



Genetic and Cellular Diversity in Cytoplasmic Human Cells

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DESCRIPTION

Intracellular heterogeneity is critical to the pathophysiology and physiology of some debilitating diseases. This is heavily influenced by distinct organelle populations, and strategies for extracting and studying organelles from specific locations within tissues are required to understand disease causation. They explain the development of a subcellular biopsy technique that makes it easier to isolate organelles from human tissue, such as mitochondria. They compared Laser Capture Micro Dissection (LCMD), the industry standard for extracting cells from the tissues around them, to subcellular biopsy technology. They first establish that LCMD has an operating limit (>20 μm), and then show that subcellular biopsies can be utilized to isolate mitochondria in human tissue beyond this limit.

Inter-tissue and inter-cellular heterogeneity is thought to influence a wide range of human diseases, including cancer, cardiovascular disease, metabolic disease, neurodegeneration, neurodevelopmental disorders, and pathological aging. However, evaluating heterogeneity at the cellular and tissue levels sometimes renders subtle subcellular and organelle heterogeneity difficult to detect. Because of their own multi-copy genome, mitochondria exhibit genetic variation in addition to the morphological and functional variability observed in other organelles. Homoplasmy, in which all mitochondrial DNA (mtDNA) molecules are consistently wild-type at birth in healthy people, is distinguished from heteroplasmy, in which mutations result in a mix of wild-type and mutant mtDNA molecules.

Low levels of heteroplasmy can be tolerated, but if enough mutant mtDNA molecules accumulate and spread, oxidative phosphorylation can become blocked, which frequently leads to mitochondrial disease. This method, known as clonal expansion, has an unknown mechanism. Investigating clonal proliferation at the subatomic level may help us characterize mitochondrial disease and better understand the underlying mechanisms. In general, a better understanding of the physiological (and pathological) relevance of intracellular organelle heterogeneity

with subcellular specificity will most likely aid in effective illness detection and therapy; nevertheless, this requires the appropriate technology.

To fully benefit from single-cell multiomics, nano probe-based technologies can overcome some of the issues that arise when analyzing subcellular molecules, such as: Scanning probe microscopy is frequently used in conjunction with nano probe technology to achieve nanometer-level accuracy both inside and outside cells. The comparatively small probe size has little effect on cell viability or the cellular environment, allowing for sampling from live cells. Scanning probe microscopy is routinely combined with nano probe technology to obtain nanometer-level accuracy both within and outside of cells. The comparatively small probe size has little effect on cell viability or the cellular environment, allowing for sampling from live cells.

In 2014, the co-workers developed a nano biopsy approach that extracts mitochondria and mRNA from the cytoplasm of cultured fibroblasts using a nanopipette loaded with an organic solvent. This method is based on a technique known as electro wetting, which involves applying a voltage to a liquid-liquid interface in order to aspirate a target from the cytoplasm of living cells. Fluid Force Microscopy (FFM), dielectrophoretic nano tweezers, and nano pipettes were recently used to successfully sample cytoplasmic proteins and nucleic acids from grown cells.

The cytoplasmic proteins and nucleic acids of cultured cells have recently been successfully sampled utilizing FFM, dielectrophoretic nano tweezers, and nano pipettes. However, none of these technologies have been used to investigate tissue samples used in clinical or molecular pathology. This study sought to examine whether nano biopsy might be adjusted to sample from human tissue samples. They show that subcellular biopsy, a variant of nano biopsy, has the potential to overcome present methodological restrictions by comparing it to Laser-Capture-Micro Dissection (LCMD), the most common approach for studying individual cells in tissue samples.

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