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DATASHEET

Krios Rx Cryo-TEM

Pharma-dedicated cryo-TEM solution for single particle analysis and structure-based drug design

As the flagship of the iSPA Workflow, the Krios Rx Cryo-TEM offers the highest productivity, unprecedented ease-of-use, and a pharma-dedicated service package for guaranteed reliability.

Structure-based drug design requires expedient delivery of a *de novo* structure, followed by repeat structures of the target in combination with candidate compounds. As drug targets become more challenging, it becomes harder to solve structures quickly enough to match your timeline for lead identification and optimization. Cryo-electron microscopy (cryo-EM) Single Particle Analysis (SPA) allows you to visualize difficult-to-crystalize molecules at near-atomic resolution. It is the structure determination method of choice to address intractable targets, such as membrane proteins or large macromolecular complexes.

While SPA has clear advantages in structure-based drug design, as a structural biologist or a lab manager you need to overcome current workflow challenges that may slow down your structure generation. To meet the pace of drug discovery in pharma, you need a streamlined SPA workflow that requires minimal user input or cryo-EM expertise. You need reliable, trusted instruments that reduce costs and give you the peace of mind to focus on drug discovery.

Key Benefits

- **Highest productivity** with a guaranteed throughput of over 400 high-quality images per hour
- **Easy to use** with simplified workflow and unattended multi-grid data collection ideal for non-expert microscopists
- **Highly reliable** microscope with a pharma-dedicated service package and 90% uptime guarantee
- **Future-proof platform** with automated and programmable loading door to be ready for robotic sample loading
- **Compact design** and active vibration dampening system allows for easy installation and avoids costly room renovations

iSPA Workflow

The industrialized SPA (iSPA) Workflow is the first complete SPA-dedicated solution specifically designed to support the drug discovery process, from sample vitrification to data collection. Created in partnership with customers like you, this innovative cryo-EM solution is optimized to offer the highest productivity with unprecedented ease-of-use, and guaranteed reliability of your instruments.

Krios Rx Cryo-TEM

The Thermo Scientific™ Krios™ Rx Cryo-Transmission Electron Microscope (Cryo-TEM) is the flagship of the iSPA Workflow, streamlined for the pharma drug discovery process. This high-end microscope has a fixed voltage (300 kV) with a configuration optimized for SPA. Standard equipped with a Thermo Scientific Falcon™ 4 detector in combination with a number of next-level EPU automations, and a pharma-dedicated service package, the Krios Rx Cryo-TEM is the only microscope that guarantees a throughput of over 400 high-quality images per hour and 90% uptime.

The integrated vibration isolation system (iVIS) ensures active vibration dampening for enhanced system performance. With a height less than 3 meters, the system fits in a standard room allowing easier installation and saving you challenging and costly room renovations.

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Highest productivity and ease-of-use

The Krios Rx Cryo-TEM is optimized for the drug discovery process with the highest productivity for high resolution imaging—a guaranteed throughput of over 400 high-quality images per hour. This is ideal to help you generate new and repeat structures quickly to match your timeline for lead discovery and optimization.

The traditional workflow includes many manual steps to set up data acquisition and change grids, requiring expertise and significant time at the microscope. With the Krios Rx Cryo-TEM, it's faster and easier than ever to set up and run your microscope using a simplified workflow that is ideal for non-expert microscopists. It requires less training and allows you to get up to speed faster. Innovative new features, such us auto-microscope optimization that uses a traffic light cue, make sure you do not need advanced expertise to set up the Krios Rx Cryo-TEM for data collection. This self-diagnostic function makes sure the microscope is fully tuned to its optimal starting point for SPA.

