Editorial

Mechanistic Biomarkers: The Field for the Development of Non-Pharmaceutical and Pharmaceutical Approaches to Diagnostics, Prevention and Treatment of Chronic Diseases

Igor A. Sobenin

Alexander N. Orekhov

Keywords: Biomarkers, chronic diseases, non-communicable diseases, complementary medicine, alternative medicine, medicinal plants, phytochemicals.

Chronic non-communicable diseases, which are the main causes of poor health, disability, death and health-care expenditures, start long before the overt clinical manifestations occur, and the hidden progression of pathology takes years and even decades [1-3]. During this time, no preventive measures can be foreseen to decline the development of the overt disease. It should be noted that the set of adequate biomarkers and diagnostic methods to disguise the hidden but progressing pathology at the very early stages is still insufficient. Therefore, there is no formal reasons for physician to perform preventive intervention in the individual who is considered healthy at the present time. More and more new approaches to early diagnostic, prevention and treatment of chronic diseases are required. To address the chronic disease burden in effective and equitable way, it is necessary to deploy integrated strategies and interventions, and address many risk factors and conditions simultaneously [4-6].

This thematic issue includes the papers from the team of international experts in the field, outlining the various aspects of the challenges mentioned above. The exposure of individuals to early life risk factors may induce the development of chronic diseases in adulthood, as well as the the presence of premature risk factors can influence gene expression. The large number of scientific papers published in this research area makes it difficult for the healthcare professional to keep up with individual results and to establish association between them. Emerging biomarkers, including chemical, imaging or genomic biomarkers hold great promise for early diagnosis of disease and as prognostic tests for managing treatment of chronic diseases such as cardiovascular disease, cancer, osteoarthritis, Alzheimer disease, etc. To advance the success of treating and managing these diseases, efforts are needed to establish the temporal relationship between changes in biomarkers with the progression of the chronic disease. Clinical biomarkers, once qualified, are useful for facilitating drug development as well as for implementing individualized medicine, including approaches developed in the field of complementary and alternative medicine. Therefore, the recent approaches to estimating of novel diagnostic methods and evolving biomarkers are disguised in this thematic issue, aimed to evaluation of preclinical pathology in humans and finding molecular and pathway targets for further development of pathogenesis-targeted therapy.

The good portion of review papers in this issue describes some aspects of the current perspectives of use of biologically active phytochemicals for prevention and treatment of various chronic non-communicable diseases, thus suggesting them as a template for new drug development using recent scientific principles. It is necessary to consider wider application of complementary and alternative therapies, which can enhance current practice and reduce the use of pharmacological interventions. Complementary and alternative practice does not exclude pharmacological interventions, but adds a trend to introducing non-pharmacological options that can have an important role in chronic disease management [7]. Several review papers in this issue are addressed to acquisition of adequate biomarkers and diagnostic methods, which should help disguising the hidden but progressing pathology in humans at the very early stages. The search of novel biomarkers and their combinations to identify subjects with high risk of development of chronic non-communicable diseases is the keystone of these papers. Early diagnostics of premorbidic condition or subclinical disease is very important for alternative medicine. The fact is that the impact of alternative medicine is primarily pathogenetic, but not symptomatic one. Alternative approaches may be used in situation, when there are no symptoms of overt disease, and therefore no targets and indications for conventional intervention exist. That is why the early detection of pathological processes is essential, thus allowing proper identification of apparently healthy individual at risk or a patient with more poor prognosis, as well as early preventive or therapeutic intervention.

The review paper by Orhan (Turkey) focused on examples of monoamine oxidase-inhibiting natural compounds from a wide variety of chemical classes isolated from plants. Considering the need for novel monoamine oxidase inhibitors due to side effects of the current ones, natural products have become attractive targets for researchers due to strong monoamine oxidase inhibitory activity of flavonoids, xanthone, alkaloids, and coumarin derivatives from herbal sources [8].

Autism is a comprehensive growth abnormality in which social skills, language, communication, and behavioral skills are developed with delay and as diversionary. Bahmani *et al*. (Iran) reviewed the recent findings, pathophysiology, and etiology of autism, as well as promising results of herbal remedies that have been considered to treat autism, with a special focus on *Ginkgo biloba* [9].

Parvez *et al*. (Saudi Arabia) discuss the recent developments in anti- hepatitis B virus natural products. All currently approved antiviral drugs have their limitations: interferon alpha has limited efficacy and a high incidence of adverse side-effects; nucleoside analogues are very effective in treating chronic hepatitis B, but long-term therapy eventually leads to drug-resistance. As an alternative approach, a broad spectrum of phytochemicals including flavonoids, terpenes, alkaloids, polyphenolics, saponins and lignans are investigated for anti-HBV activities. These promising compounds have different and overlapping mechanisms of action by either inhibiting viral antigens secretions or suppression of DNA replication [10].

Shishodia *et al*. (USA) focused on the anti-cancer properties, molecular targets, and the apoptotic effects of guggulsterone, a plant sterol derived from the gum resin of the tree *Commiphora wightii*. Ethnobotanical data provides enough evidence to suggest guggulsterone as a template for new drug discovery using modern scientific principles. Overall, guggulsterone shows great potential for development new anticancer drug [11].

