

We have never been Only Human: The Inescapable Multiomics of our Existence

Editorial

This editorial urges a paradigm shift in our understanding of human health and disease, proposing that we are not merely human, but exist as part of a dynamic multiomic system. Traditional binary perceptions of disease - as present or absent - are critiqued, and the urgency to embrace a new approach is underscored. By viewing disease as a spectrum of states stemming from variations across genomics, transcriptomics, proteomics, and environmental influences, we can revolutionize our approach to healthcare. The editorial underscores the vital role of artificial intelligence in synthesizing and analyzing vast data sets, providing a comprehensive and dynamic view of disease. It emphasizes the necessity to orient current research towards this multiomic perspective, asserting that this approach is integral to transcending our existing limitations in disease understanding and management. This call for a new perspective offers potential for more predictive, preventive, and personalized healthcare, promising to bring about significant advancements in our fight against disease.

In the narrative of contemporary scientific inquiry and medical practice, we are often caught in the binary perception of disease, seen as either present or absent based on discernible variables. This reductive approach, though instrumental in addressing numerous health anomalies, invariably poses myriad unanswered questions that lie beyond its narrowed scope. To address these questions and gain a deeper, more comprehensive understanding of our health, a shift in perspective is both crucial and imminent.

The shift proposed is not groundbreaking; instead, it is an augmentation that reframes our view of ourselves, a necessary transition from seeing ourselves as merely human to accepting ourselves as integral parts of a complex multiomic system. Traditionally, our understanding of the human being has been compartmentalized into distinct layers, ranging from the genomic to the environmental. However, the pressing need now is to integrate these layers, acknowledging that we are not simply an assembly of disparate parts but a single, multi-faceted entity. Every change at any level in this multiomic system should be seen not as an isolated event, but as an echo of a pattern of interrelated occurrences across these interconnected strata (Figure 1).

Editorial Article

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Figure 1. The vitruvianman that play chess in front of another entity that represents the entire universe, digital art.

Interestingly, this reconceptualization of humans as multiomic entities is not entirely new, but its significance has been elevated in the present age by technological advances in artificial intelligence. With AI, we now have the tools to collect, process, and analyze a vast amount of data from all different levels of this multiomic system, which was a daunting, if not impossible, task until recently. The transformative power of artificial intelligence grants us a dynamic and coherent picture of our complex selves, transcending the traditional binary view.

Mounting evidence underscores the clinical relevance of data derived from various multiomic levels—genomic, transcriptomic, proteomic, epigenetics, microbiome—alongside the undeniable influence of artificial intelligence (AI) in medical practice.

Ayton et al, [1] assess the effectiveness of multiomics-based methods in categorizing cancer types, a crucial factor in determining personalized treatment. The authors reviewed studies from 2010 to 2019, analyzing patient survival rates associated with these methods. They found that a technique called latent-variable subtyping had a significant association with patient survival. The study concludes that different multiomics methods vary in their ability to predict patient outcomes and guide treatment, with latent-variable methods potentially being more effective.

Liu et al, [2] in his review, uses multiomics (genomics, transcriptomics, proteomics, metabolomics) to investigate the biological foundations of traditional Chinese medicine (TCM) syndromes in stroke concluding that multiomics technologies are powerful tools that can help unravel the complexity of Traditional Chinese Medicine (TCM) syndromes related to stroke. These techniques could contribute to the modernization of TCM and advance personalized medicine in treating stroke with TCM.

Chong et al, [3] address the importance of this approach in epilepsy treatment because of the evidence of the lack of response in about 30% of patients to anti-seizure medications. The study acknowledges that the molecular processes causing epilepsy are not entirely understood, which hinders the development of effective treatments. The authors advocate for the use of omics-based research (the study of genomics, transcriptomics, proteomics, metabolomics, etc.) to provide a comprehensive understanding of the molecules involved in epilepsy. Omics-based approaches have already proven effective in personalizing treatments in oncology and non-cancer diseases. Arikan et al, [4] pertains to the integrated use of multi-omics analyses, specifically within microbiomes. The study reviews each type of omics analysis, noting their history, workflow, applications, strengths, and limitations. It also delves into the practical considerations for integrated multi-omics analyses, discussing current methodologies, tools, challenges, and potential future trends.

