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Editorial

Feature Papers in *BioChem*, 2nd Edition

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1. Introduction and Scope

As mentioned in the Editorial of the first edition of the Special Issue on "Feature Papers in *BioChem*", biochemistry acts as a key cog in the "clock of the knowledge, permitting that wheels from several science areas move each other" [1]. Moreover, the understanding of life on earth is a perpetual topic in biochemistry, with boundaries dependent on the specificities of each time period and scientific environment [1]. Thus, following the first edition, this Special Issue on "Feature Papers in *BioChem*, 2nd Edition" still emphases interdisciplinary research in diverse and interconnected scientific areas, with a majority from molecular medicine, cell biology and of course biochemistry (Table 1). Among these scientific fields, a wide range of topics were addressed, as expressed by the diversity of the titles and keywords that can be found in each contribution (Table 1).

Table 1. Type of contribution, scientific area, title and keywords of the 16 contributions of the SI, according to the order of publication.

Contribution/ Type/Scientific Area	Title	Keywords
Contribution 1/ review/cell biology	Advances in Personalized Cancer Vaccine Development: AI Applications from Neoantigen Discovery to mRNA Formulation	personalized cancer vaccines; neoantigen prediction; codon optimization; 5′ UTR; mRNA design; deep learning; immunotherapy
Contribution 2/ review/microbiology	From Microbes to Molecules: Synthetic Biology Approaches for Advanced Materials Design	synthetic biology; biopolymer; nanotechnology; biomineralization; MICP
Contribution 3/ review/medicine	The Mini-TRH Test, Dopamine Transmission, and Schizophrenia Symptoms	schizophrenia; dopamine; TRH; positive symptoms
Contribution 4/ review/cell biology	Single-Cell Transcriptomics in Spinal Cord Studies: Progress and Perspectives	single-cell RNA sequencing; spinal cord; transcriptomics; spinal cord injury; neurodegeneration; developmental biology; spatial transcriptomics; multi-omics integration; cell atlas; regenerative medicine
Contribution 5/ article/medicine	HCC in MASLD and ALD: Biochemical Pathways, Epidemiology, Diagnosis, and Treatment	hepatocellular carcinoma; HCC; liver cancer; MASLD; MASH; alcohol-related liver disease; ALD

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Table 1. *Cont.*

Contribution/ Type/Scientific Area	Title	Keywords
Contribution 6/ review/medicine	The Occult Cascade That Leads to CTEPH	pulmonary hypertension; pulmonary emboli; microthrombi
Contribution 7/ review/cell biology	Enhancing Mitochondrial Maturation in iPSC-DerivedCardiomyocytes: Strategies for Metabolic Optimization	mitochondrial maturation; iPSC-derived cardiomyocytes; oxidative phosphorylation; mitochondrial biogenesis; fatty acid oxidation; energy metabolism; metabolic preconditioning; cardiac regeneration; regenerative medicine
Contribution 8/ review/medicine	Cancer Therapy-Related Left Ventricular Dysfunction: Are There New Gatekeepers?	cardio-oncology; cancer therapy-related cardiac dysfunction; tailored approach; left ventricular impairment
Contribution 9/ review/biotechnology	Therapeutic Potential of Essential Oils and Their Bioactive Compounds Against Colon Cancer: Focus on Colon-Specific Micro- and Nanocarriers	anticancer essential oils; bioactive compounds; colon cancer; colon-targeted drug delivery; micro- and nanoapproaches
Contribution 10/ opinion/medicine	An Opinion on the Supplementation of Folic Acid 1 mg + Iron (Ferrous Sulfate) 90 mg in the Prevention and Treatment of Anemia	anemia; iron deficiency; folic acid; supplementation; ferrous sulfate
Contribution 11/ review/medicine	Osteoporosis: Focus on Bone Remodeling and Disease Types	osteoporosis; pathogenesis; secondary osteoporosis
Contribution 12/ article/biochemistry	AI-Assisted Identification of the Functional Residues of Ginsenoside Biosynthesis-Associated UGTs	UGT; ginsenoside biosynthesis; functional residue; artificial intelligence; 3D structure
Contribution 13/ review/medicine	RASopathy and Sudden Cardiac Death: A Literature Review	RASopathy; RASopathies; sudden cardiac death; sudden death
Contribution 14/ feature paper/biochemistry	Polyoxometalates' Progress for the Treatment of Alzheimer's Disease	polyoxometalates; Alzheimer's disease; β-amyloid aggregation; neurotoxicity; blood–brain barrier; reactive oxygen species production;β-amyloid disaggregation; acetylcholinesterase inhibitors; transition metal chelators; nanoparticles
Contribution 15/ article/medicine	Drug Allergy in Hospitalized Patients: Three Years of Consultation Experience in a Tertiary Care Setting	allergy consultation; drug allergy; adverse drug reaction; epidemiology; inpatient allergology; anaphylaxis; scar; drug allergy diagnosis; desensitization; allergy stewardship
Contribution 16/ review/biotecnhology	Lactic Acid Bacteria: From Bioprocessing to Nanomedicine	lactic acid bacteria; nanomedicine; *Lactobacillus*; postbiotics; paraprobiotics; probiotics; encapsulation; functional foods; nanoparticles

