

## Higher precision 3D analysis from structure to function

### Combining cryo-electron microscopy with mass spectrometry

Determine how proteins function within the cellular environment by combining the near-atomic resolution of cryo-electron microscopy (cryo-EM) with advanced biomolecular mass spectrometry (MS). Integrating several complementary techniques can help you move beyond protein structure to understand the function and dynamics of large molecular machines.

Below are just a few examples of how various mass spectrometry techniques can be combined with cryo-EM to provide unique insights beyond protein structures. This includes native MS screening of sample quality prior to vitrification, crosslinking MS to increase the resolution of cryo-electron tomography (cryo-ET) structures, and hydrogen-deuterium exchange to provide a dynamic view of static protein structures. Integrative structural biology offers you the solutions to tackle today's most challenging scientific questions.

#### Accelerated adoption of integrated workflows that use mass spectrometry and cryo-EM.

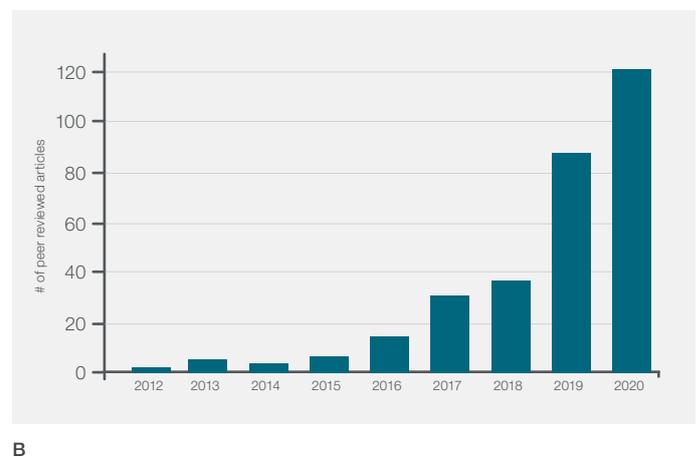
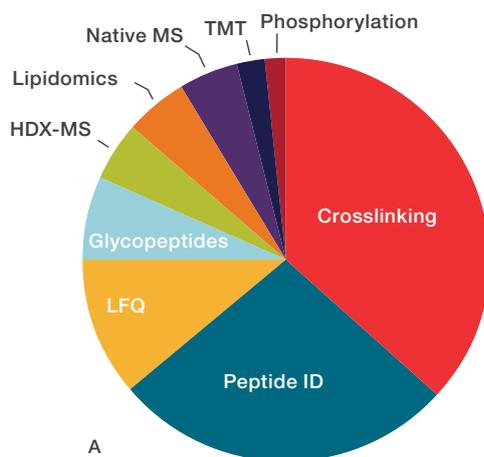


Figure 1. A) the most common mass spectrometry applications that are used to supplement cryo-EM. B) the rapidly growing number of articles that feature Thermo Scientific™ cryo-EM and Orbitrap™ mass spectrometers.

