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## **Cryo-correlative strategies and genetically encoded multimeric particle tags for protein localisation in cellular cryo-ET**

Cryo-ET offers a powerful way to visualise the sociology of biomolecules in the cellular context. However, since cryo-ET is a label-free imaging method, a major challenge remains in the precise localisation of structures in cryo-electron tomograms. Through registration with fluorescence data, correlative light and electron microscopy (CLEM) can be used to guide FIB lamella preparation and cryo-ET imaging of whole cell specimens. I will outline a 3D CLEM-guided imaging workflow we recently streamlined [1]. Despite the added precision, CLEM can suffer from localisation errors due to the diffraction limit and sample deformation. Molecular tags of an identifiable size, shape and density, thus, provide a complementary visual solution for protein localisation. I will describe our current efforts to engineer a genetically encoded multimeric particle (GEM) tag for endogenous protein labelling in human cells.

[1] Klumpe\*, Fung\*, Goetz\* et al. eLife. 10, e70506 (2021).

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