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

Noemi Malandrino · Lorenzo Leggio ·
Giovanni Addolorato · Giovanni Gasbarrini ·
Esmeralda Capristo

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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.

References

1. Goodwin PJ, Ennis M, Bahl M et al (2008) High insulin levels in newly diagnosed breast cancer patients reflect underlying insulin resistance and are associated with components of the insulin resistance syndrome. *Breast Cancer Res Treat*. doi:10.1007/s10549-008-0019-0
2. Capristo E, Malandrino N, Farnetti S et al (2006) Metabolic alterations as a risk factor for cancer. *Intern Emerg Med* 1:29S–35S
3. Malmström R, Taskinen MR, Karonen SL et al (1996) Insulin increases plasma leptin concentrations in normal subjects and patients with NIDDM. *Diabetologia* 39:993–996. doi:10.1007/BF00403921
4. Mueller WM, Gregoire FM, Stanhope KL et al (1998) Evidence that glucose metabolism regulates leptin secretion from cultured rat adipocytes. *Endocrinology* 139:551–558. doi:10.1210/en.139.2.551
5. Greco AV, Mingrone G, Vettor R et al (2002) Lowering of circulating free-fatty acids levels and reduced expression of leptin in white adipose tissue in post-obesity status. *J Investig Med* 50:207–213. doi:10.2310/6650.2002.33435
6. Perera CN, Spalding HS, Mohammed SI et al (2008) Identification of proteins secreted from leptin stimulated mcf-7 breast cancer cells: a dual proteomic approach. *Exp Biol Med* 233:708–720. doi:10.3181/0710-RM-281

N. Malandrino (✉) · E. Capristo
Institute of Internal Medicine, Metabolic Unit, Catholic
University of Rome, Largo A. Gemelli 8, 00168 Rome, Italy
e-mail: noemi.malandrino@edu.rm.unicatt.it

L. Leggio · G. Addolorato · G. Gasbarrini
Institute of Internal Medicine, Catholic University of Rome,
Largo A. Gemelli 8, 00168 Rome, Italy

7. Slattery ML, Wolff RK, Herrick J et al (2008) Leptin and leptin receptor genotypes and colon cancer: gene–gene and gene–lifestyle interactions. *Int J Cancer* 122:1611–1617. doi:[10.1002/ijc.23135](https://doi.org/10.1002/ijc.23135)
8. Stattin P, Söderberg S, Hallmans G et al (2001) Leptin is associated with increased prostate cancer risk: a nested case-referent study. *J Clin Endocrinol Metab* 86:1341–1345. doi:[10.1210/jc.86.3.1341](https://doi.org/10.1210/jc.86.3.1341)
9. Ramani K, Yang H, Xia M et al (2008) Leptin's mitogenic effect in human liver cancer cells requires induction of both methionine adenosyltransferase 2A and 2beta. *Hepatology* 47:521–531. doi:[10.1002/hep.22064](https://doi.org/10.1002/hep.22064)
10. Koda M, Sulkowska M, Kanczuga-Koda L et al (2007) Expression of leptin and its receptor in female breast cancer in relation with selected apoptotic markers. *Folia Histochem Cytobiol* 45:S187–S191
11. Soma D, Kitayama J, Yamashita H et al. (2007) Leptin augments proliferation of breast cancer cells via transactivation of HER2. *J Surg Res*. doi:[10.1016/j.jss.2007.10.012](https://doi.org/10.1016/j.jss.2007.10.012)