## Mass spectrometry toolbox for structural biology

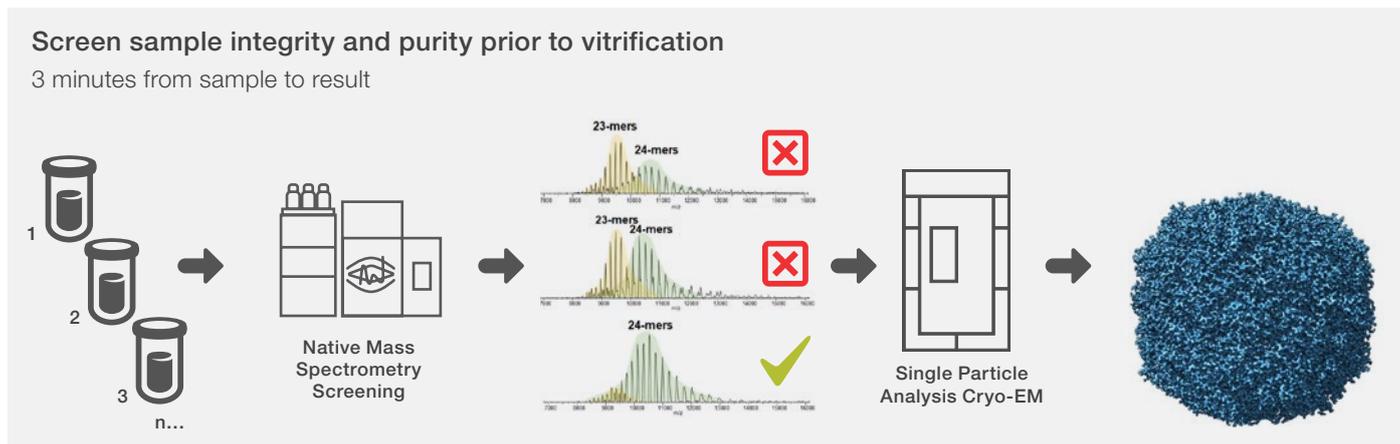


Figure 2. High-throughput native mass spectrometry: from sample to result in just three minutes.<sup>1</sup>

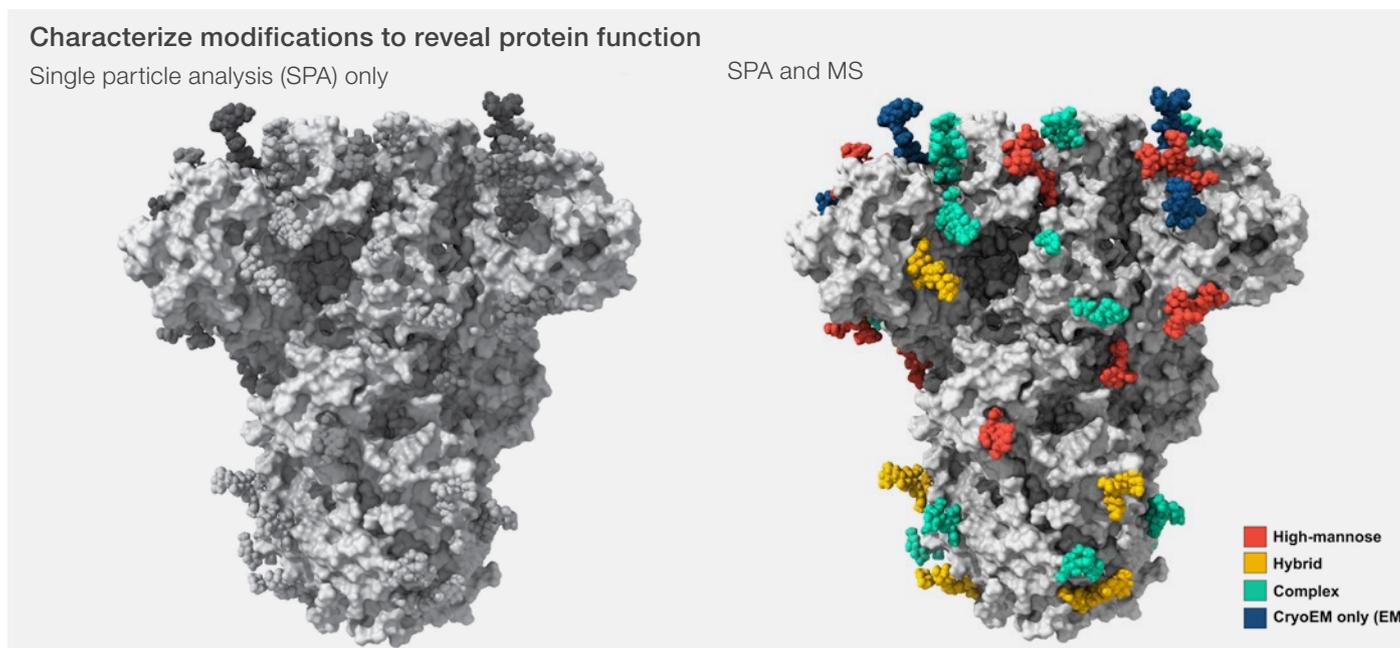


Figure 3. Glycoproteomics: characterization of the 5-glycan shield of coronavirus S glycoproteins (MERS-CoV S).<sup>2</sup>

