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New nanoarray technologies for single cell omic analysis: Why and how?

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Cell heterogeneity is intrinsic to both genetically programmed differentiation and stochastic/epigenetic variation. The scientific and technological challenge is to quantitatively study the nature and extent of the heterogeneity of populations of cells. In order to reach this goal, scientists need to measure the complete molecular content "omes" of single cells. This is not achievable by the classical approach implementing chromatography/electrophoresis microsystem separation and analysis by mass spectroscopy and nuclear magnetic resonance, due to their lack of high throughput technology and their lack of sufficiently high detection sensitivity. Here we propose that single cell "omic" measurements can be realized with the new interdisciplinary nanotechnology combining physics and chemistry with biology. Our nanoscience approach is based on the implementation of novel Nano in Micro Array (NiMA) biosensor chip platform that can analyze the complete proteome and glycome by means of accommodating up to 2,500 different cell samplings (positioned in microwells) and 250,000 probe markers (positioned in nanowells) per chip. Using a combination of chemical, mechanical, optical, and electrical detection with Secondary Ion Mass Spectrometry (SIMS) and by Scanning Probe Microscopy (SPM), we can quantify all biomolecules approaching detection of a single protein molecule. The gained knowledge about molecular heterogeneity quantified at the single molecular level within each individual cell in the form of "omes" (proteome, glycome, transcriptome, and metabolome) is fundamental to our understanding of causative relationships and formulations of natural laws. This will be a large step toward comprehension and prediction of processes associated with complex living systems like the evolution of life, embryogenesis and morphogenesis, immunity, adaptivity, selfnonself recognition, neural plasticity, and learning, as well as driving forces leading to diseased states of living organisms such as cancer, bacterial, and viral disease, neurodegenerative disorders, and autoimmunity.