1873-4286/16 $58.00+.00

International team from Australia and Russia chaired by Bobryshev focused mainly on tumor-induced pathways of a downregulation of dendritic cells in Barrett's esophagus, known as a premalignant condition strongly associated with esophageal adenocarcinoma, a very often deadly cancer. Some possibilities to use dendritic cells for immunotherapeutic approaches in cancer treatment were discussed [12].

Several papers were aimed to find and demonstrate the consensus between ancient traditional medicine and contemporary evidence-based medicine. Thus, international team from China and UK in the review paper by Wang *et al*. tried to put a bridge between Traditional Chinese medicine and western medicine, using estrogen deficiency, a major pathogenetic factor in bone loss after menopause or oophorectomy and osteoporosis, as an example. The fusion of Traditional Chinese medicine with western medicine will put the way forward for new translational advances [13].

International team (Australia and Iran) have presented a rather unusual review by Emami *et al*., which describes mainly the results of search in ancient major Islamic Traditional Medicine textbooks for definition, etiology and medicinal plants used to manage paresthesia, a common symptom of multiple sclerosis and peripheral neuropathies. The direct comparison of ancient knowledge and current achievements of experimental and clinical medicine certainly deserve interest [14].

International team from China and Canada (review paper by Wang *et al*.) summarized current knowledge on *Herba Epimedii* and its constituents to provide anti-resorptive and bone formation-stimulating effects, which target different pathways in the bone remodeling cycle. These compounds may provide new perspectives in alternative treatment regimes and reveal novel chemical scaffolds for the development of anti-osteoporotic drugs. Again, the interest this paper should arise is a direct comparison of approaches of Traditional Chinese Medicine and current achievements of experimental and clinical medicine [15].

Zarshenas *et al*. (Iran) has compiled a concise but critical review over reported liver diseases and concerned medicinal plants from perspectives of Persian medicine. Five main ancient pharmaceutical manuscripts of Persian medicine, as well as the latest and largest medical textbook of Persian medicine were studied. The mechanisms or pharmacological activities of reported medicinal plants in the field of liver diseases were cited and discussed. Apart from the historical clarification, current investigation compiled an evidence-based study on reported herbal single remedies for liver diseases from the standpoints of Persian scholars [16].

Núñez-Cortés *et al*. (Spain) have reviewed the recent findings on cardiometabolic risk and the binomial hypertriglyceridemia-low HDL cholesterol. The data for this review were derived from Hypertriglyceridemia Registry of the Spanish Association of Arteriosclerosis. The main finding was that combination of hypertriglyceridemia between and low HDL cholesterol has very high prevalence, and it is related to overweight-obesity and other metabolic disorders as mellitus diabetes with or without metabolic syndrome. In this context, triglyceride-lowering treatment was suggested to address the residual atherosclerotic cardiovascular disease risk [17].

The research group from Brazil has presented a review by Klafke *et al*., which demonstrates novel biomarkers as an alternative to early detection of subclinical atherosclerosis. One of the proposed biomarkers is the ischemia-modified albumin, and another marker is the advanced oxidation protein product. In this review also is evidenced the use of plants and natural products to reduce protein oxidation and improve the availability of nitric oxide and consequently vascular function, reducing the risk for development of cardiovascular disease [18].

Nagai *et al*. (Japan) have discussed visit-to-visit blood pressure variability a new independent risk factor for stroke, with the class of antihypertensives being suggested to be an important determinant of visit-to-visit blood pressure variability. This review article summarizes the recent literature on these topics [19].

Sazonova *et al*. (Russia) discussed the data on using next generation sequencing technology in studying mitochondrial genome mutations associated with atherosclerosis and its risk factors, such as mitochondrial diabetes, mitochondrial cardiomyopathy, diabetic nephropathy and left ventricular hypertrophy. Genetic diagnostics of individual predisposition to atherosclerosis may provide a set of informative biomarkers to disguise the hidden but progressing pathology at the very early stages. The new paradigm of crosstalk between non-pharmaceutical (including molecular and genetic) and true pharmaceutical approaches may be developed to fill the niche of effective and pathogenically targeted pretreatment and treatment of preclinical and subclinical atherosclerosis to avoid the development of chronic life-threatening disease [20].

International team from USA, UK and Iran chaired by Mobarhan and Avan highlighted the recent findings from preclinical and clinical studies on the role of miRNAs in myocardial infarction, novel miRNA-based therapeutic approaches for therapeutic intervention, and potential of circulating miRNA to be served as biomarkers in patients with suspected myocardial infarction [21].

Thus, in this issue, a team of international experts discusses the hot topics on emerging mechanistic biomarkers and the development of non-pharmaceutical and pharmaceutical approaches to diagnostics, prevention and treatment of chronic diseases. We would like to thank the contributors to this thematic issue for their participation, and hope that this issue will be helpful for the development of novel methods of diagnostics and therapy of chronic diseases.

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Igor A. Sobenin

Department of Cardiovascular Pathology
Russian Cardiology Research and Production Complex
15A 3rd Cherepkovskaya Str.
121552 Moscow
Russsia
Tel: +7 926 359 00 50
Fax: +7 495 415 95 94
E-mail: sobenin@cardio.ru

Alexander N. Orekhov

Laboratory of Angiopathology
Institute of General Pathology and Pathophysiology
8 Baltiyskaya Street
125315 Moscow
Russia
Tel: +7 903 169 08 66
Fax: +7 495 415 95 94
E-mail: a.h.opexob@gmail.com