Altogether, this Special Issue shared three articles, one opinion, one feature paper and eleven reviews, coming to a total of 16 contributions. A total of 53 authors from 9 countries, namely, Italy (5), USA (4), Portugal (2), Korea (2), Japan, Finland, Bulgaria, Indonesia and Iran, were involved, with the majority of topics being related to medicine, biochemistry and biotechnology. Whereas the eleven contributions of the first edition have gathered 32 citations and 50,114 views as of 20 March 2026, indicating an average of 2.9 citations and 4555 views per publication, these 16 contributions have already gathered 31 citations and 52,707 views, indicating an average of 1.4 citations and 3294 views per publication.

2. Contributions

This Special Issue contains three articles (contributions 5, 12, 15), one opinion (10), one feature paper (14) and eleven reviews (1–4, 6–9, 11, 13, 16), for a total of 16 contributions. The first article contribution published in the present Special Issue (SI) is entitled "HCC in MASLD and ALD: Biochemical Pathways, Epidemiology, Diagnosis, and Treatment" (contribution 5) and it deals with hepatocellular carcinoma (HCC) with metabolic-dysfunction-associated steatohepatitis (MASH) and alcohol-related liver disease (ALD). The authors emphasize the consensus regarding the screening of HCC in cirrhosis patients, and the lack of consensus on screening strategies for non-cirrhotic MASH patients who are also at risk for HCC. It was concluded that multidisciplinary and personalized approaches to prevention, diagnosis, and treatment are crucial for improving outcomes in HCC, especially for groups affected by MASH and ALD, thus preventing healthcare disparities. A recent review from Dr Patel analyzed glucagon-like peptide-1 receptor agonists (GLP-1 RAs) in the reduction of alcohol use and in the treating of alcohol use disorder [2]. The second article (contribution 12) is entitled "AI-Assisted Identification of the Functional Residues of Ginsenoside Biosynthesis-Associated UGTs" and the authors identified amino acid residues in UGTs (UDP-dependent glycosyltransferases) that may alter their reaction kinetics. They also identified, using AI, several other residues that potentially change ligand interactivity of ginsenoside biosynthesis-associated UDP-dependent glycosyltransferases (UGTs) in plant enzymes. As referenced in the article, the conversion of ginsenosides into various molecules presents numerous pharmaceutical applications such as anti-cancer, anti-diabetic, cardio-protective, anti-osteoporosis, antiviral, and anti-Parkinson's disease, among many others, highlighting how modulating the sugar moiety of ginsenoside molecules may alter their pharmaceutical activity. Recent studies from Professor Kim's research group, which also used structure-based AI models, described four promising amyloid-β amino acid residues to be targeted which might treat Alzheimer's disease [3]. The third article (contribution 15) is about "Drug Allergy in Hospitalized Patients: Three Years of Consultation Experience in a Tertiary Care Setting". The study aims to characterize the clinical features of patients referred for allergology consultation due to suspected drug allergy, since drug hypersensitivity reactions (DHRs) are an important cause of morbidity in hospitalized patients.

Also based on clinical experience, and from another hospital medical research team, we received an opinion paper (contribution 10) about "An Opinion on the Supplementation of Folic Acid 1 mg + Iron (Ferrous Sulfate) 90 mg in the Prevention and Treatment of Anemia". The authors discussed the recommendation of using folic acid 1 mg + iron (ferrous sulfate) 90 mg supplementation in the prevention and treatment of anemia in adults. Following a similar concern, Professor Hugo and collaborators' recent publications include a review about the appropriate prescription of non-steroidal anti-inflammatory drugs (NSAIDs) in geriatric patients [4]. This SI also contains a feature paper about "Polyoxometalates' Progress for the Treatment of Alzheimer's Disease" (contribution 14). Behind the inorganic biochemistry perspective of the evolution of the utilization of polyoxometalates' in Alzheimer's disease (AD), focusing on the diverse types of POM structures, the POMs' effects and future directions in the field, the authors also aim to bring together AD caregivers, doctors, psychologists, nurses and family members. Recent studies from Professor Aureliano's research group include new polyoxometalates with anti-cancer properties and Ca^{2+}-ATPase inhibition potential [5,6].