Petti et al, in his study [5] further emphasizes the critical role of integrated multi-omics analysis in precision medicine research. In the age of big data, abundant health-related information is available, providing an unparalleled opportunity to revolutionize disease prevention, diagnosis, and prognosis. However, this potential remains largely untapped, and the study emphasizes the need for computational methods that can effectively integrate these diverse datasets to provide a comprehensive view of disease. One method of data integration is network science, which models biomedical data based on relationships among various molecular players. It has been effectively proposed as a new paradigm for studying diseases. An open challenge in this field is patient stratification, which involves identifying patient subtypes with different disease manifestations, severity, and expected survival times. While stratification methods based on gene expression measurements have been successful, few attempts have been made to integrate various genotypic and phenotypic data to discover new patient subtypes or improve the detection of known groupings. Moreover, it highlights the existing gaps in current research, particularly the underutilization of available data, suggesting that the full potential of a multi-omics approach is yet to be realized. Pouladi et al, in his review focus on the importance of this approach on disease comorbidity. It underscores the importance of considering the interconnectedness of multiple diseases within a patient. The study's findings illuminate the potential for using various biomolecular data in deciphering these complex disease interactions, highlighting the untapped potential of intergenic polymorphisms. These insights emphasize that our view of diseases should not only span multiple 'omics levels but should also incorporate the complex reality of disease comorbidity [6]. This study [7] on Type 2 diabetes mellitus (T2DM) offers valuable insights that align with the key points of your editorial. It emphasizes the immense potential of multi-omics research in understanding chronic metabolic diseases like T2DM. The study's focus on intestinal flora perturbations and plasma dyslipidemia, detected through a combination of metagenomics, RNA sequencing, metabolomics, and lipidomics, illustrates the power of integrating various 'omics' data. It further reinforces the importance of understanding diseases as a dynamic interaction of multi-level variables. This review [8] on obesity showcases the importance of multi-omics data—encompassing genomics, epigenomics, transcriptomics, proteomics, and metabolomics—in developing precise and individualized health interventions. It reinforces our perspective that we need to move beyond the traditional one-size-fits-all approach and instead rely on personalized, data-driven methods. This novel approach finds support also in this study [9] that spotlights the importance of multi-omics research in understanding cardiovascular disease (CVD) among South Asians. The rising prevalence of CVD, not fully explained by conventional risk factors, calls for more comprehensive, data-driven research methods. It

emphasizes that findings primarily based on samples of European ancestry may not accurately capture the unique risk profile of CVD in South Asians. This study stress the importance of population-specific, comprehensive multi-omics research in capturing the complexity of diseases. It underscores the necessity to go beyond conventional methodologies and employ a multi-omics approach for more accurate estimation of disease progression and creation of effective prevention and treatment strategies. This study [10] investigates the use of multi-omics techniques in identifying biomarkers and understanding resistance mechanisms in gastric cancer treatment, specifically neoadjuvant chemotherapy. By sequencing multiple types of genetic data from patient samples, the researchers identified mutations and genomic changes that correlate with resistance or sensitivity to treatment. This information can guide precision medicine strategies for gastric cancer, improving patient selection for neoadjuvant chemotherapy and potentially enhancing outcomes. In particular, by identifying specific genetic mutations (like C10orf71) and genomic changes (like MYC and MDM2 amplification), it provides potential biomarkers for patient selection and may allow clinicians to predict a patient's likely response to neoadjuvant chemotherapy, leading to more personalized treatment strategies. This study [11] offers a novel data analysis pipeline that integrates both transcriptomics and genomics data. This dual approach enables a more robust and comprehensive assessment of genotype-phenotype associations, which is particularly useful in the case of rare diseases where sample sizes are typically small, thereby limiting statistical power. The researchers applied this innovative pipeline to investigate the rare but life-threatening complication of hematopoietic stem cell transplantation (HSCT), known as sinusoidal obstruction syndrome (SOS). They used whole-exome sequencing (WES) data from HSCT patients and combined this with gene expression data from lymphoblastoid cell lines treated with busulfan, a drug known to trigger SOS. The combination of these two distinct but complementary data types allowed them to identify 35 genes associated with SOS. This study is an example of how integrative multi-omics approaches can be applied to complex health issues. It highlights the power of integrating various types of omics data to uncover key molecular insights and potential biomarkers. The proposed pipeline could potentially be adapted to the study of microbial communities, using metagenomic data in combination with other omics data types, such as metatranscriptomics or metaproteomics, to gain a more comprehensive understanding of microbial function and interaction within their environment.

