Cystic fibrosis (CF) is a prevalent genetic disease that causes respiratory and digestive issues due to mutations in the CFTR gene [1]. The proper functioning of CFTR protein is influenced by lipids [2]. Recent research has unveiled various lipid abnormalities in CF, including disturbances in lipid rafts, increased saturated fatty acids, ceramide build up, and heightened oxidative stress [3].

Traditional vibrational spectroscopy techniques have limitations in analysing specific membrane regions, hindering the identification of distinct lipid and protein [4] alterations in CF lung cells [3]. This impedes the development of drugs to regulate CFTR protein activity.

To address this, our study employs innovative nanoscale resolved infrared spectroscopy techniques: scattering-type scanning near-field optical microscopy (s-SNOM) and nano FT-IR spectroscopy. For the first time, we will investigate changes in lipid composition, distribution, and orientation within the cell membranes of CF-affected lung cells. s-SNOM surpasses the diffraction limit of light, providing sub-wavelength resolution imaging. Unlike fluorescence microscopy and mass spectrometry, s-SNOM enables label-free, high-resolution imaging of biomolecules without the need for external labels or tags. Nano FT-IR spectroscopy utilizes synchrotron radiation to acquire point infrared spectra at the nano-scale, complementing the observations from s-SNOM images.

Our initial focus is on developing a novel methodology for s-SNOM imaging of biological membranes, overcoming challenges associated with nanoscale measurements in thin samples like cell membranes.

The CFBE41o- human CF bronchial epithelial cell line, extensively studied in CF research [1,2,3], will be employed. Our objective is to detect lipid changes and analyse their nanoscale distribution within the membrane systems.

Additionally, we aim to investigate whether lower levels of polyunsaturated fatty acids (PUFA) observed during disease progression [3], when replicated in the culture medium, exacerbate CF cell deterioration.

These findings have the potential to drive the development of novel treatments and therapies, ultimately enhancing the quality of life for individuals with cystic fibrosis.

This innovative approach integrates advanced spectroscopy techniques, includes disease-relevant components, and focuses on understanding membrane remodeling processes associated with cystic fibrosis. It has the potential to unveil novel insights into the role of CFTR and lipids in membrane function and cystic fibrosis pathology, paving the way for future therapeutic strategies and interventions.

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