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Cytomics Column

Cytomics: An Entry to Biomedical Cell Systems Biology

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BACKGROUND

The introduction of high throughput and high content screening has induced a prolific growth of *-omic* terms such as genomics, proteomics, cytomics and many others (1).

Cytomics, for example, may be considered a new name for cytometry. It is legitimate to ask why a successful effort should have a new name because previous work may get lost in searches as a counterproductive byproduct. Nevertheless, it seems important to consider potentials and challenges of cytomics in the cytometry field.

CYTOMETRY

Cytometry as a technologically oriented science is focused on the multiparametric determination of molecular or morphologic cell parameters by flow or image cytometry. Despite rapid technologic progress (2), the incremental gains in biomedical knowledge has remained in recent years under the true potential of the technology.

This becomes clear when considering the current practice of flow cytometry. Multiparameter measurements are typically performed to discriminate very specific cell populations to confirm or refute a preconceived hypothesis. Only a fraction of the available information is usually extracted by visual evaluation of multiparametrically gated histograms or by quantification of marker positive or negative cells.

CYTOMICS

In this situation, the conceptual dimensions of cytomics (3,4) emerge. Cells constitute the elementary building units of organisms. Diseases are induced by systematic changes of certain molecular cell phenotypes in the background of the full heterogeneity of cells and cell systems (cytomes). Further, molecular cell phenotypes evolve in individuals during their lifetimes due to genotype and exposure to external or internal influences. Differential single-cell screens of diseased versus healthy cytomes using hypothesis-driven parameter panels uncover disease-induced cell phenotype changes. Cytomics are operationally defined as the multimolecular cytometric analysis of cell and cell system heterogeneity in combination with exhaustive bioinformatic knowledge extraction from all measured cells (1). Cytomics enables the correlative analysis of differential individual cellular information with regard to future (prediction) or current (diagnosis) disease states of patients. Disease-associated cytomes are typically investigated, but no detailed a priori knowledge on specific disease-inducing mechanisms is required. This is powerful because it permits one to uncover molecular networks of as yet unknown functionality during the exhaustive knowledge extraction phase of this inductive approach.

CYTOMICS AND BIOMEDICAL CELL SYSTEMS BIOLOGY

A considerable conceptual difficulty currently exists in understanding the corroborative action of the 30,000 to 40,000 genes of the genome by *bottom-up* analysis from the genome level via the proteome, the metabolome (1) including all the low-molecular-weight molecules, the organelle compartments up to the level of cells, cell systems, organs, and organisms (5). The *top-down* approach by cytomics as an alternative represents an efficient and simplifying research strategy that often leads to new hypotheses. Patient-derived molecular data patterns of 20 to 40 gene products are typically obtained from cytomics data pattern differentials. These data patterns are of immediate relevance for everyday medicine because they provide therapy-re-

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lated, individualized, disease-course predictions for patients (4). In addition, the molecular reverse engineering and modeling of the underlying pathways by biomedical cell systems biology has the potential to uncover practically important molecular disease-inducing pathways and new drug targets. In a more general sense, molecular reverse engineering seems important for the analysis of very complex systems because it may be impossible to forward engineer them, given the infinite number of exposure conditions upon a multitude of genetically heterogeneous individuals.

CONCLUSION

The top-down cytomics approach has the potential to advance general health care by therapy-related individualized disease-course predictions. It also provides the potential to uncover practically relevant disease-inducing molecular pathways by biomedical cell systems biology and to identify new drug targets within such pathways. The incentive for the development of sensitive single-cell technologies for research and medicine and the provision of advanced software for analysis and standardized data management represent further important facets of this challenge.

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