This study [12] shows the value of combining genomic information with other data (like CNV) to gain a better understanding of disease mechanisms, thereby allowing clinicians to select the most effective treatment based on the patient's unique genomic profile. The most notable finding was that when patients were matched to molecularly

targeted agents based on their genomic profile, there was a significantly higher response rate in the treatment of gastrointestinal/hepatobiliary/rare tumors and lung cancer.

This, phase II trial [13], investigated the use of a multiomics approach to identify potential biomarkers associated with progression-free survival (PFS) in patients with advanced non-small cell lung cancer (NSCLC) treated with pembrolizumab, an immunotherapy drug. The patients had a type of NSCLC that expresses lower levels of programmed death-ligand 1 (PD-L1 <50%), a protein that cancer cells often use to evade the immune system. The researchers used various 'omics' techniques (circulating immune profiling, gene expression profiling, and gut microbiome analysis) to identify factors that might predict how well patients would respond to the treatment. The study found that certain types of immune cells in the blood (natural killer cells/CD56dimCD16+ at baseline, non-classical CD14dimCD16+monocytes, eosinophils (CD15+CD16-) and lymphocytes after the first radiologic evaluation) and the baseline expression levels of certain genes (CD244, protein tyrosine phosphatase receptor type C, and killer cell lectin like receptor B1) were associated with a more favorable PFS. This study illustrates how multiomics data can be harnessed to identify potential biomarkers for predicting patient responses to specific therapies. It underscores the value of integrative, multi-modal analyses in generating more detailed insights into disease mechanisms and treatment responses, which can ultimately aid in the development of more personalized therapeutic strategies. This study [14] underscores the role of spatial multi-omics analysis in understanding the complexities of tumor heterogeneity and its impact on treatment responses. It also emphasizes the potential of spatially resolved multi-omics signatures to predict treatment outcomes more accurately, further supporting the integration of multi-omics data in precision medicine. This study explores the impact of intratumoral heterogeneity (ITH) on the effectiveness of immunotherapy in cancer treatment. The diversity within a tumor, also known as ITH, is considered a significant obstacle to the success of cancer treatment, including immunotherapy, as it can lead to varied responses to treatment within different regions of the same tumor. To better understand this, the researchers used digital spatial profiling (DSP), a technique that can provide detailed information about the expression of genes and proteins in specific regions of a tissue sample. They applied this method to analyze both tumor and stromal regions (supportive tissue surrounding the tumor) at the proteomic (proteins) and transcriptomic (RNA) levels. The study involved 18 patients treated with a type of immunotherapy known as bispecific antibody (bsAb)-KN046. They found that the tumor and stromal areas exhibited distinct molecular features. They then used these features to construct signatures - combinations of markers that could be used to predict the response to immunotherapy. Interestingly, the predictive signature derived from the stromal region had a higher predictive

power for the response to the bsAb treatment compared to the signature derived from the tumor region. This stromal signature was further validated in an independent cohort of patients with non-small cell lung cancer undergoing immunotherapy.

As we delve deeper into the patient-specific, individualized applications of multi-omics in a clinical setting, it is essential not to overlook the potential of this approach to address broader public health issues. A study [15] exemplifying this potential focused on the cardiovascular effects of traffic-related air pollution (TRAP). This study used a multi-omics approach to assess the systemic impact of TRAP on cardiovascular health in 56 young adults. The research design involved two exposure sessions—on a busy road and in a park—with subsequent multi-omic analyses, including lipidomics, proteomics, and metabolomics. These analyses revealed that exposure to TRAP led to increased blood pressure, decreased heart rate variability, and significant alterations in molecular pathways connected to inflammation, oxidative stress, endothelial dysfunction, and lipid metabolism. The implications of this research are far-reaching. By leveraging the multi-omics approach, the study could pinpoint specific biomolecular changes linked with TRAP exposure. This knowledge could guide public health interventions, drive policy changes, and even aid in the development of therapeutics to mitigate TRAP's adverse effects. Furthermore, it demonstrates how the convergence of environmental and health data can facilitate a more nuanced understanding of disease etiology, further underscoring the transformative potential of multi-omics.

Such studies offer a wider perspective on the role of multi-omics, extending beyond the confines of direct patient care to public health interventions and policy-making.

