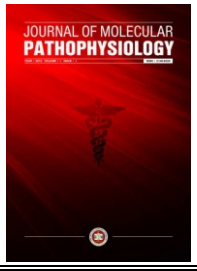
GESDAV

Journal of Molecular Pathophysiology

available at www.scopemed.org



Editorial

A New Hope in Biomedical Research Area; Journal of Molecular Pathophysiolog

Ahmet Korkmaz, Turgut Topal

Gulhane School of Medicine, Department of Physiology, Turkey

Received: June 01, 201; **Accepted:** June 04, 201; **Published Online:** June 10, 2012; **DOI:** 10.5455/jmp.20120604123051
Corresponding Author: Ahmet Korkmaz, Gulhane School of Medicine, Department of Physiology, Ankara, Turkey, korkmaza@gata.edu.tr

One of the greatest of all men of science and father of physiology, Claude Bernard (1813-1878) described the "Constance of the **internal environment** is the condition for a free and independent life" mostly known underlying principle of "*homeostasis*". The word "*homeostasis*" was coined by Walter Bradford Cannon (1871-1945) from the Greek homoios (same, like, resembling) and stasis (to stand, posture). He wrote "The Wisdom of the Body", a fascinating description of the factors involving in the preservation of the internal equilibrium of the body (homeostasis). The book often reads like a book of wonders as it describes the extraordinarily complex internal world of the human, animal and the mechanisms by which the body acts to maintain the balance essential for continuing existence. How, for example, the water, sugar, and salt content of the blood is kept constant; how the body temperature, exposed to great fluctuations from within and without, maintains constancy. There is no doubt that essential elements can be deadly if their concentrations become low or high. Even tiny fluctuations in pH, calcium, hormones etc. are inconsistent with being healthy and life. What we learned from patients suffering hyperglycemia let us to refer even glucose as a "vital poison". Paracelsus (1493–1541), a popular scientist, unknowingly intimated that "all things are poison and nothing is without poison, only the dose permits something not to be poisonous". His intuition still appears valid today.

After second part of 20th century, something in biomedical research area has been changed forever by several discovery such as Harman's intriguing "free radical theory of aging" [1], exploration the structure of DNA by Watson and Crick [2] and invention of propranolol, the β-adrenergic receptor antagonist that revolutionized the medical management of ischemic heart disease, by Sir James Black [3]. From 1960s to date, astonishing progress have revealed in the pathophysiologic mechanisms and treatment of diseases. The pharmacologic adventure of coping with the diseases of civilization is, therefore, basically started from early 1960s by modulating a cell membrane receptors (β-adrenergic receptor-propranolol), accelerated by discovery of Endothelium Derived Relaxing Factor (EDRF) is nitric oxide (NO) [4] and a variety of NO-related mechanisms [5], understanding of cellular signal transduction [6] and finally reached to astonishing nuclear receptors-epigenome-genome connections [7] while becoming progressively sophisticated.

Along with enormous pharmacologic achievement, patients suffered from toxicity [8-10] caused by novel medicines targeting several molecules like cyclooxygenase (COX)-2 inhibitors [11, 12], thiazolidinedione (TZD)s [10, 13] and statins [14, 15]. Unfortunately, the World Health Organization (WHO) estimates that around one billion people throughout the world are overweight and that over 300 million of these are obese and the number of overweight persons will increase to 1.5 billion by 2015. How about the other diseases of civilization? Cancer, diabetes, hypertension, metabolic syndrome and neurodegenerative disorders such as Parkinson and Alzheimer's disease have the same destiny. We will see more than one billion individual who suffer from these chronic, debilitating, non-curable diseases by 2015. Recent epidemiological studies [16, 17] and accumulating evidence regarding childhood and adolescent obesity [18, 19] horribly

verify the WHO's estimations.

As the future researches dig out the nucleus, which seems to be the final organelle to find out novel targeting molecules, nuclear receptors and epigenetic regulations of genes for new therapeutics [20], it might be useful to use a systems-chemistry approach to modify integrated outcomes rather than targeting single molecules with the hope that the desired systematic effect might be generated, as recently suggested by Hotamisligil [21]. It is to say that, establishing a "new homeostasis" will require the modification of more than one target since the diseases of civilization, caused by disrupted environment, develop through on damaged homeostasis.

