Review of Clinical Pharmacology and Pharmacokinetics

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GENERAL INFORMATIONS

REVIEW OF CLINICAL PHARMACOLOGY AND PHARMACOKINETICS

publishes Applied Pharmacology and Current Therapeutics Reviews, Review Articles on Drugs and Drug Therapy, Original Papers and Practical Therapeutics Articles.

The *scientific standard* of the papers, which are accepted for publication, is controlled by the Editorial Board or by other Experts in the various fields of Pharmacology and Pharmacokinetics.

Manuscripts: These should mention, on the first page, the *Title*, *Author(s)* and the *Name of the Institution* at which the work was done. The complete *address* of the author, including Postal area code number, should be given under the rubric *Send reprint requests to*. Papers should follow the general form: *Introduction, Materials and Methods, Results, Discussion* and *References*. Drugs must be referred to by their generic or chemical name, but may be identified by trade name in parenthesis or o footnote. All papers should be submitted in duplicate.

Summary: A summary in English (maximum length 200 words) must accompany all manuscripts.

Key words: A list of key words should be submitted.

References: These should be numbered in the paper and listed under *References* in order of their appearance in the text. The author(s) surname followed by the initials should be given first, then the complete title of the article, the name of the Journal or Magazine (abbreviated according to the Index Medicus), the volume number, page numbers and year of publication in parenthesis.

Papers should be submitted to the Editors-in-Chief: Prof. S.T. Plessas or Dr C.T. Plessas.

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Letter from Guest Editor

The progress and contributions of 20th century pharmacology has been immense with over 20 pharmacologists to have received Nobel Prizes. This field of medical studies covers many areas; it is built upon and at the same time incorporates many disciplines such as biochemistry, biology physiology, pathology, anatomy, molecular biology, while the development of new analytical and experimental techniques and instruments has given a new boost in pharmacological research. Yet, although a remarkable progress has been made in developing new drugs and in understanding how they act, the challenges are endless. Integrating a depth of knowledge in many related scientific disciplines, pharmacologists offer a unique perspective to solving drug and chemical related problems which impinge on human health, with ultimate goal the treatment and prevention of major diseases.

The 5th Panhellenic Congress of Pharmacology focuses on four *hot* subjects: Regenerative Pharmacology, Herbal Medicines, Pharmacology of Abuse and Dependence, and Education in Pharmacology.

- *Regenerative Pharmacology* is one of the newest areas in Pharmacology, represents a groundbreaking field of research and has the potential to radically alter the treatment of diseases and disorders.

- *Herbal Medicines* have acquired an important percentage among the drug used; according to WHO 80% of people worldwide rely on herbal medicines for some aspect of their primary health care. This continuously increasing use of plant medicines imposes the need for establishing new regulations.

- *Pharmacology of Abuse and Dependence*, still not a well defined area, presents a lot of challenge for researchers and clinicians.

- *Education in Pharmacology* remains a hot subject in the Medical education, following the knowledge *explosion* of the last decades accompanied by a decreasing reliance on didactic teaching. The crucial question is: how and what should we teach?

We hope that the round table discussions along with the invited lectures, included in this abstract book, will raise new and intriguing ques-

tions that will further stimulate research, and will contribute to new therapeutic approaches and attitudes.

I would like to thank the Editorial Board of *Review of Clinical Pharmacology and Pharmacokinetics* in particular Journal Editors Prof. S.T. Plessas and Dr C.T. Plessas for invitation and for providing the suitable and high-standard forum through which new research findings will become available to the scientific community.

The Guest Editor

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REVIEW OF CLINICAL PHARMACOLOGY AND
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Neuroprotection: The difficult Journey from the Bench to the Bedside

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Neurodegenerative diseases are a varied assortment of central nervous system disorders characterised by the gradual and progressive loss of neural tissue or nerve cells. Two of such diseases that have a major public health impact are Alzheimer Disease (AD) (5% of the population older than 65 years) and Parkinson Disease (PD) (1% of the population older than 65 years).

Currently, symptomatic treatment of AD is only modestly efficacious (anticholinesterase inhibitors, memantine). On the other hand the symptomatic treatment of the motor symptoms of PD is highly efficacious (levodopa, dopamine agonists, MAO-B inhibitors, COMT inhibitors, deep brain stimulation). Yet, despite these circumstantial differences both diseases are far from being controlled. All the expectations and dreams about controlling AD or PD are mostly based in the concept of halting or slowing the progression of disease, mostly by interfering with the processes that lead to neuronal death.

Target Discovery is very much disease specific. The amyloid and tau hypothesis underlying the physiopathology of AD have been a fertile field to generate compounds to be tested in clinical trials. AD Epidemiological research also contributed to the identification of clinically testable compounds (AINES, COX-2 inhibitors, statins, estrogens). In the field of PD the most recent advances in target search have been accrued in the field of genetics. However, so far most of the compounds tested in clinical trials have been supported by non-genetic concepts: mitochondrial dysfunction, oxidative stress (selegiline, CoQ10, creatinine).

Until now not a single compound succeeded to be proven as being a disease modifier (neuroprotector) in clinical trials. There are many reasons to justify this daunting scenario, which we intend to discuss in some details. Those reasons can be classified in 2 main types: (1) the compound is not sufficiently active to have clinical expression. (2) The clinical trial design and implementation are not adequate to detect the clinical expression of the effect. For the time being our evaluation of the data available suggests that the first reason is the most common.

The lack of high potential compounds is probably the biggest shortcoming in the field. However many of the bottlenecks are technological or methodological and must be mastered if a disease modifying intervention is to be found. At the lab level issues like the lack of positive predictability of in vitro and in vivo models must be solved. Methods to establish plausible dose ranges must be developed. This, in part, depends on the validation of biomarkers.

At the clinical level the validation of progression biomarkers is critical (diagnostic and progression biomarkers should be distinguished). To much emphasis and work have been put, so far, in innovative trial designs (futility, two period designs).

We will summarize the controversy surrounding these topics, providing our personal insights on the matter.

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