Editorial

New Therapeutic Targets in Clinical Medicine

Antonino Tuttolomondo

Clinical medicine is the study of diseases and of their treatment by direct examination of the living patient and pharmacological therapy represent a fundamental branch of this discipline.

New agents directed at selected multiple targets have been increasingly explored for enhanced therapeutic efficacies, improved safety profiles, and reduced resistance activities by simultaneously modulating the activity of a primary target and the counteractive elements. New therapeutic targets represent a very important resource against several disease to improve treatment of those already treatable and to offer a treatment to those so far untreatable.

In this issue of Current Pharmaceutical Design several authors with their review articles will summarize pathogenetic pathways and potential therapeutic targets in some diseases of widely interest.

Kenichi Matsushita *et al.* will evaluate pathogenetic pathways of cardiorenal syndrome and their possible therapeutic implications [1]. Cardiorenal syndrome (CRS) is the term used to describe disorders of the heart and kidneys whereby acute or long-term dysfunction in one organ may induce acute or long-term dysfunction of the other [2,3]. The management of cardiovascular diseases and risk factors may influence, in a beneficial or harmful way, kidney function and progression of kidney injury. In this review author will ases therapeutic strategies and discuss treatment options for the management of patients with heart failure with decreased kidney function and highlight recent evidences suggesting the limited importance of renal blood flow reduction as a mediator of in favoir of a pathogenetic mechanism more strictly linked to increased venous pressure and to neurohormonal mediators such as renin-angiotensin system, sympathetic nervous system [4,5].

In another review article of this issue, Luis Castilla-Guerra *et al*. [6] will analyze the present and the future statin role in stroke prevention. Stroke incidence is related with increasing age and although eidemiological have not reported a clear association between cholesterol levels and all causes of stroke, statin trials in patients with established cardiac heart disease (CHD) or at high risk for CHD have shown that statins decrease stroke incidence in these populations [7,8]. This is the so-called "*cholesterol paradox*". In their review, Castilla-Guerra *et al*. will summarize results of more recent trials with statins on stroke prevention and they will evaluate possible new therapeutic "cholesterol target" (e.g PCSK9) that may represent useful future therapeutic target to optimize cholesterol reduction strategy in view of a perspective of stroke reduction.

In another review, Machado and Pinheiro da Silva [9] will analyze the role of Intestinal Barrier Dysfunction in Human Pathology and Aging. The intestinal epithelial monolayer constitutes a very important physical and functional barrier between the organism and the external environment due to the fact that epithelial cells are linked by means tight junctions that the passage of charge entities, whereas mild irritants, proinflammatory cytokines, toxins and pathogens, and adverse environmental conditions open tight junctions and increase paracellular permeability [10].

An impaired barrier function results from activation of signalling pathways that lead to alteration of junctional proteins expression and/or distribution is linked in vivo to intestinal barrier dysfunction that has been reported as associated with various intestinal and non-intestinal disorders that the authors will evaluate in their review.

Furthermore, de Ramon *et al*. [11] will evaluate the role of new targets in RNAi-based therapy in experimental ischemia-reperfusion injury. In their review authors will analyze molecular and cellular mechanism of ischemia and reperfusion injury and in acute renal failure. They also evaluated the role of RNA-based therapeutics in renal ischemia and reperfusion injury and in particular they reviewed therapeutic role of antisense oligonucleotides (ASO), small interference RNA (siRNA) and antagomirs also known as anti-miRs or blockmirs, a class of chemically engineered oligonucleotides used to silence endogenous microRNA (miR) [12-14].

Della Corte *et al*. [15] in their review will evaluate the role of arterial stiffness indexes as potential targets in cardiovascular clinical medicine. Arterial stiffness is an important surrogate marker that describes the capability of an artery to expand and contract in response to pressure changes. It can be assessed with different techniques, such as the evaluation of pulse wave velocity (PWV) and augmentation index (AIx). It is related to central systolic pressure and it is an independent predictor of cardiovascular morbidity and mortality in hypertensive patients, type 2 diabetes, end-stage renal disease and in elderly populations [16-19]. In this review authors will analyze the role of arterial stiffness, endothelial dysfunction and immunoinflammatory markers as surrogate endpoint, assessing the correlations between these markers and evaluate the therapeutic perspectives that these findings may offer to clinicians as potential therapeutic targets [20-24].

Another review by Tuttolomondo *et al*. [25] will review available scientific and therapeutic data about rare diseases such as IgG4 related systemic disease (IgG4-RSD). This is a very complex disease. One of the first organ to be involved is pancreas (type 1 autoimmune pancreatitis) but similar IgG4 extrapancreatic lesion can occur in almost any organ during clinical course sometimes simultaneously and often metachronously hepatobiliary tract, salivary glands, orbit, lymphonodes, retroperitoneum, kidney, skin, prostate, lung, mediastinum, aorta, breast, central nervous system, thyroid leading to the wide spectrum manifestations of IgG4-related disease as sclerosing cholangitis, sclerosing sialoadenitis, lymphadenopathy, retroperitoneal fibrosis [25,26]. To date epidemiological data are not available in occidental countries and most of the epidemiological data has been reported by Japanese groups [27-29]. Authors reviewed the role of drugs such as immunosoppressive agents, rituximab and Bortezomib whereas a better knowledge of pathogenetic pathways of this complex of diseases will be useful to address future therapeutic targets.

Finally, Di Raimondo *et al*. [30] will review the role of specific interventions aimed to implement physical activity levels of the general population are of certain efficacy both for primary and for secondary prevention of the major chronic diseases and constitutes an excellent cost/effective tool to improve the health status of different categories of patients [31,32].

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Exercise represents a unique case in which a single intervention is useful against a broad range of diseases and risk factors, this knowledge should lead to an ever-increasing use of this lifestyle change.

Characterization of new therapeutic targets is a primary goal of research in Clinical Medicine in order to improve the treatment of diseases for which already a therapeutic standpoint is present both to provide adequate care to diseases till today lack an effective cure.

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