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An Overview of Omics Approaches

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Abstract:

The advent of cutting-edge techniques has spawned the concept of "omics," enabling a systematic and comprehensive exploration of cellular systems. However, the relentless discovery of novel and control mechanisms has continually refined our understanding of cellular machinery, rendering the field of cell omics increasingly complex and dynamic. As a consequence, attaining a thorough comprehension of cellular systems poses significant challenges. To navigate this intricacy, it is essential to evaluate current advancements and future prospects in translating omics insights into effective disease control strategies that minimize cellular disruption. This focuses on the interconnected relationships between the "four big omics" – genomics, transcriptomics, proteomics, and metabolomics – as well as epimics and interactomics. We examine existing technologies for cellular interrogation, highlighting their strengths and limitations. Furthermore, we anticipate the emergence of redoxomics as a novel omics layer, which conceptualizes cellular decision-making between physiological and pathological states as a delicate balance of redox reactions. This perspective underscores the importance of integrating omics approaches to elucidate the complex interplay between cellular components and their role in disease pathology.

Keywords: Transcriptomics, proteomics, metabolomics, redoxomics

Introduction:

The integration of "omics" technologies has transformed the landscape of biological research, enabling the simultaneous analysis of vast, complex datasets. This shift has facilitated a more comprehensive, systems-level understanding of intricate biological processes, seamlessly merging "top-down" and "bottom-up" approaches. Consequently, the investigation of multifaceted diseases has evolved from fragmented, low-throughput analyses to cohesive, high-throughput explorations of dynamic, multi-layered modifications spanning the genomic, transcriptomic, proteomic, and metabolic axes. By leveraging

the fundamental principles of the central dogma, a diverse array of omics technologies has emerged, illuminating the intricate, interdependent relationships governing genomic, transcriptomic, and proteomic interactions. These technologies enable the capture of genomic alterations, transcriptomic fluctuations, and proteomic dynamics across spatial and temporal dimensions. Furthermore, the omics landscape has expanded to encompass epigenomic, interactomics, and phenomic analyses, providing a more comprehensive understanding of disease mechanisms and hallmarks.

The convergence of multiple omics disciplines has given rise to a paradigm shift, enabling researchers to elucidate comprehensive causal relationships between molecular patterns and phenotypic outcomes. The advent of single-cell sequencing has further augmented our understanding, providing unprecedented resolution. As the omics landscape continues to evolve, novel technologies are being developed to unravel the intricate molecular mechanisms governing complex biological processes. Despite these advances, the intricate dynamics of cellular behavior and decision-making processes remain a driving force behind innovation in omics technologies. This exhaustive review provides a comprehensive overview of the four primary omics domains – genomics, transcriptomics, proteomics, and metabolomics – as well as their intersections with epigenomics and pairwise interactomics. Furthermore, we anticipate emerging trends, including the burgeoning field of "redoxomics," which promises to reveal new insights into cellular machinery and its role in maintaining homeostasis.

Transcriptomics and Genomics:

Integrating genomics and transcriptomics has transformed research and clinical applications across various fields. Biomedical scientists must now possess skills to manage and analyze large-scale genomic and transcriptomic data. Recent advancements in next-generation sequencing technologies have enabled high-throughput data generation for genomes, epigenomes, and transcriptomes. Nucleic acid-based omics approaches involve five major steps: sample collection, nucleic acid extraction, and library preparation. Post-sequencing data analysis encompasses a multi-step workflow, including data refinement, filtration, assembly, alignment, variant detection, annotation, and predictive functional analysis. Supplementing these analyses with pathway and network evaluations provides crucial biological contextualization. However, the integration of heterogeneous datasets poses significant challenges due to discrepancies in quality assurance protocols, quality control measures, and data normalization methodologies. The advent of cutting-edge technologies, such as single-cell sequencing and extended-read sequencing, introduces additional layers of complexity, including the necessity for optimal sequence coverage and robust statistical modeling. Nevertheless, sequencing-driven platforms offer unparalleled opportunities for generating high-fidelity data from minute tissue samples or individual cells, thereby facilitating a broad range of biological inquiries.

