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Leptin and Mast Cells: A Novel Adipoimmune Link

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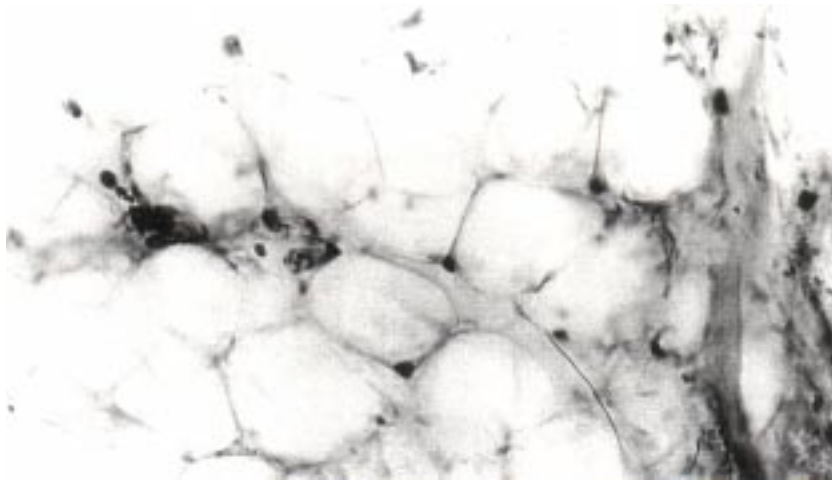
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In addition to its role in regulating feeding behavior and energy homeostasis, leptin, an adipokine (adipose tissue-secreted cytokine) (1,2), may also control lymphocyte and macrophage functions (3). However, until now, there is no published work, to our knowledge, about the possible role of leptin in the biology of mast cells (MCs). Here we report that an increased plasma level of leptin positively correlates with the number of adipose tissue MCs in patients with metabolic syndrome, a clinical disorder characterized by the clustering of atherogenic cardiovascular risk factors in one individual (4 and Refs therein).

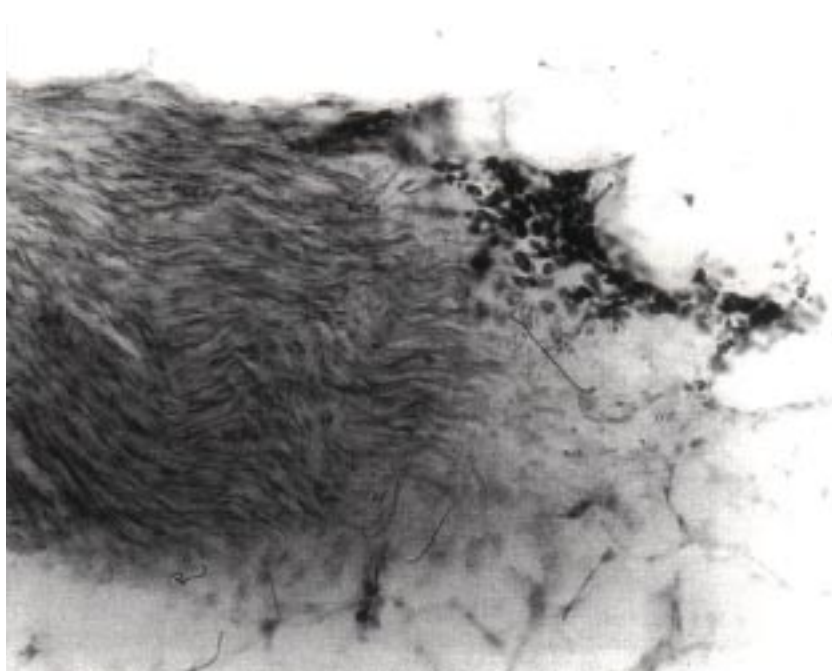
We studied 23 patients with metabolic syndrome, 20 females and 3 males (aged 45.69 \pm 2.18). The control group comprised 10 age-matched healthy subjects, 7 females and 3 males (aged 42.50 \pm 2.75). Informed consent was obtained from all the subjects studied. All medication was withdrawn 10 days before the collection of both blood and adipose tissue samples. The concentration of leptin present in the plasma was measured by radioimmunoassay using the kit by Alpha Diagnostics, San Antonio, TX, USA. For histological analysis, abdominal subcutaneous adipose tissue was collected by biopsies from the same patients and the same control subjects. The specimens were fixed in 4% paraformaldehyde in 0.1M phosphate buffer, pH 7.4, and sections stained with 0.5% toluidine blue (pH 2.5) for MCs (Fig. 1 A-B). Cell counting expressed as number per mm² was evaluated with a Zeiss microscope and analyzed by a PC using a specific software package (IAS 2000, Delta Sistemi, Rome, Italy). The data were expressed as

means \pm SEM. Analyses of variance (ANOVA) were used to determine statistical differences in the leptin levels and the number of MCs between metabolic syndrome patients and controls, taking also into account the sex factor.

The amount of plasma leptin (ng/ml) in metabolic syndrome patients was higher (6.76 \pm 0.46) than in controls (1.13 \pm 0.12) ($p < 0.01$). The number/mm² of MCs were increased in the adipose tissue of metabolic syndrome patients (59.17 \pm 6.60) when compared with controls (13.10 \pm 1.09) ($p < 0.01$). A significant correlation was observed between leptin levels and numbers of MCs in metabolic syndrome patients ($r = 0.71$, $p < 0.01$) but not in controls ($r = 0.44$, $p < 0.23$). It is noteworthy that the plasma level of nerve growth factor, a known growth factor of MCs (5), was significantly decreased in the metabolic syndrome patients when compared to control subjects examined (4). Altogether, the present findings suggest a stimulatory action of circulating leptin on adipose mast cell growth. Whether leptin stimulates proliferation and/or inhibits apoptosis of MCs remains to be evaluated. Another pressing question is whether brain MCs (6), as well as MCs associated with other organs (7), including lymph nodes (our unpublished data), could also be targets for leptin. Note that (i) a greater number of adipose MCs are reported in obese mice when compared to nonobese mice (8), and (ii) the adipose tissue surrounding lymph nodes is involved in various immune-inflammatory responses (9). We therefore suggest that further studies may contribute to the better understanding of the adipoimmune link (Table), and also adiponeuroimmune interactions (see Fig. 1, lower panel, and Refs 2, 4, 10).



A



B

Figure 1. Two photomicrographs of toluidine blue-stained sections of abdominal subcutaneous adipose tissue, obtained by biopsy from patients with metabolic syndrome. The upper panel illustrates several mast cells located between adipocytes. The lower panel illustrates a cluster of mononuclears and few mast cells associated with nerve bundle. x 200.

Table: Adipoimmune mediators.

| Adipokines | Immune cells | References |
|---------------------|--------------------------|---------------|
| Adiponectin | Macrophages | 1 |
| FIZZ1* | Lymphocytes | 10 |
| Nerve growth factor | Mast cells | 11 |
| Interleukin-8 | Macrophages | 12 |
| Leptin | Lymphocytes, macrophages | 3 |
| Leptin | Mast cells | Present study |

* Abbreviation of Found in Inflammatory Zone.

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