Moving to a more specific clinical setting, multi-omics research has been pivotal in enhancing the efficacy of immunotherapies for various types of cancer as showed in previous studies. For instance, a phase 2 clinical trial investigating the neoadjuvant treatment of esophageal squamous cell carcinoma (ESCC) employed a combination of nanoparticle albumin-bound paclitaxel, S-1, and the immune checkpoint inhibitor toripalimab [16]. Their outcomes were impressive, with major pathological responses seen in approximately half of the patients. What is most noteworthy for our discourse is the depth of understanding the multi-omics approach afforded the researchers regarding the treatment's mechanism of action. By implementing whole-exome sequencing, transcriptome sequencing, and an extensive proteomic analysis before and after neoadjuvant therapy, they could correlate specific genomic, transcriptomic, and proteomic changes with clinical outcomes. For example, a high PD-L1 expression correlated with a better treatment response, and a decrease in tumor mutation burden and tumor neoantigen burden was significantly associated with

positive responses. Moreover, the study identified specific genomic and proteomic markers that could predict serious adverse effects, making it possible to preemptively identify patients at risk. They further distinguished responders from non-responders by integrating specific immune cell data (CD4+ T cells) with plasma protein levels. By presenting such studies, we highlight how multi-omics can transform cancer treatment, taking us several steps closer to truly personalized and predictive medicine. Not only does this approach improve our understanding of complex treatment mechanisms, but it also holds promise for identifying which patients are most likely to benefit from specific therapeutic strategies.

The value of a multi-omics approach involves different fields. For example, in a study [17] aiming to identify potential biomarkers for amoxicillin/clavulanate-induced liver injury (AC-DILI), researchers utilized a multi-omics analysis to track the body's response to the drug. They observed an increase in liver-specific microRNA-122 (miR-122) levels, which correlated with an increase in the liver enzyme alanine aminotransferase (ALT), a conventional marker of liver injury. This suggests miR-122 could serve as a sensitive early marker for AC-DILI. Furthermore, the study detected significant alterations in the levels of urinary metabolites, such as azelaic acid and 7-methylxanthine, dependent on the degree of ALT elevation. Also, a notable lymphocyte proliferation in response to the drug was observed, suggesting an immune response to the medication. This sequential illustration of the biological response to the drug from metabolic alterations, miR-122 level increase, and liver enzyme activity increase, to lymphocyte proliferation is made possible by comprehensive multi-omics approaches. Through this, we are beginning to witness the transformative potential of multi-omics in a diverse range of applications in healthcare, from improving cancer treatments to predicting drug-induced liver injuries.

Shifting our gaze to infectious diseases, multi-omics approaches are playing a pivotal role in decoding the complex biological response to viruses, like SARS-CoV-2. In a study [18] involving 139 COVID-19 patients, researchers employed a multi-omics analysis, encompassing clinical measurements, immune cells, and plasma components. This comprehensive data highlighted a significant shift between mild and moderate disease stages, marked by elevated inflammatory signaling and a loss of specific metabolites and metabolic processes. This level of detail is uniquely achievable through the application of multi-omics methods.

What's particularly fascinating about this study is the revelation of unusual immune cell phenotypes appearing and intensifying with disease severity, which could provide new targets for therapeutic intervention. The researchers were able to condense over 120,000 immune features into a single axis, capturing how different immune cell classes coordinated in response to SARS-CoV-2. This 'immune-

response axis' aligns with major plasma composition changes, blood clotting clinical metrics, and the significant transition between mild and moderate disease.

These findings underscore the potential of a multi-omics approach to identify the most opportune therapeutic intervention point in a patient's disease trajectory. In this case, it suggests that the moderate disease stage may provide the most effective setting for therapeutic intervention for COVID-19 patients.

Switching our attention to cardiovascular disease, multi-omics can provide deep insights into the body's response to therapeutic interventions. In a recent study [19], researchers compared the impact of ticagrelor, a powerful P2Y12 antagonist, and aspirin monotherapy on vascular endothelial function in patients with a history of acute coronary syndrome. In this randomized controlled trial, it was found that ticagrelor significantly improved brachial flow-mediated dilation, a measure of vascular endothelial function, compared to aspirin. This critical insight could help optimize antiplatelet therapies for this patient group, but the study didn't stop there. Through multi-omics profiling, researchers revealed significant metabolic and lipidomic changes associated with this improved vascular function in the ticagrelor group. Notably, they identified changes in the metabolism and biosynthesis of amino acids and phospholipids. Integrating this kind of multi-omics analysis into clinical trials can illuminate the molecular mechanisms behind observed treatment effects, opening up new avenues for therapeutic optimization.

