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iPSZÜRICH

A Lecture Series Focused on Induced Pluripotent Stem Cells

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INTEGRATED INTRACELLULAR ORGANIZATION AND ITS VARIATIONS IN HUMAN iPS CELLS

Understanding how a subset of expressed genes dictates cellular phenotype is an enormous challenge due to the large numbers of molecules, their combinatorics, and the plethora of cellular behaviors they determine. We reduced this complexity by focusing on cellular organization, a key readout and driver of cell behavior, at the level of major cellular structures representing distinct organelles and functional machines, and generated the "hiPSC Single-Cell Image Dataset" with over 200,000 live cells in 3D spanning 25 major cellular structures. The scale and quality of this dataset permitted the creation of a generalizable analysis framework to convert raw image data of cells and their structures into dimensionally reduced, human-interpretable quantitative measurements and to facilitate data exploration. This framework embraces the vast cell-to-cell variability observed within a normal population, facilitates integration of cell-by-cell structural data, and permits quantitative analyses of distinct, separable aspects of organization within and across different cell populations. We found that the integrated intracellular organization of interphase cells was robust to the wide range of cell shape variations in the population, that the average locations of some structures became polarized in cells at the edges of colonies while maintaining the "wiring" of their interactions with other structures, and that, in contrast, structure location changes during early mitotic reorganization were accompanied by changes in their wiring.

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