Besides the above contributions, this SI also contains eleven review papers. The first review published is about "Advances in Personalized Cancer Vaccine Development: AI Applications from Neoantigen Discovery to mRNA Formulation" (contribution 1). This contribution is a review about the recent developments using AI-driven tools to enhance

personalized cancer vaccines, although this is still in its early stages. The second review (contribution 2) is "From Microbes to Molecules: Synthetic Biology Approaches for Advanced Materials Design". This article seeks to present a review of recent developments in microbial-mediated synthesis of inorganic and organic materials, and it explores the mechanisms of microbial biomineralization, particularly how microorganisms influence the formation of the mineral deposits and participate in key biogeochemical cycles. The next review is entitled "The Mini-TRH Test, Dopamine Transmission, and Schizophrenia Symptoms". The author mentions that in psychotic patients, care must be taken to reduce the effect of stress on the thyrotropin-releasing hormone (TRH) analysis and the mini-TRH test, including the use of local anesthesia to control stress induced by blood extraction. In fact, in psychotic patients, the assessment of unstimulated stress is not easy. It was concluded that correlative analyses of symptoms may provide information on symptom-specific alterations in dopamine transmission in non-affective psychotic symptoms. Following a similar concern, recent studies from the same author stated that the most common symptoms of schizophrenia, paranoid delusions and hallucinations, were not significantly associated with the mini-TRH test. However, if individual symptoms of schizophrenia could be associated with basal blood prolactin level, the mini-TRH could help discover whether it could be associated with dopamine inhibition of prolactin secretion [7]. The following review entitled "Single-Cell Transcriptomics in Spinal Cord Studies: Progress and Perspectives", related to spinal cord research and single-cell RNA sequencing (scRNA-seq) analysis, summarizes recent progress in the application of scRNA-seq to spinal cord development, injury, and neurodegenerative diseases. scRNA-seq platforms and their contributions to spinal cord research are described along with current challenges and future directions. The 5th review is about "The Occult Cascade That Leads to CTEPH". Chronic thromboembolic pulmonary hypertension (CTEPH) is a rare, progressive form of pre-capillary pulmonary hypertension. The authors concluded that the ongoing research into molecular mechanisms and biomarker-driven diagnostics promises earlier identification and more personalized management.

The 6th review is entitled "Enhancing Mitochondrial Maturation in iPSC-Derived Cardiomyocytes: Strategies for Metabolic Optimization" and highlights the potential of using pluripotent stem cell-derived cardiomyocytes (iPSC-CMs) for cardiovascular regenerative medicine, although their clinical application is hindered by suboptimal mitochondrial maturation and metabolic inefficiencies. The authors point out that metabolic preconditioning with fatty acids and oxidative phosphorylation enhancers improves mitochondrial architecture, cristae density, and ATP production. Recent studies from Professor Sugiura and collaborators include the exploration of extracellular vesicles (EVs) as powerful mediators of mitochondrial transfer and cardiomyocyte repair of mitochondrial dysfunction in cardiac disease [8]. The 7th review, also associated with cardiovascular diseases, is about "Cancer Therapy-Related Left Ventricular Dysfunction: Are There New Gatekeepers?". The authors mention that although the growing success of oncologic therapies has led to a significant improvement in patient survival, this has been accompanied by an increasing incidence of cardiovascular adverse events, particularly cancer therapy-related cardiac dysfunction (CTRCD). Specifically, the authors summarized the molecular mechanism of damage of the most dangerous drugs that cause left ventricular (LV) impairment, with the molecular mechanisms of anthracycline-induced cardiotoxicity highlighted, as well as the "new gatekeepers", that is, the drugs preventing ventricular dysfunction such as angiotensin-converting enzyme inhibitors, angiotensin receptor blockers and β-blockers. Recent studies from authors of this research group include the need to identify and implement more sensitive and specific biomarkers for cardiovascular disorders in clinical practice [9].

The next review is about "Therapeutic Potential of Essential Oils and Their Bioactive Compounds Against Colon Cancer: Focus on Colon-Specific Micro- and Nanocarriers". Lifestyle and dietary factors, namely high consumption of processed foods, red meat, and alcohol, coupled with sedentary behavior, are well known contributors of the development of colon cancer, ranking among the most prevalent and lethal cancers worldwide. Although essential oils cannot replace conventional chemotherapy, they can mitigate some of its adverse effects and improve the efficacy of associated chemotherapy drugs. Current advancements in micro- and nanoencapsulation techniques for essential-oil-targeted delivery to the colon are also explored. The authors from this research group have also published recent studies about humic substances as therapeutic agents and the use of essential oils in enhancing sports performance and recovery [10,11]. Another review (9th) in the field of molecular medicine is about "Osteoporosis: Focus on Bone Remodeling and Disease Types". It is also known that aging, hormonal changes, comorbidities, and drugs influence the process that leads to osteoporosis. Osteoporosis is a skeletal disease that leads to increased bone fragility, associated with increased risk of fracture. The review describes the main pathways involved in osteoclasts differentiation and bone resorption, and osteoblasts differentiation and proliferation, since osteoporosis results from a chronic imbalance in bone remodeling, where bone resorption by osteoclasts exceeds bone formation. As referenced in this review, the multidisciplinary nature of osteoporosis intersects with many fields of molecular medicine, making it a common challenge across specialties.

