Editorial Preface

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Adiposopathy in cancer and (cardio)metabolic diseases: an endocrine approach – Part 1

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This special issue of the journal *Hormone Molecular Biology and Clinical Investigation (HMBCI)* includes two parts (1 and 2) intended to organize around the central topic of adiposopathy numerous pertinent manuscripts demonstrating the tremendous growing implication of “sick fat” in the initiation and development of important pathophysiological events in the human body, which result in severe (chronic) diseases and possible early mortality. Among the pleiotropic entanglements of adiposopathy in multiple biological disturbances, we have decided to focus this special issue on its role in cancer and (cardio) metabolic diseases, the two major “socio-epidemic” illnesses in terms of prevalence and morbidity/mortality in Western industrial countries and now also in newly developing countries. According to the World Health Organization, more than 1.4 billion adults are overweight and more than half a billion worldwide are obese. Obesity is a fundamental contributor to insulin resistance, type 2 diabetes mellitus (T2DM), metabolic syndrome, and cardiovascular diseases, but it is also an important risk factor for some cancers, such as colorectal, hepatic, kidney, breast, endometrium, and prostate.

What is the link between adiposopathy and these crucial pathologies? The concept of adiposopathy or “sick fat” can be defined as any abnormal distribution of excessive adipose tissues (fat mass) in the whole body, as is observed essentially in overweight and especially in obese patients but also more widely in some cases of lipodystrophy.

Obesity occurs when the energy (caloric) balance is positive (excess of food intake relative to energy expenditure). This expansion of adipose tissue is necessary to sequester cytotoxic free fatty acids and lipid metabolites and emanates principally from hypertrophy and/or hyperplasia of adipocytes (fat cells).

In this context, adiposity and the anatomical distribution in the body of white adipose tissue, subcutaneous or visceral, have important repercussions in pathophysiology because they can involve, respectively, either the

“beneficial” or the very detrimental effects of obesity. Excess fat in the upper part of the body, or central abdominal (android or male-type) adiposity, correlates more with increased early mortality and risk of severe cardiometabolic dysregulation, compared with lower body, or gluteofemoral, peripheral deposit (gynoid or female-type of fat distribution). Thereby, the visceral fat (intra-abdominal) is associated with more aggressive metabolic and vascular disturbances, particularly by alteration of plasma triglycerides, lipoprotein-lipid levels, and insulin resistance. Thus, subcutaneous fat differs intrinsically from visceral fat and is thought to protect from cardiometabolic diseases.

At a local level, an excess of fat can be deposited within specific organs (or around them), including the liver, pancreas, skeletal and cardiac muscle, blood vessels, breast, or bone, to form an accumulation of lipid droplets. This excess of ectopic stored lipids can cause cellular damage (steatosis) and cell death (fibrosis) and can eventually lead to tumor formation. Other distinct fat deposits, including mammary fat, perivascular, epicardial, or bone marrow adipose tissues, operate to modify tumoral and cardiovascular morbidity risks or tissue regeneration.

All these adiposopathy-associated deleterious states derive from profound fat cell dysfunction, which induces inaccurate endocrine (paracrine, autocrine, and intracrine), immune and metabolic physiological responses often associated with formation of a chronic low-grade inflammation status, to promote and increase the risk of cancer and/or cardiometabolic pathologies. Furthermore, obesity is closely associated with aberrant production and functions of adipo(cyto)kines secreted from dysfunctional adipose tissues.

Indeed, throughout the last two decades, adipose tissue has progressively divulged its true nature as one of the largest, most complex, sophisticated, regulatory, and original endocrine multi-sided organs in the human body. In addition to its well-known functions of mechanical protective support tissue, as well as metabolic passive storage and release of triacylglycerols from lipid droplets, adipose tissue possesses surprising properties of secretion,

adaptative plasticity, and crosstalk with many peripheral and central organs or tissues, including bone, liver, pancreas, skeletal and cardiac muscle, blood vessels, kidney, brain, and breast. Above all, fat cells largely secrete more than 100 different adipocyte-derived factors [adipo(cyto)kines], including steroids and specific hormones (e.g., leptin, adiponectin, resistin, visfatin, apelin), cytokines, chemokines, and prostaglandins, in various concentrations according to the lean or obese tissue status and nature of fat deposits.

In this way, fat tissue emerges as one paramount coordinator of key biological processes such as differentiation, tissue regeneration, cell growth, apoptosis, reproduction, immunity, inflammation, angiogenesis, metabolism, and thermoregulation; its dysfunction can lead or contribute to multiple pathologies such as obesity, T2DM, dyslipidemia, hypertension, atherosclerosis of coronary/cerebral/peripheral vessels, metabolic syndrome, cognitive alteration, or cancer.

Part 1 (*HMBCI*, Vol. 20, Issues 1 and 2) of our special series on “Adiposopathy in Cancer and (Cardio)Metabolic Diseases: An Endocrine Approach” essentially concerns papers dealing with adiposopathy and cardiometabolic disease. As will be described in this series of articles, numerous endocrine events can initiate obesity-related cardiometabolic disorders.

The first issue summarizes the cellular and molecular pathways underlying obesity-related metabolic disorders, notably, the role of macrophage infiltration in the genesis of insulin resistance and/or obesity (L.K. Heilbronn and B. Liu), the effects of sex and sex steroids in regional body fat distribution (S. Santosa and M.D. Jensen), and the pathophysiological mechanisms in aging that can induce

obesity, sarcopenia, osteoporosis, and cardiovascular complications (S. Migliaccio et al.). This is followed in the second issue by four articles describing the contribution of nutrition (G. Tarantino), vitamin D (I.N. Sergeev), and sex hormones and the nuclear hormone receptor peroxisome proliferator-activated receptor γ (PPAR γ) (H. Sato et al.) to control nonalcoholic fatty liver disease, obesity, cardiovascular dysfunction, and/or cancer. In particular, the implication of mutated PPAR γ in the occurrence of familial partial lipodystrophy syndrome and/or diabetes is investigated (O. Astapova and T. Leff).

We are indebted to all the scientists, widely recognized in their field, who have kindly contributed to this special issue and provided a state-of-the-art update on adiposopathy in cancer and (cardio)metabolic diseases, an exciting new topic that has profound clinical consequences on the health and well-being of millions of individuals around the world. We sincerely hope that readers of *HMBCI* will enjoy finding some answers and perhaps it will encourage submission of interesting original articles related to cancer and all adiposopathy-associated cardiometabolic disorders.

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