

# **Correlative Light and Electron Microscopy (CLEM)** Dr. Yannick Schwab

EMBL, Heidelberg

# **TUTORIALS IN LIFE SCIENCES**





14 September 2017, 9.00 am Philippstr. 13 Building 18, Maud Menten Hall (3rd floor) 10115 Berlin

Tutorials in Life Sciences feature expert speakers who provide insight into current research fields of Life Sciences and their methods.









# Summary

#### Correlative Light and Electron Microscopy (CLEM)

CLEM regroups a set of techniques that aim to image the same region of a sample with both light and electron microscopy in order to benefit from the advantages of both modalities. On one side, light microscopes, and more specifically fluorescence imaging benefit from a large field of view, can identify molecular species utilizing specific probes, and are compatible with imaging living samples. On the other side, electron microscopy uniquely reveals the rich and complex ultrastructure of cells at high resolution. This lecture will provide an overview of the methods currently used in CLEM and will cover practical aspects including sample preparation, probes, correlation strategies and dedicated tools applied to a variety of specimens from cells in culture to model organisms.

Towards a quantitative description of subcellular phenotypes by CLEM

A variety of strategies are now available to correlate live cell or in vivo imaging to EM, but they often suffer from tedious workflows. The Schwab team activities are centred on the development of new methods that increase the throughput of correlation on both cultured cells and multicellular specimens. By elaborating on the capacities of the focused ion beam-scanning electron microscope, automated correlation enables the acquisition of dozens of selected cells in a fully unattended fashion. The selection is performed by high-throughput screening at the light microscopic level which defines objective criteria to select the sub-populations of cells to be further analysed by electron microscopy. As a result, impact of various treatments, such as siRNA, on organelle morphology and distribution can be analysed at the ultrastructural level on multiple cells. On multicellular specimens, the major challenge is the navigation within the volume of the samples to reach the region of interest. Precise targeting is mandatory in order to make the correlation efficient. By using microscopic X-ray computed tomography as a bridging modality, the 3D data obtained by in vivo imaging, which reveals the targeted cells' position, is registered to the topology of the resin embedded specimen. With this information, exposing the sub-volume of interest is fast and precise. This workflow opens to the transversal observation of dynamic events such a tumor-cell extravasation in a mouse model of brain metastasis.

## Info

**Dr. Yannick Schwab** is team leader in the Cell Biology and Biophysics Unit and head of the Electron Microscopy Core Facility at the European Molecular Biology Laboratory (EMBL) in Heidelberg. The Schwab team is interested in developing tools for the 3D correlation of data generated by fluorescent imaging and by electron microscopy.

### www.iri-lifesciences.de

Funded by the resources of the Humboldt-Universität zu Berlin as part of the Excellence Initiative of the federal and state government





