



# Emerging and Promising Keywords in Biomolecules and Therapeutics for 21st Century Diseases

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## Abstract

Recent technological advancements and environmental changes are leading to an increase in various diseases such as obesity, fibrosis, metabolic disorders, and degenerative diseases associated with aging. Additionally, micro- and nanoplastics are emerging as potential contributors to many of these conditions, posing a serious threat to human health. This special issue aims to explore new directions and opportunities for future drug development through recent review articles published in the issue, focusing on these key medical topics.

**Key Words:** Obesity, Fibrosis, Metabolic disorders, Degenerative diseases, Micro- and nanoplastics

## INTRODUCTION

In recent years, technological advancements and the emergence of new environmental risk factors have led to an increase in global disease occurrences, bringing forth new keywords that require our attention. We aim to review research trends by compiling seven key papers spanning diverse topics, including obesity, fibrosis, metabolic and degenerative diseases, cancer and nerve connectivity, microplastics, the gut microbiome, natural compounds, and stem cell therapies. Through this comprehensive review, we aim to extract integrative ideas from these different keywords and generate insights for future advancements in biomedical research and innovative drug development.

## KEYWORDS IN BIOMOLECULES AND THERAPEUTICS FOR 21ST CENTURY DISEASES

### Obesity: GLP-1 agonist & beyond

The first paper focuses on obesity, for which drug development research is actively ongoing by global and domestic pharmaceutical companies (Special issue 1) (Kim and Kim, 2025). As is well known, the increasing trend of obesity triggers numerous complications, including allergies, psoriasis, type 2 diabetes, cardiovascular diseases, and specific cancers, ne-

cessitating a multifaceted approach to treatment. The *Biomolecules & Therapeutics* journal has also seen an increase in obesity-related papers in recent years (Hwang *et al.*, 2020; Piao *et al.*, 2022; Cha *et al.*, 2023; Han *et al.*, 2023b). While existing anti-obesity drugs have achieved some success, new drug developments that go beyond simply reducing energy intake show promising potential for achieving greater weight loss and improving obesity-related complications (Müller *et al.*, 2022; Novikoff *et al.*, 2024). We believe that a combination of innovative drug therapies and lifestyle changes can provide new hope for addressing obesity, a global health challenge.

### Metabolic dysfunction-associated steatotic liver disease and hepatic fibrosis: AMPK inhibitor

Moreover, as metabolic dysfunction-associated liver disease (MASLD) and other chronic liver diseases increase, the development of new strategies for liver protection and disease progression prevention has become crucial (Raza *et al.*, 2024). The second paper specifically addresses these new strategies (special issue 2) (An *et al.*, 2025). AMP-activated protein kinase (AMPK) activators have already emerged as promising candidates for various diseases due to their broad regulatory effects on major metabolic and inflammatory pathways (Jeong *et al.*, 2016; Rho *et al.*, 2021; Penugurti *et al.*, 2024; Pokhrel *et al.*, 2024). By modulating lipid metabolism, insulin resistance, and inflammatory cascades, AMPK activators show potential

**Open Access** <https://doi.org/10.4062/biomolther.2024.007>

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Received Dec 16, 2024 Revised Dec 26, 2024 Accepted Dec 26, 2024

Published Online Dec 31, 2024

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to halt or reverse the progression of MASLD, liver fibrosis, and even hepatocellular carcinoma.

### **Kidney Disease: natural products**

The global burden of increasing kidney diseases, particularly diabetic kidney disease (DKD) as a complication of diabetes mellitus, necessitates a paradigm shift in treatment strategies (Wada and Makino, 2016; Natesan and Kim, 2021). Traditionally, treatment for diseases like DKD has focused on symptom management and slowing disease progression. However, recent studies exploring the role of natural compounds and combination therapies have emphasized their potential not only to prevent but also to reverse kidney damage (Sun *et al.*, 2022; Jung *et al.*, 2023; Ahn and Park, 2024; Choi *et al.*, 2024). Bioactive substances, such as polyphenols found in various foods, have emerged as promising candidates for preventing diabetic nephropathy and mitigating oxidative stress and inflammation, which contribute to kidney dysfunction (Special issue 3) (Natesan and Kim, 2025). As these compounds are further scientifically investigated, the therapeutic potential of natural substances in kidney disease treatment could offer a new complementary approach to existing pharmacological interventions.

