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Link between insulin and metabolic disorders in cancer: does leptin play a key role?

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To the Editor,

We read with great interest the recent paper by Goodwin et al. [1] on the association between insulin resistance and other components of the metabolic syndrome (e.g., obesity, high waist–hip ratio, impaired lipid profile) in patients affected by breast cancer. As correctly reported by the authors [1], a state of hyperinsulinemia can act on breast cancer prognosis through several mechanisms, such as: (i) a direct interaction between insulin and insulin/IGF receptors able to stimulate cell proliferation; (ii) some indirect effects of insulin on the circulating levels of both IGF and of insulin/IGF binding proteins; (iii) an effect of insulin on the free circulating estrogen levels.

A further explanation supporting this hypothesis could be related to the ability of insulin to stimulate the expression and secretion of leptin by adipocytes [2–5]. Therefore, hyperleptinemia is usually present in some states of hyperinsulinemia like in obesity [2–5]. Consistently, a possible role of leptin in the development and progression of breast cancer has been suggested [2]. In fact in addition to its neuroendocrine functions (i.e., regulation of appetite and energy expenditure), leptin can act as a mitogen and angiogenic factor via paracrine and autocrine mechanisms. Due to its mitogen effect, a condition of hyperleptinemia could favour the development of malignancies. In close agreement with this hypothesis, several lines of evidence

support the role of leptin in the neoplastic processes [6–9]. Moreover, this is further supported by some genetic evidences showing a correlation between serum leptin levels, leptin receptor polymorphisms, and the risk of breast cancer [10, 11]. In sum, although further prospective data are needed, leptin should be mentioned among the key factors in understanding the relationship between hyperinsulinemia and related metabolic factors in subjects with cancer risk. This also gets the basis for future potential therapeutical approaches (i.e., leptin-inhibiting drugs, strict adherence to weight-reducing programs) in the prevention and treatment of malignancies.

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