In the current context with enormous technological advancements, we insist on looking inside the cells to show a novel pathway, a newly discovered molecule or transcription factors those affect the genes and change the fate of the cells either keeping them alive and functional or killing them through apoptosis/necrosis. Although today we know a lot about how a cell acts under a variety of circumstances and we have plenty of pharmacological drugs to treat the human diseases, we still have a nodding acquaintance with how human body reacts as a whole. Today plenty of drugs mean not only plenty of treatment modalities but plenty of side effects as well. Among a variety of reasons, a prominent one might be that we have forgotten to look at the big picture, namely human body as a whole. Through first issue of a new journal, Journal of Molecular Pathophysiology, we made an attempt to look at inside the cell in order to see the big picture. I hope this will be a successful story in near future and will be a new hope to understand the magic of human body as indicated by Walter Bradford Cannon.

1. Harman D. Aging: a theory based on free radical and radiation chemistry. J Gerontol 1956; 11:298-300.
2. Watson JD, Crick FH. The structure of DNA. Cold Spring Harb Symp Quant Biol 1953; 18:123-131.
3. Black JW, Duncan WA, Shanks RG. Comparison of some properties of pronethalol and propranolol. Br J Pharmacol Chemother 1965; 25:577-591.
4. Ignarro LJ, Buga GM, Wood KS, Byrns RE, Chaudhuri G. Endothelium-derived relaxing factor produced and released from artery and vein is nitric oxide. Proc Natl Acad Sci U S A 1987; 84:9265-9269.
5. Pacher P, Beckman JS, Liaudet L. Nitric oxide and peroxynitrite in health and disease. Physiol Rev 2007; 87:315-424.
6. Nishizuka Y. The Albert Lasker Medical Awards. The family of protein kinase C for signal transduction. Jama 1989; 262:1826-1833.
7. Glass CK. Going nuclear in metabolic and cardiovascular disease. J Clin Invest 2006; 116:556-560.
8. Chang CY, Schiano TD. Review article: drug hepatotoxicity. Aliment Pharmacol Ther 2007; 25:1135-1151.
9. Johnson DE, Rodgers AD. Computational toxicology: heading toward more relevance in drug discovery and development. Curr Opin Drug Discov Devel 2006; 9:29-37.
10. Maddrey WC. Drug-induced hepatotoxicity: 2005. J Clin Gastroenterol 2005; 39:S83-89.
11. Maxwell SR, Webb DJ. COX-2 selective inhibitors--important lessons learned. Lancet 2005; 365:449-451.
12. Beardsley S. Avoiding another Vioxx. Sci Am 2005; 292:16, 18.
13. Isley WL. Hepatotoxicity of thiazolidinediones. Expert Opin Drug Saf 2003; 2:581-586.
14. Davidson MH, Robinson JG. Safety of aggressive lipid management. J Am Coll Cardiol 2007; 49:1753-1762.
15. Mukhtar RY, Reckless JP. Statin-induced myositis: a commonly encountered or rare side effect? Curr Opin Lipidol 2005; 16:640-647.
16. Reynolds K, He J. Epidemiology of the metabolic syndrome. Am J Med Sci 2005; 330:273-279.
17. Ogden CL, Yanovski SZ, Carroll MD, Flegal KM. The epidemiology of obesity. Gastroenterology 2007; 132:2087-2102.
18. Bibbins-Domingo K, Coxson P, Pletcher MJ, Lightwood J, Goldman L. Adolescent overweight and future adult coronary heart disease. N Engl J Med 2007; 357:2371-2379.
19. Caspary T, Cleary MA, Baker CC, Guan XJ, Tilghman SM. Multiple mechanisms regulate imprinting of the mouse distal chromosome 7 gene cluster. Mol Cell Biol 1998; 18:3466-3474.
20. Korkmaz A, Manchester LC, Topal T, Ma S, Tan DX, Reiter RJ. Epigenetic mechanisms in human physiology and diseases. J Exp Integr Med 2011; 1:139-147.
21. Hotamisligil GS. Inflammation and metabolic disorders. Nature 2006; 444:860-867.