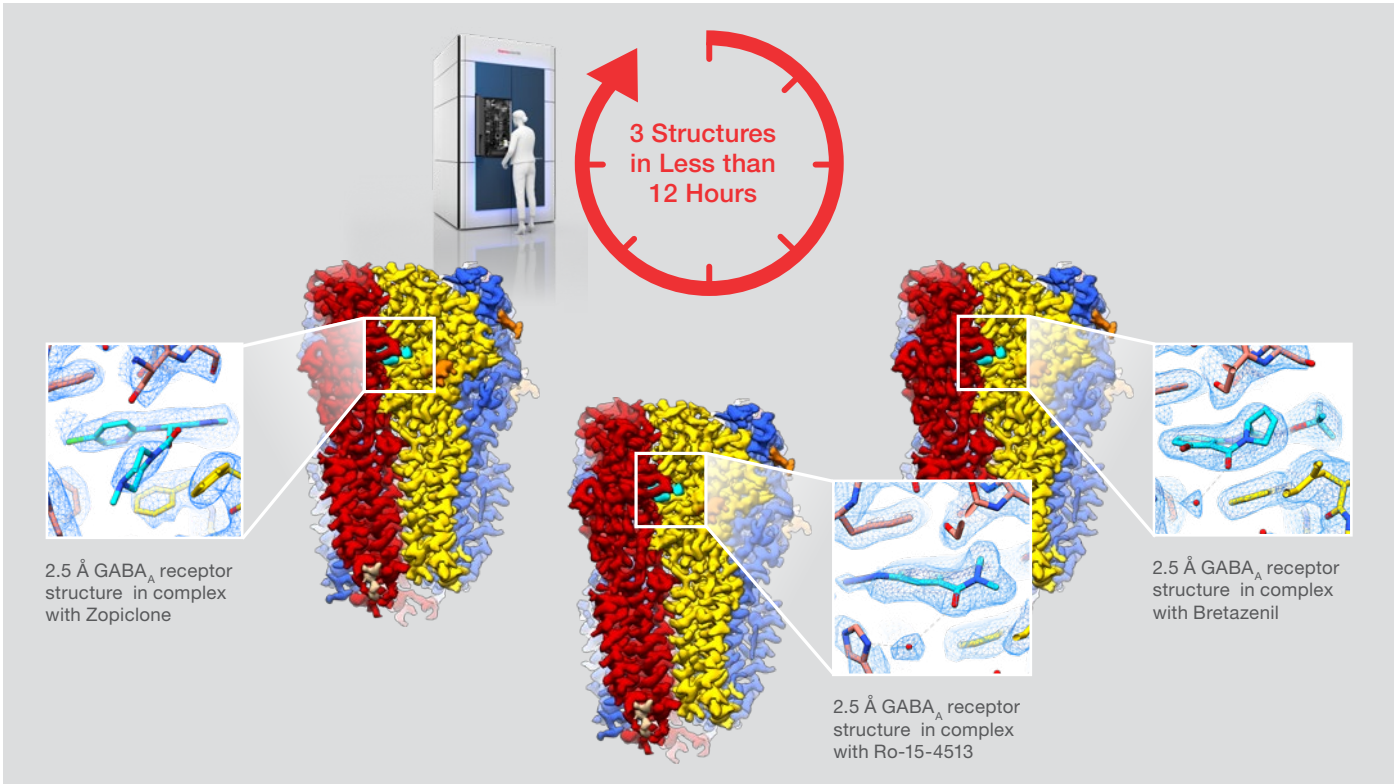
Our EPU enhanced package for unattended multigrid data acquisition feature will allow you to collect more datasets per day with minimal user input. Innovative enhancements in automation reduce the set-up time to under 30 minutes. You can now also run the microscope unattended—including overnight or over the weekend—to collect near-atomic resolution images from multiple samples of up to 12 grids. EPU Quality Monitor (EQM) on-the-fly pre-processing tool evaluates the quality of the images during the actual acquisition process. This allows you to judge and optimize the quality of the data collection while it is happening. EPU Data Management (powered by Thermo Scientific Athena™ Software) allows for automatic organizing and viewing of SPA data and metadata. It enables the best connectivity for reproducible operation and secure sharing.

The Falcon 4 detector, combined with optical and throughput enhancement modes, accelerates automated data acquisition by up to 10x. Aberration Free Image Shift (AFIS) functionality uses image beam shifts rather than a number of mechanical stage movements, while Fringe Free Imaging (FFI) ensures you can collect more images per foil hole at the highest quality. To overcome data overload for increasingly large datasets, the Falcon 4 uses the Electron Event Representation (EER) data format. This enables substantial, lossless data compression, while retaining super-resolution information for better resolution of generated structures. Together, these enhancements streamline instrument operation and maximize your productivity.

Additionally, the Krios Rx Cryo-TEM is future proof for the next level of automation. If you need further ramp-up of throughput, the automated and programmable loading door enables compatibility with robotic sample loading in the future.

Guaranteed reliability

A vital element of the Krios Rx Cryo-TEM is the unique suite of service offerings specifically targeted to the pharma industry. The Accelerate Rx comprehensive support portfolio validation service to ensure your Krios Rx Cryo-TEM achieves an output of over 400 high-quality images per hour, and on-site and remote applications support to train you in all aspects of your workflow. Access to a Connected Care Portal, which includes a productivity monitoring dashboard, will help you identify opportunities for performance improvement to maximize system usage. Through our system remote monitoring service, we will monitor critical system parameters, help you resolve any issues, and deliver recommendations for operational improvements. Through these measures, we can deliver a system performance commitment of 90% to ensure that your microscope operates at maximum efficiency to help you accelerate your structure-based drug discovery process.



