Molecular medicine in the translational research era

Welcome to this thematic issue of *Annals of Translational Medicine* on the recent advances of the ever-expanding field of molecular medicine. The present volume attempts to cover current genetic, molecular, or cellular aspects of main subject areas including microbiology, haematology, biomechanics, oncology, endocrinology, pharmacology, cardiology and hepatology. It is primarily focused on recent developments on molecular biomarkers and current technologies that elucidate disease pathogenesis and may lead to the design of specific tools for diagnosis, treatment, or disease prevention.

The first article of the volume provides current insights on the effective and reliable laboratory diagnosis of microbial infections with emphasis in detection of antimicrobial resistance biomarkers. The recent applications of mass spectrometry and especially the new technology of matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF) has revolutionized pathogen identification and has immensely accelerated detection of antimicrobial resistance in aerobic and anaerobic bacteria, fungi and viruses.

The second article addresses the role of non-coding RNAs as key signal transduction molecules in carcinogenesis regulating tumor cell development and progression. The clinical aspects of non-coding RNAs as prognostic and diagnostic tumor biomarkers are extensively discussed and therapeutic targets are proposed.

The third article explores the molecular, genetic and epigenetic profiling of hematopoietic disorders implicated in all aspects of clinical practice including diagnosis, prognosis and prediction of response to treatments. Novel molecular methods and advanced technologies currently applied in the challenging haematological disorders are described.

The fourth article is an original research study of apoptotic biomarkers in osteoarthritis. A detailed quantitative analysis of *BCL2* family genes has been performed in the articular cartilage of an experimental animal model of osteoarthritis, revealing an important role of the apoptotic *BAX* and *BCL2L12* genes. Upregulation of these molecules in the osteoarthritic samples compared to healthy controls indicates their significance as potential therapeutic targets.

The following article is an interesting technical paper on genomic research data processing. Adamopoulos *et al.* describe the design and applications of the "Alternative Splicing Detection Tool" (ASDT), a novel PERL algorithm that allows sensitive detection of alternative splicing events from next-generation sequencing data, thus facilitating their precise and efficient analysis.

Moving to the next section of biomechanics, the molecular pathogenic aspects of psoriasis are discussed with emphasis to the mechanical stimulation of keratinocytes and the underpinning mechanotransduction pathways. Key mechano-induced signaling pathways and emerging mechanosensitive molecules appear to have a potential diagnostic and therapeutic utility in the management of psoriasis.

Along this line, the role of transient receptor potential (TRP) channels acting as mechanoreceptors in bone is extensively described in the following article authored by Katsianou *et al.* TRPPs are capable to sense external mechanical forces including strain, stretch and fluid shear stress, triggering a cascade of signaling pathways involved in osteoblastogenesis and bone formation, while aberrant function may be associated with the pathogenesis of bone maladies.

The next section is focused on state-of-the-art advances in molecular oncology. The article by Anestis *et al.* explores the challenges of targeting hepatocyte growth factor (HGF)/c-mesenchymal-epithelial transition (c-Met) pathway in gastric adenocarcinomas. HGF/c-Met signaling pathway plays a pivotal role in tumor growth, survival and invasiveness and its inhibition holds great promise for therapy. Clinical testing of c-Met targeted therapeutic agents is also addressed in this review.

The following article provides recent data on the genetic and epigenetic landscape of pediatric brain tumors. The authors critically discuss the emerging role of tumor-specific histone modifications that affect chromatin remodeling and ultimately alter gene expression. They also highlight the therapeutic potential of histone modifications targeting in the management of pediatric brain tumors.

The progress in the molecular pathology of melanocytic tumors and especially the molecular alterations that characterize the challenging diagnostic group of spitzoid lesions are discussed in the next article. The authors describe in detail novel molecular markers that may assist the differential diagnosis of melanoma, particularly from malignant peripheral nerve sheath

tumors. They also offer insights on the progress that has been made towards targeted therapy.

Molecular profiling data for urothelial carcinoma are summarized in the following article by Mendiratta and Grivas. Emerging biomarkers that may predict response to cisplatin-based chemotherapy, immunotherapy, arising targeted therapies and promising combination strategies are extensively described along with a few examples of 'precision medicine' trials aiming to improve outcomes in urothelial carcinoma patients.

Molecular characterization of low- and high-grade pediatric gliomas has immensely improved histological evaluation and therapeutic targeting. The next article provides a detailed account of the pathological aspects underlying pediatric gliomas, highlighting current clinical diagnostic criteria and extensive treatment options.

Moving to the section of molecular endocrinology, the first article unravels the genetic and molecular mechanisms of neuroendocrine neoplasms pathogenesis. Emerging molecular markers have improved current diagnosis and targeted therapy of neuroendocrine neoplasms towards a more efficient patient's management.

The second article in this section focuses on adrenal neoplasms, presenting recent data on the role of insulin-like growth factor (IGF) and epidermal growth factor (EGF) pathways in adrenal development and tumorigenesis. The potential implication of these pathways in the treatment of adrenocortical carcinomas is explored attempting to improve the very poor prognosis of this malignancy.

Moving towards molecular pharmacology, the role of thyroid receptor α1 (TRα1) as a novel therapeutic target of tissue repair is discussed in the first article. TRα1 being essential for cell proliferation and differentiation is also highly involved in the process of repair/regeneration in the heart and other tissues. Thyroid hormone (TH) treatment in clinical settings of ischemia/reperfusion such as by-pass surgery seems to be cardioprotective against ischemic injury. Furthermore, TH therapy of donors is shown to result in organ preservation and improved post-transplantation graft survival.

In the following article, interesting experimental and clinical data indicate the potential efficacy of dipeptidyl peptidase-4 (DPP-4) inhibitors in Alzheimer's disease. These drugs that are currently used in diabetes mellitus type II treatment are also shown to specifically suppress Aβ accumulation, tau hyper-phosphorylation, neuroinflammation, mitochondrial dysfunction and reactive oxygen species (ROS) formation, resulting in the inhibition of cognitive impairment.

An insight into molecular cardiology reveals the fundamental role of proper mitochondrial function in cardiovascular diseases. Mitochondrial dysfunction has been associated with the development of several cardiac diseases such as atherosclerosis, ischemia/reperfusion injury, hypertension, diabetes, cardiac hypertrophy and heart failure, due to the uncontrolled production of ROS. Therefore, early control of mitochondrial dysfunction is a crucial step in the therapy of cardiac disorders, while a number of anti-oxidant molecules and medications have been currently developed.

Finally, moving to the area of molecular hepatology, treatment of acute liver injury remains challenging with very few available pharmacological options. The last article in this issue provides an overview of the biological role of fibroblast growth factor (FGF) family members and especially the endocrine hormones FGF19 and FGF21, which exert a profound influence in systemic metabolism and important hepatoprotective activities. The authors further highlight their potential therapeutic application in the clinical management of acute liver injury.

In concluding of this preface, we wish to thank again all authors for their original and valuable contributions, hoping that the present thematic issue will be of substantial interest to the broad readership of the journal.

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