### **Neurodegenerative disease: probiotics**

Recently, many researchers have significantly increased their focus on brain and neurological disorders, as well as the development of treatments for these conditions (Han *et al.*, 2023; Creekmore *et al.*, 2024; Kim, 2024; Lefevre-Arbogast *et al.*, 2024; Nixon and Rubinsztein, 2024; Yajing *et al.*, 2024). The occurrence of neurodegenerative diseases (NDDs), such as Alzheimer's and Parkinson's disease, further emphasizes the complexity of modern healthcare (Coukos and Krainc, 2024; Jackson *et al.*, 2024; Korczyn and Grinberg, 2024; Morris *et al.*, 2024). These diseases are characterized by progressive neurodegeneration and pose substantial challenges to global health systems. In response to these challenges, the gut microbiome has emerged as a novel therapeutic approach (Kwon *et al.*, 2024; Lee *et al.*, 2024; Seo and Holtzmann, 2024). Research into the gut-brain axis and the role of microorganisms in neurodegeneration has opened new pathways for understanding how external factors influence brain health (Special issue 4) (Kim *et al.*, 2025). In particular, probiotics have garnered attention for their potential to modulate neurodegenerative processes and provide therapeutic benefits. Specific probiotic strains, such as *Lactobacillus plantarum*, *Bifidobacterium breve*, and *Lactobacillus rhamnosus*, may offer novel approaches to managing these debilitating diseases, providing potential benefits that go beyond symptom management.

### **Cancer-nerve intersection: DX2**

Interest in brain and neuroscience is rapidly expanding within the field of cancer (Hutchings *et al.*, 2020; Lee *et al.*, 2020; Winkler *et al.*, 2023; Lyu *et al.*, 2024; Poh, 2024). Specifically, research that previously focused on the microenvironment in cancer is now also drawing attention to the neural microenvironment, which contributes to immune suppression (Mancusi and Monje, 2023; Xu *et al.*, 2024). In addition to the numerous research trends studying how nerves interact within the cancer microenvironment, recent approaches have increasingly emphasized applying cancer research findings to neurode-

generative brain diseases. This research trend is particularly addressed in this special issue (Special issue 5) (Baek, 2025). Survival genes like DX2 play crucial roles in both cancer and neurodegeneration. DX2, a spliced variant of AIMP2 with deletion of exon 2, is overexpressed in various cancers and regulates cell death pathways, presenting a potential target for anti-cancer therapies. Interestingly, genes traditionally considered oncogenes, such as AKT and XBP1, are now being studied for their neuroprotective effects in neurodegenerative diseases, bringing about strategic changes in therapeutic applications.

### **Osteoarthritis: stem cell**

Following the potential of treating neurodegenerative brain diseases using microbiome, research on treating degenerative diseases using stem cells and their derived exosomes continues steadily (Ni *et al.*, 2020; Ehioghae *et al.*, 2024; Kim *et al.*, 2024; Li *et al.*, 2024; Tian *et al.*, 2024). In the musculoskeletal health field, osteoarthritis remains a major cause of disability, with current treatments primarily focused on symptom management. However, stem cell therapy for knee joint cartilage regeneration is considered a promising alternative (Special issue 6) (Lee *et al.*, 2025). Stem cell injections offer the potential to provide long-term relief for osteoarthritis patients by promoting cartilage regeneration and reducing pain and inflammation, thereby opening a path to avoid more invasive procedures like joint replacement surgery. We anticipate that stem cell-based therapies will expand to address a wider range of degenerative diseases.

### **Micro- and nanoplastics: new emerging etiology**

One of the most serious consequences of widespread plastic use is environmental pollution by microplastics (MPs) and nanoplastics (NPs), along with the diseases they may cause (de Oliveira *et al.*, 2024; Goswami *et al.*, 2024; Liao *et al.*, 2024; Liu *et al.*, 2024; Sun *et al.*, 2024; Zhao *et al.*, 2024; Zheng *et al.*, 2024). These small plastic particles, created as plastic products break down, have been found in marine organisms, wildlife, and even in human bodies. However, despite their widespread presence, recent reports have highlighted their potential role as disease agents, yet our understanding of their immunological impacts remains limited (Special issue 7) (Dan *et al.*, 2025). Preliminary research suggests these particles can interact with the immune system in complex ways, potentially exerting differential effects depending on their material, size, and shape. As global efforts to reduce plastic pollution intensify, it is critically important to comprehensively understand the impact of MPs and NPs on immune health, especially given their potential to exacerbate or trigger diseases.

## **CONCLUSION**

In this special issue, we have published review articles covering keywords related to both recently emerging and longstanding yet unresolved diseases. Through the exploration of these individual keywords and new efforts to understand them comprehensively, we believe we can continue to make progress towards innovation in addressing 21st-century diseases.

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