From microscope setup to data collection in less than 12 hours: GABA$_A$ receptor and three repeat structures in combination with their ligands at 2.5 Å resolution.
Images courtesy of Simonas Masiulis, Radu Aricescu, MRC-LMB Cambridge and Evgeniia Pechnikova, Abhay Kotecha, Thermo Fisher Scientific

Flagship of the iSPA Workflow

With the iSPA Workflow, you no longer need to be a cryo-EM expert to collect good quality datasets for your most challenging targets. Gain efficiency in your target selection, lead identification, and lead optimization by generating timely structures at near-atomic resolution, at a significantly reduced cost per structure. With innovative features and automation for the highest productivity and ease-of-use, and guaranteed instrument reliability, the Krios Rx Cryo-TEM will power structural insights that meet the pace of your drug discovery.

Technical Highlights

- Fixed accelerating voltage at 300 kV
- High-brightness field emission gun (X-FEG)
- Cryo-Autoloader for automated and contamination-free loading of cassettes, containing up to 12 Autogrids
- Integrated cryo box, fixed to the objective lens, providing temperature stability and preserving cryo specimen quality
- Temperature management software, including liquid nitrogen autofill and scheduling of cool down after cryo cycle
- Extremely stable 300 mm diameter column
- Automatic Condenser C2 and Objective, factory aligned C1, C3 and SA apertures
- Cryo-stage with single axis holder for optimized stability and drift performance
- Constant power lens design; minimizes lens hysteresis and image aberrations during mode switching (imaging modes and diffraction)
- Symmetric Constant-Power™ C-TWIN objective lens, combining excellent resolution with high contrast under cryo condition (focal length = 3.5 mm, Cs = 2.7 mm, Cc = 2.7 mm)
- Optics electronics that enable rotation-free imaging, and allow for fast switching of modes, magnifications, conditions and techniques, all with minimized stabilization time. This is crucial for full automation of Single Particle Analysis.
- Three-condenser lens system, resulting in parallel illumination over a wide and variable field-of-view, providing flexibility of throughput and resolution
- Low hysteresis design with minimized crosstalk, which allows much better predictability of the electron beam position. This is essential for the implementation of automated alignments and applications software and makes the operation of the system much more reproducible, which is extremely important for high throughput applications.
- High-speed, digital search-and-view camera (FluCam)
- Linear distortion < 0.5% between 18 kx and 155 kx in TEM microprobe and nanoprobe modes
- The microscope is fully aligned at 300 kV in the factory. At this pre-aligned acceleration voltage, critical microscope characteristics are optimized, ensuring ultimate performance in imaging and analysis.
- Advanced Performance Monitoring: self-assessment of microscope status, combined with automated alignments, ensuring optimal experimental conditions
- Falcon 4 Direct Electron Detector
- AFIS: Aberration-free image shift between grid holes for shorter relaxation times
- FFI: Fringe-free imaging for multiple image acquisitions per grid hole
- EER: Electron Event Representation data format for the Falcon 4 enables substantial, lossless data compression, while retaining super-resolution information resulting in better resolution of generated structures
- Integrated Vibration Isolation System (iVIS) built into the microscope to actively dampen vibration frequencies
- Thermo Scientific EPU 2 Software for automated SPA screening and data acquisition
- EPU Quality Monitor to measure key image quality parameter on-the-fly as high-resolution images are being collected in EPU
- EPU Data Management for organizing, viewing, and sharing single particle cryo-EM data
- Primary control unit including two 30” monitors and hand panels to be placed within 15 meters from the column and the option to extend up to 300 meters from the column
- Windows® 10 Operating System

Accelerate Rx

Integrated service and applications support packages to accelerate customer innovation and enhance productivity.

- Customer success manager
- Customer enablement plan
- On-site applications training and support (20 days)
- Remote applications support (100 hours)
- Workflow validation service *
- Scientific Workflows app
- System remote monitoring
- Quarterly performance reviews
- Connected Care Portal
- Throughput validation service
- 90% performance commitment **
- Productivity monitoring

* Vitrification onsite will be performed in case customers own a Vitrobot 4 or higher version and make this Vitrobot available to execute this service. If no Vitrobot is available onsite, the test will be performed with a pre-vitrified sample.

** The committed uptime is 90%. If the Gatan BioContinuum filter and K3 camera are added to the system configuration, then the committed uptime is 85%.

Optional Configurations

- Advance Rx service portfolios
- Gatan BioContinuum energy filter and K3 camera

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Notes

Find out more at **thermofisher.com/EM-Sales**

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