Preface

Adipose tissues are responsible for the control of energy balance and lipid homeostasis. Only in the last decade the complex functions of adipose are clarifying, and it becomes evident that other than serving the purpose of energy storage in the form of triglyceride depots, adipose is responsible for secreting hormones and cytokines, so it is connected to the endocrinal system as well. Adipose is now known to also host mesenchymal stem cells (MSCs) with potential of tissue repair and regeneration.

With respect to the energy storage capacities of adipose tissues, conventional thinking is that adipogenesis initiates when energy intake exceeds nutritional requirements which then affects different biochemical pathways. However, a different thinking is currently becoming recognized, that adipogenesis is also a mechanosensitive-regulated process, and so, mechanotransduction plays a major role in the development and progression of obesity, as well as of related diseases including type-2 diabetes and insulin resistance, hyperlipidemia and hypercholesterolemia, vascular diseases, metabolic inflammations, and several cancers. This volume describes the state-of-knowledge in the study of the intriguing relationships between mechanical loading states in tissues and cells, and these serious, yet common pathophysiologies that are all related to the increase in mass of adipose tissues and/or hyperglycemia.

As revealed by our own research (reviewed in this volume), there appears to be fundamental interactions between the loading states in tissues and cells and adipogenesis. The *Israel Science Foundation* kindly provided us a 4-year grant (ISF grant no. 611/12) to research these relationships to depth, given that obesity and diabetes are now seen as epidemics in developed as well as in developing countries. Actually, obesity and diabetes are so close together in underlying factors and complications that they are sometimes being referred to as one single disease —"diabesity." In addition to carbohydrate-rich and sugar-rich nutrition, risk factors for obesity and diabetes relate to gender, age, pre-existing medical conditions, and also, clearly to the genetics of the individual, but all these were heavily studied before. Mechanotransduction as a direct, primary factor leading to, or accelerating

obesity and diabetes is a new and emerging concept, and this book summarizes the pioneering efforts in this regard across the leading laboratories in the world.

Our growing understanding is that diseases and conditions that traditionally were never thought to relate to biomechanics (such as breast cancer or infertility) are now fully appreciated as such, particularly at the cellular and subcellular levels. This is truly fascinating in the sense that (bio)mechanics is found to be involved nearly everywhere in the body! And, obesity appears to be no exception. Not only with regard to the fact that abnormal bodyweight is causing well-documented secondary orthopedic disorders, e.g., gradually deforming the feet and impairing the gait pattern, or contributing to osteoarthritis and accelerated joint wear-out (topics that are also covered in this book). In a much more fundamental sense, biomechanics and mechanobiology are at the roots of obesity and diabetes themselves, and begin to play a role at the cellular, the subcellular, and even at the molecular scales.

These roots of the diseases can, for example, be seen to originate in the MSCs that are, as mentioned above already, hosted by adipose tissues. MSCs are known to have the potential to differentiate into either adipose cells (adipocytes) or to other, e.g., myogenic or osteogenic cell types. Indeed, one of the chapters here is focusing on the role of mechanical stimulations in directing MSC adipogenesis. Even after differentiation, adipocytes are still influenced by their mechanical loading environment and actively respond to it; specifically, as demonstrated by our own work, adipocytes have been shown to respond to static loading regimes by accelerating adipogenesis. We summarize our research in this regard in the book, by describing the adipogenesis spiral, and particularly how a sedentary life style and hormonal effects at a cell scale can manifest as abnormal rise in fat tissue mass at the whole-body scale. The mechanical behavior of fat tissues is still insufficiently understood, and one of the chapters is a comprehensive review of work to characterize this behavior and properties in the large-deformation and viscoelastic testing domain. It is known however that internally in adipose tissues, the mechanical stiffnesses of both the cells and extracellular matrix play a role in determining the profile of the adipogenesis process. Indeed, one chapter discusses how matrix stiffness interacts with adipose tissue metabolism and also with inflammation, which could be chronic in adipose of morbidly obese individuals. Both the cell-scale mechanical loading conditions and the inflammatory condition connect to mechanically activated signaling pathways and molecular mechanisms, and these are discussed in several chapters as well. Finally, the interactions of adipocytes with cells of the immune system, the vascular system and cells with a malignant phenotype are discussed, to show how diabetes, vascular diseases, and cancers all relate to obesity through cellular signaling and molecular mechanisms. The roles and potential of state-of-the-art experimental cellular and biomolecular measurement techniques, as well as sophisticated mathematical and computational bioengineering modeling, are evident throughout the book in exploring all these exciting relationships.

The book hence summarizes the efforts of an international group of authors, from universities and government research institutes in the USA, Japan, the Netherlands, Australia, Finland, and Israel. The chapters included altogether make an extremely unique comprehensive, rigorous, and concise description,

summarizing the state-of-science in the journey toward understanding the role of mechanotransduction in obesity and related diseases. We are certain that scientists working in the fields of obesity, diabetes, hypertension, hyperlipidemia, orthopedic, and cancer research (which is actually where most of the biomedical research efforts are currently focused) will find this book very useful, and so will graduate students in medicine, bioengineering and biophysics, and medical doctors with an interest in basic and medical sciences. Obesity is not only a metabolic disease, it is also a mechanobiological disorder, and the present book provides the compilation of evidence to describe it as such.

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