Proteomics:

Proteomics enables the quantification of proteins in various sample types using shotgun and targeted approaches. Recent mass spectrometry (MS) advancements have increased sensitivity and reduced sample requirements, allowing for detection of subtle protein abundance differences, post-translational modifications, and other applications. Quantitative proteomics involves six major steps: sample collection, protein extraction, enzymatic digestion, liquid chromatography separation, MS analysis, and peptide/protein identification and quantification. Additional bioinformatics analyses, such as pathway and network analyses, provide further insights. The field has evolved from 2D-PAGE-based approaches to system-wide screening methods using label-based techniques like SILAC, iTRAQ, and TMT, or label-free methods. Both approaches have yielded favorable results in diverse biological matrices. Despite ongoing efforts through the Proteomics Standards Initiative, a consensus on data formatting, cleaning, and normalization has yet to be established. Nonetheless, proteomics continues to advance biomedical research, including diagnosis, biomarker development, and therapeutics.

Metabolomics:

Metabolomics serves as a crucial link between the genome, transcriptome, proteome, and phenotype, enabling the discovery of the genetic basis of metabolic variation. This field involves the analysis of various biological samples, including cells, tissues, biofluids, and organisms, to determine the relative and absolute amounts of diverse metabolites. Metabolomics employs a range of techniques, including nuclear magnetic resonance (NMR) spectroscopy and mass spectrometry (MS), often coupled with chromatography or electrophoresis. The major steps involved in metabolomics analyses encompass experimental design, sample collection, metabolism quenching, metabolite extraction, and data analysis. Data analysis in metabolomics is complex and variable, depending on the platform and instrument used. Different approaches are required for targeted and untargeted analyses, with the latter typically used for discovery and hypothesis generation. The combination of liquid chromatography-mass spectrometry (LC-MS) and gas chromatography-mass spectrometry (GC-MS) provides comprehensive coverage of the chemical space presented by a biological sample.

Epigenomics:

Epigenomics elucidates the dynamic alterations in gene regulation that occur without modifying the underlying DNA sequence, thereby modulating gene transcription. This field encompasses the characterization of higher-order chromatin structures, including the DNA-DNA interactome, as well as DNA and RNA modifications, such as methylation. The Hi-C technique provides a comprehensive approach to capturing chromosome conformation by crosslinking chromatin with formaldehyde, followed by digestion and re-ligation. Through this process, chimeric DNA ligation products are selectively purified and subsequently analyzed by deep sequencing. The retained ligation products preserve spatial information

regarding their genomic positioning and three-dimensional genome architecture, thereby providing invaluable insights into chromatin topology and gene regulatory mechanisms.

Trends in Omics Technology Development:

The suffix "omics" symbolizes the groundbreaking technological progress made over these years, enabling the simultaneous analysis of thousands of molecules. The four big omics have paved the way for the development of their respective epimomics fields, including epigenomics, epi transcriptomics, and epi proteomics. Additionally, these foundational omics disciplines have led to the emergence of interactomics, encompassing various interaction-based fields such as DNA-RNA, RNA-RNA, DNA-protein, RNA-protein, protein-protein, and protein-metabolite interactomics. Furthermore, knowledge-based omics fields like immunomics and microbiomics have also evolved. The completion of the human genome sequence has catalyzed significant advancements in personalized medicine, where genetic and genomic information informs decisions on disease prevention, diagnosis, and treatment. Genomic data have been instrumental in developing predictive disease models and guiding therapeutic strategies, particularly in cancer treatment. Similarly, metabolomics has uncovered novel biomarkers, shedding light on metabolic pathway disruptions that impact substance levels, such as fatty acids and bile acids. This leads to finding of biomarkers for early hepatocellular carcinoma diagnosis. Despite these breakthroughs, the omics sciences face substantial challenges, including data complexity, management, and integration with external data sources, such as clinical data from routine medical visits. Addressing these challenges is crucial to fully harnessing the potential of omics-driven personalized medicine.

Conclusion:

The intricate association of cellular systems has made hurdle to translational omics, with multi-layered heterogeneity being a primary contributor. While omics technologies provide a snapshot of cellular systems at a specific level, cells are dynamic entities that exist in diverse states. Moreover, cells within tissues or biopsies exhibit pronounced heterogeneity, rendering accurate interpretation of omics data a formidable challenge. This complexity is further exacerbated by inter-patient variability in clinical manifestations and treatment responses. To navigate this complexity, there is a growing trend toward integrating omics datasets of a particular research domain. This integrated approach has given rise to interdisciplinary fields like immunomics and microbiomics. By consolidating omics datasets, scientists can create a systematic view of a research area, uncovering novel insights into the intricate relationships between disparate biological components. This approach is particularly valuable when investigating complex biological processes that impact human cells, such as the delicate balance between homeostasis and malignant transformation.

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