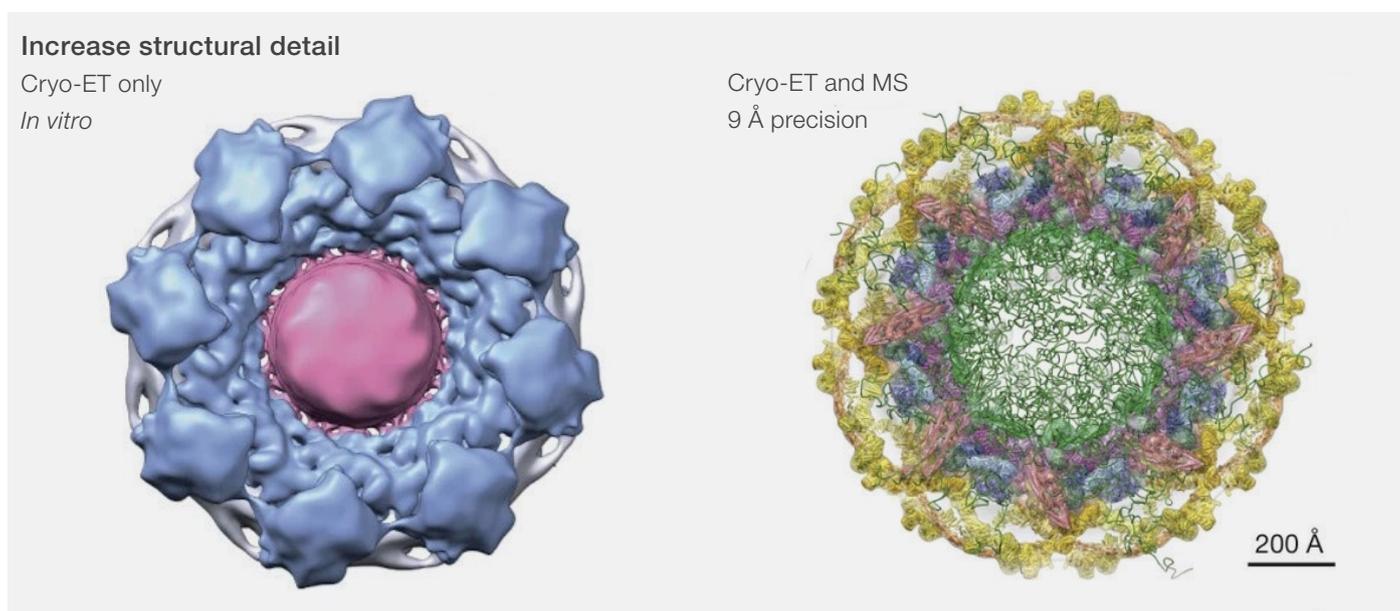


Figure 4. Crosslinking MS (XL-MS) with high-resolution cryo-ET provides detailed structural and functional insights into the nuclear pore complex a nuclear pore complex.<sup>3</sup>

