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Correlative cryo-fluorescent and electron microscopy for biological applications.

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Chemical fixation is a standard procedure used in preparation for optical microscopy of biological samples. Unfortunately, chemical fixation produces various artefacts and may destroy cellular ultrastructure. Cryo-fixation offers an alternative way of preserving a sample in a life-like state. While cryo-fixation poses challenges for subsequent imaging, it also allows for different imaging modalities. The photo-physical properties of fluorescent labels can be very different at low temperature, so the combination of fluorescent labels and light imaging methodology needs to be reevaluated. Furthermore, good ultrastructure preservation allows for subsequent high-quality electron microscopy imaging, thus permitting correlated optical and electron microscopy imaging. We will describe the instruments and methods we developed for preparation and imaging of cultured cells using cryo-fluorescent and electron microscopy.