The 10th review paper is entitled "RASopathy and Sudden Cardiac Death: A Literature Review". It discusses how the increased risk of sudden cardiac death, especially in relation to hypertrophic cardiomyopathy (HCM) and ventricular arrhythmias, is associated with RASopathies, genetic syndromes caused by germline mutations in gene-encoding proteins of the RAS/MAPK pathway. The review provides an updated overview of the main RASopathies with cardiac involvement. Genotype–phenotype correlations, pathogenic mechanisms underlying sudden cardiac death, and current diagnosis, monitoring, and prevention strategies are explored. Exploring similar concerns, recent studies from the authors have analyzed the causes of youth sudden cardiac death [12]. Finally, the 11th and last review paper is entitled "Lactic Acid Bacteria: From Bioprocessing to Nanomedicine", which aimed to explore a new horizon for future research and development to exploit the capabilities of lactic acid bacteria across biotechnology, food science, and nanomedicine. The authors concluded that although the biological origin of biosynthesized nanoparticles (NPs) may confer greater biocompatibility and biodegradability than physically or chemically synthesized nanoparticles (NPs) using lactic acid bacteria, thereby reducing the risk of in vivo toxicity, the safety of nanomaterials remains a crucial challenge, especially concerning their long-term use. In fact, despite using safe substances and synthesis methods, the bioaccumulation of NPs in tissues, along with their potential cytotoxicity and genotoxicity, are among the critical concerns, which can arise from repeated administration and the interactions between NPs and cells. Recent studies from the authors included the applications of bioactive glass nanoparticles in dentistry [13].

The understanding of human health is an endless topic in biochemistry. As can be observed in Table 1, the majority of the keywords are associated with medicine, such as drug allergy, Alzheimer's disease, osteoporosis, cardiac dysfunction, sudden cardiac death, pulmonary hypertension, anemia, schizophrenia as well as hepatocellular carcinoma, colon cancer and cancer vaccines. Besides human diseases, others complementary keywords such as dopamine, mRNA design, nanotechnology, mitochondria biogenesis, bioactive compounds, essentials oils, iron deficiency, ginsenoside biosynthesis, polyoxometalates, ß-amyloid aggregation, acetylcholinaesterase inhibitors, transition metal chelators and nanoparticles can be found, highlighting the cellular and molecular basis of biochemistry

in the understanding of diseases. Allegorically, biochemistry represents a fundamental knowledge base, being a scientific safe harbor that provides molecular understanding for the treatment of several human diseases such as Alzheimer's disease, osteoporosis, cardiac diseases, pulmonary hypertension, anemia, drug allergy, schizophrenia, and cancer, among others.

In addition, this Special Issue also reflects on the emerging direction of biochemistry, i.e., from "Understanding Life" to "Designing Life". The first notable feature of this is the growing role of data-driven methodologies, especially deep learning and artificial intelligence, in elucidating biomolecular structure–function relationships and enabling rational therapeutic design. These advances are not only accelerating the identification of clinically actionable targets, such as neoantigens in cancer immunotherapy, but are also reshaping our ability to engineer biomolecules with enhanced precision, as exemplified by innovations in mRNA optimization and enzyme functional annotation.

Equally significant is the expansion of biochemistry into multi-scale and systems-level investigations. The integration of single-cell and spatial transcriptomics, together with multi-omics approaches, is redefining our understanding of cellular heterogeneity, tissue organization, and disease progression. Such approaches are particularly transformative in complex biological contexts, including neurodegeneration, spinal cord injury, and metabolic and cardiovascular disorders, where the interplay between molecular pathways and cellular environments is critical.

Taken together, the contents of the two Special Issues in *BioChem* follow overall global trends in the field of biochemistry, namely, structural biology revolution in AI protein folding prediction, RNA therapeutics explosion, single-cell and spatial omics, and translational and clinical focus. Finally, while chemical biology and small molecule mechanisms are less emphasized in this issue, interested readers can find them in the first Special Issue.

Again, we hope that this Special Issue will serve as both a valuable resource and a source of inspiration for researchers across disciplines, fostering continued advances at the frontiers of biochemistry.

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