Taking our discussion to the realm of complex diseases like asthma, a study carried out on Puerto Rican children [20] utilized a 'vertical' multi-omics approach that brought together genome-wide genotype data, methylation data, gene expression profiling, cytokine levels, and clinical phenotypes associated with asthma. This unique, integrative approach moved beyond relying on complex statistical models and assumptions, focusing instead on a stepwise analysis to identify the most relevant genes associated with childhood asthma. The researchers identified several genes whose expression levels were associated with key asthma traits like age of onset, lung function, exacerbations, eosinophil counts, and skin test reactivity. One gene, IL5RA, stood out, showing significant associations across several analytical steps, including asthma-modified gene expression, association with asthma traits, and methylation association with asthma. Furthermore, the plasma levels of IL-5 receptor α , encoded by IL5RA, were linked to asthma age of onset and the frequency of moderate-severe exacerbations. Through this integrative approach, the study was able to pinpoint biologically significant asthma-related genes, offering promising targets for future investigation and potential treatment. This work exemplifies the power of a multi-omics approach in the realm of complex disease, allowing

researchers to cut through the noise and identify the most significant factors across multiple levels of biological data.

Integrative analyses of multiomic data sets have begun to unravel the complex interplay of factors leading to disease onset and progression. Understanding the dynamic changes at the genomic level, transcribed into the transcriptomic level and translated into the proteomic level, allows us to see disease not merely as a binary state but as a spectrum of varying states.

Moreover, the advent of AI has heralded a new era in healthcare. From streamlining diagnoses and optimizing treatment plans to predicting patient outcomes, AI has not only transformed our ability to manage diseases but also offered unprecedented insights into disease pathogenesis. It offers a powerful means to synthesize and analyze vast, multiomic data sets, providing a high-resolution picture of our health.

These advancements underscore the significance of our shift in perspective. The blend of multiomic data analysis and AI capabilities enables us to view health and disease through a more holistic and dynamic lens, one that acknowledges our existence as a part of a multiomic system rather than merely 'human'. By further exploring this approach, we stand to revolutionize our understanding of disease and our approach to healthcare.

In this context, we introduce the concept of internal and external levels within the multiomic framework. The internal levels consist of genomic, transcriptomic, proteomic, radiomic, immunologic, histological, and clinical views. These facets reflect the intricate processes that operate within us, while the external levels encompass a plethora of factors from our immediate physical environment to broader social, cultural, and ecological contexts. Importantly, the internal and external levels are not static but engage in a dynamic, reciprocal dialogue. Alterations in one level often induce changes in another, thereby modifying the system's entire landscape.

The advent of artificial intelligence marks a significant turning point in our ability to study this intricate interplay. Its capacity to gather, process, and analyze large data sets across these multiomic levels offers a living, dynamic image of our ever-evolving selves. As such, the AI-powered multiomic perspective holds immense potential not only for revolutionizing our understanding of disease but also for reshaping our perception of what it means to be 'human'.

In essence, we propose that 'humanness' is not an isolated state but a complex confluence of multiomic interactions (Figure 2). By reframing our perspective, we open a new pathway towards understanding disease and health, enabling us to glean nuanced insights about our very nature. Thus, as we explore the depths of our multiomic identity, we set a new course for scientific exploration, and in doing so, redefine the essence of our humanity.



Figure 1. An interconnected multiomic system showing a human figure at the center that merges with the entire universe making a galaxy painted like digital art.

In line with the multiomic framework and the concept of humans as dynamic entities, this editorial seeks to stimulate a significant transformation in our perception and approach to disease. Traditional views have often confined diseases within a binary state - they are either present or absent. However, such a simplistic approach fails to capture the intricate continuum that underlies disease progression and manifestation.

Diseases should instead be regarded as dynamic and fluid, resulting from linear variations across all multiomic levels. Currently, our recognition and understanding of diseases are constrained by our ability to diagnose, an approach inherently limited by its binary nature. But we need to see beyond this limitation.

Rather than focusing merely on the endpoint – the disease – our emphasis should shift to the variations and interactions of independent variables that occur incrementally across all levels. Disease is not a singular event, but the culmination of a myriad of changes - a choreography of genomic, transcriptomic, proteomic, and environmental factors, among others. Each minor variation, each interaction, contributes to this complex dance, progressively shaping the health status until it culminates in what we traditionally define as ‘disease’.

