Mediterranean Thematic Workshops in Advanced Molecular Imaging

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Exploring Inflammatory Pathways: Optical Nanoscopy Reveals Cytokine-Induced β-Cell Stress Signatures

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β-cell failure in both Type-1 and Type-2 Diabetes is intricately linked to the inflammatory cascade mediated by pro-inflammatory cytokines. To analyze the molecular intricacies underlying cytokine-induced β-cell dysfunction, we employed advanced super-resolution optical microscopy techniques. Specifically, we utilized Expansion Microscopy (ExM), a groundbreaking method enabling nanoscale imaging of biological specimens without the need for expensive optical instruments. In this study, we investigated the inflammatory impact of interleukin-1β (IL-1β) and interferon-γ (IFN-γ) on Insulinoma 1E (INS-1E) β-cells using ExM-based fluorescence super-resolution imaging. Our findings revealed profound alterations in β-cell morphology and subcellular organization following 24-hour exposure to IL-1β and IFN-γ. Notably, we observed an ˜80% increase in mitochondrial circularity, a ˜40% reduction in insulin granule density accompanied by mis-localization of the remaining granules, and the emergence of F-actin-positive membrane blebs. Additionally, we identified a previously unrecognized fragmentation of the microtubule network, with a ˜37% reduction in branch density. These observations provide unprecedented insights into the subcellular effects of pro-inflammatory cytokines on β-cell function, complementing existing molecular data. Our study establishes a novel optical microscopy framework for interpreting β-cell dysfunction and paves the way for future ex-vivo and in-vivo investigations aimed at unraveling the pathophysiology of Diabetes mellitus.

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