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"Adiponcosis": a new term to name the obesity and cancer link

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It is now beyond doubt that obesity is a pandemic disease that poses a great challenge to global health, since it leads to many comorbidities affecting life expectancy. In addition to cardiovascular disease and diabetes, epidemiological data clearly demonstrate a link between obesity and cancer incidence and bad prognosis in breast, colon, endometrium, kidney and esophagus cancers, for at least a quarter of the patients (1–3). Continuation of existing trends in obesity will lead to about 500,000 additional cases of cancer only in the United States by 2030 (4).

The molecular mechanisms underlying how obesity causes an increased risk of cancer are to date poorly understood and may be different depending on cancer type. Possible mechanisms could involve metabolic and hormonal dysregulation, insulin-resistance, hyper activation of the IGF-I pathway and a chronic low-grade proinflammatory state in adipose tissue, characterized by increased circulating fatty acids, and chemoattraction of immune cells, all factors able to promote tumor onset and progression. Many hormones involved in obesity play a role in the initiation and promotion of cancer at cellular, paracrine and systemic level. Obesity disrupts the dynamic role of adipocytes in energy homeostasis and changes the biology of nonadipose cells in the stromal-vascular fraction, resulting in inflammation, abnormal angiogenesis and alteration of adipocytokines (leptin, adiponectin) and inflammatory cytokines signaling that could be an active local player determining the peri-tumoral milieau which promotes tumor rise and progression (5). Chronic inflammation is a key feature of both metabolic disorders and cancer, and local adipose inflammation with crown-like foci of dead adipocytes surrounded by macrophages activated by released saturated fatty acids, is really evident in obese and overweight individuals (6). In particular, inflammasomes - multiprotein complexes that operate as platforms for the activation of caspase-1- nucleated by NLRP3 and NLRP6 integrate multiple signals from metabolic systems (ceramide, saturated free fatty acids and others) that cause pathogenic inflammation in obesity and high-fat diet (7). This innovative concept has been for the first time introduced in 2010 and inflammasomes are now emerging as a driving force for obesity and its related morbidities such as insulin-resistance and diabetes (8). Interestingly, NRLP3 and NRLP6 can influence the formation and progression of cancer, as observed for colon cancer and melanoma, through their contribution to tissue homeostasis (9). Additionally, obesity is associated with immune dysfunction and causes secondary changes that are related to lipid deregulation, factors that may also foster cancer development (10).

Noteworthy, strategies to mitigate the adverse metabolic effect of adiposity are a priority for cancer prevention since the weight gain following chemotherapy and the frequent relapses linked to this occurrence are strong links between obesity and cancer.

In the light of the evidence that the obesity-cancer link is not more a mere medical hypothesis but an evolving and currently very active area of research, we propose the new term "*adiponcosis*" derived from the fusion of the word of latin origin "adiposis" (excessive accumulation of fat in the body) and that of greek origin "oncosis" (formation of a tumor) to describe the innovative, but proved concept, that the accumulation of fat may induce the insurgence of a tumor. Therefore research in the field of *adiponcosis*, aimed to elucidate the molecular mechanisms linking obesity to cancer and to characterize the beneficial pharmacological effects of compounds acting on their converging

Abbreviations:

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pathways, is an emerging critical step for cancer prevention and treatment.

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