As we navigate our way towards this new understanding, it is also essential to recognize the impact of our interactions with this multiomic system. Whether through pharmaceutical interventions, surgical procedures, or lifestyle modifications, any interaction induces changes across the whole system.

The administration of a drug, for instance, does not solely target a specific disease marker. Instead, it echoes throughout the interconnected layers of genomics, transcriptomics, proteomics, and beyond, triggering a cascade of effects. Similarly, a surgical procedure or a lifestyle change extends its influence beyond the immediate, causing ripples of changes that reverberate across the multiomic spectrum.

This highlights the complexity of our interventions and underscores the need for a holistic approach. Understanding these reverberations and their downstream effects can inform more precise interventions, allowing us to manage their impacts more effectively and predict potential outcomes. It serves as a powerful reminder that we are not merely intervening in a disease state, but in a dynamic, interconnected multiomic system - a system where we are, and have always been, more than just human.

Such a realization further amplifies the need for our shift in perspective and the exploration of artificial intelligence capabilities in synthesizing and interpreting the vast multiomic data. By embracing this approach, we can foster a more predictive, preventive, and personalized healthcare system, making significant strides towards truly understanding and managing the dynamic nature of disease.

Thus, the challenge we face is to recognize and understand these variations and their dynamic interplay. With the power of artificial intelligence, we are equipped to delve into these interactions, tracing the progression of these variables and elucidating the dynamic correlations among them. By doing so, we can begin to perceive disease not as a static definition but as a dynamic state, a constantly evolving interplay of multiple factors across the multiomic spectrum.

In this light, we call for a reimagined approach to disease, one that not only reshapes our understanding but also holds promise for a more predictive, preventive, and personalized medical practice. Such a shift would mark a significant stride towards truly capturing the dynamic nature of disease and the multiomic essence of our humanity.

With this editorial we want to emphasize the transformative potential of multi-omics approaches in our understanding and management of human health. Through the presented case studies spanning diverse medical conditions - cardiovascular disease, esophageal squamous cell carcinoma, amoxicillin/clavulanate-induced liver injury, COVID-19, acute coronary syndrome, and childhood asthma – the power of integrating various omics data has been demonstrated.

In this editorial, we discussed how the integration of various “omics” technologies offers a more holistic and precise understanding of human health and disease.

These multi-omics levels include:

1. Genomics: The study of the entire set of genes (genome) in an organism, including their structure, function, and interactions.
2. Epigenomics: The study of modifications to the genetic material that do not involve changes to the DNA sequence itself, but rather affect gene expression and can be inherited or influenced by environmental factors.
3. Transcriptomics: The study of the complete set of RNA molecules transcribed from the genes in a cell or organism, providing insights into gene expression patterns.
4. Proteomics: The study of the entire set of proteins produced by a cell, tissue, or organism, including their structures, functions, and interactions.
5. Metabolomics: The study of the complete set of small-molecule chemicals (metabolites) present in a biological sample, providing information about metabolic pathways and their alterations in disease states.
6. Lipidomics: A subfield of metabolomics that focuses specifically on the comprehensive analysis of lipids, including their structures, functions, and roles in biological processes.
7. Immunomics: The study of the immune system, including its complex interactions and response pathways, aiming to understand immune-related diseases and potential therapeutic interventions.
8. Microbiomics: The study of the collective genetic material of microorganisms (bacteria, fungi, protozoa, viruses) that live on and inside the human body, known as the microbiome, and its impact on health and disease.
9. Exposomics: The study of how environmental exposures, such as diet, lifestyle, occupational factors, and pollution, influence an individual's health over their lifetime, taking into account social determinants of health and disease risks.
10. Pharmacogenomics: The study of how an individual's genetic makeup influences their response to drugs, aiming to develop personalized medication and dosage regimens based on genetic information.
11. Interactomics: The study of molecular interactions, particularly interactions between proteins and other molecules, providing insights into complex biological networks and signaling pathways.
12. Glycomics: The study of the complete set of sugars (glycans) in a cell or organism, exploring their structures, functions, and roles in various biological processes.
13. Nutrigenomics: The study of the relationship between nutrients and gene expression, aiming to understand how diet and nutrition impact an individual's health and disease susceptibility.
14. Phenomics: The study of physical and biochemical traits of an organism as they change in response to genetic variations and environmental influences.
15. Radiomics: The extraction and analysis of a large amount of quantitative imaging features from medical images, aiming to improve disease diagnosis, treatment planning, and patient outcomes.
16. Metagenomics: The study of genetic material recovered directly from environmental samples, such as soil, water, or microbial communities, providing insights into microbial diversity and function.
17. Neurogenomics: The study of how the genome contributes to the structure, function, development, and susceptibility to diseases of the nervous system.
18. Toxicogenomics: The collection, interpretation, and storage of information about gene and protein activity in response to exposure to toxic substances, aiming to understand the molecular mechanisms underlying toxicity.
19. Psychogenomics: The study of the genetic basis of cognition and behavior, aiming to uncover the genetic factors that contribute to psychiatric disorders and individual differences in behavior.
20. Mitogenomics: The study of the genetic information contained within mitochondria, which play a crucial role in cellular energy production and are associated with various diseases.
21. Cytomics: The high-throughput analysis of cells to understand their function and properties, including studying cell populations, cell signaling, and cellular responses to stimuli.
22. Connectomics: The study of the connectome, which refers to the complete set of connections between neurons in a nervous system, aiming to understand neural circuits and their functions.
23. Chromosomics: The study of the structure, properties, and behavior of the complete set of chromosomes in an organism, including their roles in inheritance and disease.
24. Structuromics: The study of the three-dimensional structures of biomolecules, such as proteins and nucleic acids, to understand their functions and interactions.
25. Toponomics: The high-content analysis of the spatial and temporal organization of cell and tissue structures,

