to these research needs.

Safe sample and data transfer between instruments ensure easy navigation to the cellular target regions and reliable results at subnanometer resolution.



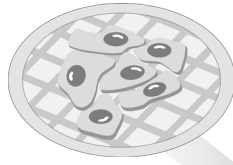
Additional fields of research

- Cell Biology
- Immunology
- Virology
- Microbiology

References

- Marx V., 2018, "Calling all cell biologists to try cryo-ET", *Nature Methods* 15: 575–578.
- Vaites L.P., Harper, J.W., 2018, "Protein aggregates caught stalling", *Nature* 555, 449-451.
- Oikonomou C.M., Jensen G.J., 2017, "Cellular electron cryotomography: towards structural biology in situ", *Annual Review of Biochemistry* 86: 873-896.
- Beck M., Baumeister W., 2016, "Cryo-Electron Tomography: can it reveal the molecular sociology of cells in atomic detail?", *Trends in Cell Biology* 26(11): 825-837.

THE FIRST INTEGRATED CRYO ELECTRON TOMOGRAPHY WORKFLOW*



Vitrification

Grow cells on an electron microscopy grid. Vitrify the sample with the automatic plunge freezer EM GP2. The cellular content stays as close as possible to the native state.

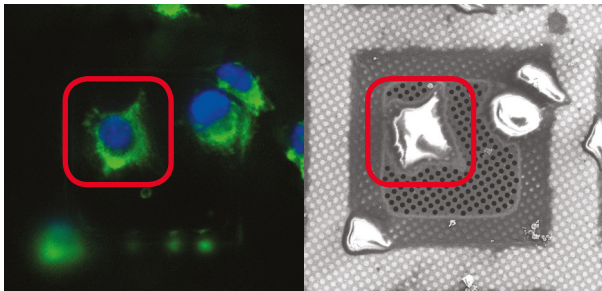


Selection

Preselect cells and target regions using the cryo light microscope EM Cryo CLEM. Transfer the sample to the Cryo DualBeam electron microscope Thermo Scientific Aquilos™ for milling.



Leica provides: Fast selection and retrieval of target coordinates.



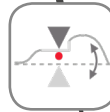
Left: Fluorescence image of a cell selectively marked with the EM Cryo CLEM.

Right: The exact same cell relocated by the Aquilos.



Milling

Retrieve the preselected target regions by coordinate locking between the EM Cryo CLEM and the Aquilos. Create a thin ice sheet (on-grid lamella) by using the focused ion beam.



Cryo Tomography

Transfer the lamella to the Thermo Scientific Krios™ G3i. The area of interest is imaged from different angles to generate a 3D tomogram. Record the lamella's content at subnanometer resolution.



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