Preface

Of Vitruvian mice and men

Leonardo Da Vinci’s Vitruvian man—often called the Proportions of Man—is a blend of art and science. Leonardo based his drawing on hints from the ancient Roman architect Vitruvius. It is an elegant illustration of his interest in both proportions and human anatomy. Today, however, we recognize that there is no such thing as a universal set of proportions for the human body. In fact, a field of research called anthropometry has been created in order to document and study these differences. In recent years, some of our proportions have begun to change at an alarming rate. The most recognizable of these is an increase in our body weight. If Da Vinci were alive today, he would find it difficult to establish universal and lasting rules of body proportions. Sixty-six percent of the US population is now considered overweight or obese and this trend is poised to continue.

Changes in our body proportions, particularly the increase in central obesity, carry serious pathological consequences. The most prominent of these is the “metabolic syndrome,” first defined by Reaven. Also referred to as “syndrome X,” the metabolic syndrome is a medical condition estimated by the American Heart Association to affect 20–25% of Americans. The condition is defined by the coincidence of three of the following clinical symptoms: insulin resistance, excessive abdominal fat, high blood sugar levels, high triglycerides, low HDL, a prothrombic state or high blood pressure. It is believed that the underlying causes of metabolic syndrome include overweight, physical inactivity and genetic factors. Metabolic syndrome increases the risk of cardiovascular diseases and diabetes and is a major contributor to morbidity and mortality.

Metabolic syndrome is a very complex condition likely reflecting multiple underlying pathologies. Some of this complexity derives from the fact that numerous physiological pathways contribute to feeding, glucose production and lipid synthesis, as well as fuel catabolism, storage and utilization. This complexity is further amplified by the diversity of the tissues and cell types (i.e. liver, muscle, fat, pancreas, adipose tissue, CNS, immune cells, etc.) contributing to and regulating these processes.

Our goal for this Special Issue was to highlight recent advances in research on various aspects of the metabolic syndrome. Among the important questions being pursued in cutting edge research in this area include the underlying pathophysiological mechanisms, the contribution of specific genes or gene families, associated diseases, and promising targets for therapeutic intervention. Special emphasis in this issue is placed on a particular group of transcription factors, the nuclear hormone receptors and their cofactors, that directly link metabolism to transcriptional regulation. In fact, eight of the reviews touch on this area. Other reviews focus on the emerging concept that inflammation and inflammatory cells contribute to progression of metabolic disease. The role of other key transcriptional pathways, such as FoxO and ChREBP, are also addressed, along with those of key metabolic effector proteins such as lipins, adiponectin and AMP-activated protein kinase. Finally, the important contributions of the CNS and circadian rhythms to metabolic control are also discussed.

And why does the obese Vitruvian mouse grace the cover? Leonardo Da Vinci was helped by comparative anatomy of the horse, birds and human legs to understand the principles of movement and flying. Similarly, in almost all the research areas discussed in this issue, the model of choice is the mouse. The study of genetic or diet-induced obese rodents as models for the effects of Western lifestyle habits has been central to many important discoveries in the field of metabolic disease. Da Vinci would no doubt appreciate the efforts by modern researchers to use animal models in order to understand the proportions and responses of the human body.

Laszlo Nagy
Department of Biochemistry and Molecular Biology
Research Center for Molecular Medicine
University of Debrecen
Debrecen H-4012, Hungary
E-mail address: nagyl@med.unideb.hu

Peter Tontonoz
Howard Hughes Medical Institute and
Department of Pathology and Laboratory Medicine
UCLA, Los Angeles, CA 90095, USA
E-mail address: ptontonoz@mednet.ucla.edu