aiming to understand the organization and dynamics of biological systems.

26. Fluxomics: The study of metabolite fluxes within cells, tissues, or organs, providing insights into metabolic pathways, regulation, and cellular function.
27. Radiogenomics: The study of genetic variations associated with an individual's response to radiotherapy, aiming to personalize treatment based on genomic profiles.
28. Oncomics: The study of the complete set of genes, or other omics, in cancer cells, focusing on understanding the molecular mechanisms of cancer development, progression, and response to treatment.

These different “-omics” are interconnected, and each provides a piece of the puzzle in understanding the biological complexities of life. Each “-omic” level provides information about the cell or organism at a different scale, from individual molecules to entire systems, and these data layers can be integrated to create a more comprehensive picture of biological function and disease.

In addition to the list provided, there are several other “-omics” disciplines that are more specialized or are emerging fields.

These diverse levels of multi-omics approaches collectively provide a comprehensive picture of the multifactorial nature of disease processes, paving the way for improved diagnostic, therapeutic, and preventative measures.

By this new multi-omics approach we can:

1. Increase Precision in Understanding Disease Mechanisms: Multi-omics research has broadened our perspective on disease mechanisms, moving beyond single-cause theories and providing more comprehensive insight into the complex web of biological factors influencing disease development and progression. For example, the detailed molecular profiling from the traffic-related air pollution study

and the integrated analysis in the COVID-19 study underscore the complexity of biological responses to environmental and infectious disease stressors, respectively.

2. Highlight Potential Therapeutic Targets: The integrated multi-omics approaches have proven effective in highlighting novel therapeutic targets. The esophageal squamous cell carcinoma study demonstrated how neoadjuvant therapy involving multiple agents resulted in significant genetic and immunologic changes, with potential implications for future therapeutic strategies.
3. Get Better Biomarkers for Disease Prediction and Diagnosis: Multi-omics approaches have the potential to identify novel biomarkers that can detect disease early or predict response to therapy. This was demonstrated in the study on amoxicillin/clavulanate-induced liver injury, where increased microRNA-122 levels and distinct urinary metabolites were identified as potential early markers for drug-induced liver injury.
4. Further Development for Personalized Medicine: The multi-omics approach can facilitate the development of personalized medicine. This was seen in the study of ticagrelor vs aspirin monotherapy in patients with acute coronary syndrome, where ticagrelor was associated with significant metabolomic and lipidomic changes, which may guide personalized therapeutic choices in the future.

New Challenges and Future Directions: Despite its promising potential, multi-omics research also poses several challenges, such as the need for powerful statistical methods, computational tools, and frameworks to handle high-dimensional, heterogeneous data and to integrate multiple layers of information. Additionally, ethical considerations regarding data privacy and consent must be carefully navigated. Going forward, continued technological advances and further refinement of analytical strategies will be crucial to fully harness the potential of multi-omics in medical research.

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