CRISTAL: Resin infused biological sample preparation for correlative light and electron microscopy analysis

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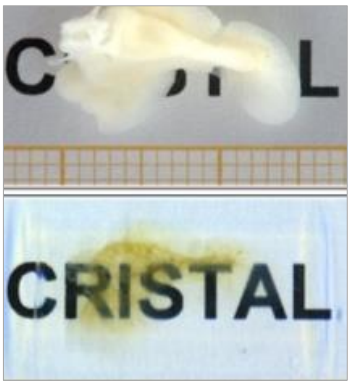
Correlative imaging allows for a comprehensive analysis of biological specimens and thus may lead to new insights in a biomedical context. Especially CLEM has already been proven addressing a resolution regime from the micro to the nano scale. However, most sample preparation methods lack from severe artifact formation ranging from movement and deformation during preparation and analysis to biological degradation and morphology changes, which results difficult comparison of the acquired data. We would like introduce a novel method for advanced specimen preparation (Fig.1) resulting in reduced artifact formation and allows correlative analysis from the macro to the nano scale. We used Scanning Laser Optical Tomography for *in toto* specimen visualization on the macroscale followed by Multi Photon Microscopy for the microscopic scale (Fig. 2) and Electron Microscopy for the nano scale on the very same specimen addressing a variety of contrast mechanisms ranging from endogenous mechanisms as autofluorescence, scattering, absorption and higher harmonic generation to exogenous markers as fluorescent and absorbing probes [1].

Fig. 1 (right): CRISTAL sample preparation of a rat lung lobe with the CRISTAL method. The accessory lung lobe of the rat is shown after fixation and after the resin-based clearing.



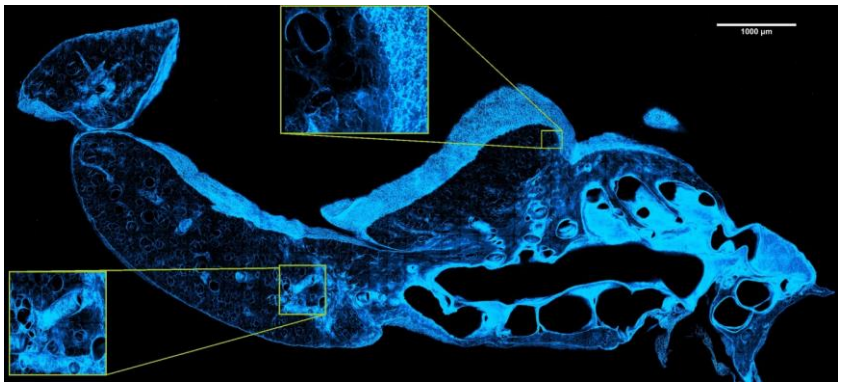


Fig. 2 (left): Maximum intensity projection of a SHG Image stack acquired with multi photon microscopy of the rat lung lobe.

References:
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3D imaging of biological samples from macro to nano scale" Scientific Reports | 6:35606 | DOI: 10.1038/srep35606