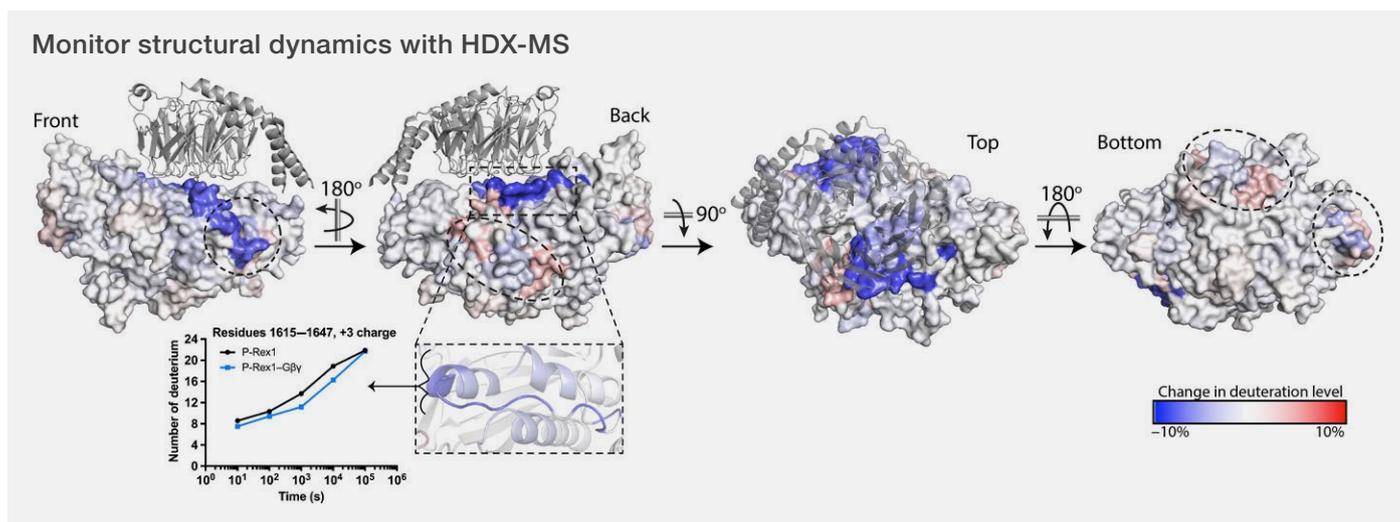


Figure 5. Hydrogen-deuterium exchange mass spectrometry (HDX-MS): ligand-binding dynamic of P-REX1 complex.<sup>4</sup>

### Cryo-EM and MS workflow for integrated structural biology

	Analytical techniques/workflow steps	MS*	Negative staining	SPA**	Cryo-ET**
Sample	Sample identity	●	○	○	○
	Biochemical optimization	●	●	◐	◐
	Sample quality screening	●	◐	●	◐
	Vitrification	○	○	●	●
Structure	Low resolution or initial model	◐	●	◐	◐
	3D construction or HR model	○	○	●	●
	Cellular information	◐	○	○	●
Function	Subunit connectivity	●	○	◐	○
	Complex dynamics	●	○	◐	○
	Lipids, ligands, modifications	●	○	◐	○

\*<https://www.thermofisher.com/us/en/home/industrial/mass-spectrometry/proteomics-mass-spectrometry/protein-structure-analysis-mass-spectrometry.html>

\*\*<https://www.thermofisher.com/us/en/home/electron-microscopy/life-sciences/learning-center.html>

### References

1. Image generated by Thermo Fisher Scientific. For more information, please watch our webinar with Dr. Paul Dominic B. Olinares of Rockefeller University: <https://www.thermofisher.com/us/en/home/global/forms/industrial/integrative-structural-biology-webinars.html>
2. Walls AC, Xiaoli X, Park Y-J, et al. (2019) Unexpected receptor functional mimicry elucidates activation of coronavirus fusion. *Cell* 176(5): 1026–1039.
3. Kim SJ, Fernandez-Martinez J, Nudelman I, et al. (2018) Integrative structure and functional anatomy of a nuclear pore complex. *Nature* 555(7697): 475–482.
4. Cash JN, Urata S, Li S, et al. (2019) Cryo-electron microscopy structure and analysis of the P-Rex1-Gβγ signaling scaffold. *Sci Adv* 5(10): eaax8855.

Learn how to **optimize your MS workflows with cryo-EM**

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