INTERNATIONAL JOURNAL OF IMMUNOPATHOLOGY AND PHARMACOLOGY Vol. 21, no. 1, 1-4 (2008)

EDITORIAL

ALLERGIC INFLAMMATION AND ADIPOCYTOKINES

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Received November 14, 2007 – Accepted November 30, 2007

Increasing evidence indicates that inflammation is a major component of a number of diseases with atopic diathesis (1), such as asthma, atopic dermatitis, contact dermatitis, and even psoriasis. A number of cytokines are clearly implicated in inflammatory processes; some of the most important ones are IL-1, IL-6, TNF-α, as well as the newly discovered IL-32 (2) and IL-33 (3). Chemokines such as IL-8, MCP-1 and RANTES are also involved (4), and are potent chemoattractants for mast cells, which are critical for atopic diseases (5). It is of interest that at least IL-1 (6) and IL-33 (7) can induce release of IL-6 and IL-13 from mast cells, selectively without histamine. Mast cells could, therefore, participate in both IgE and non-IgE- mediated hypersensitivity responses.

There are some clinical observations suggesting a relationship between inflammatory diseases and obesity (8). For instance, one recent epidemiological study using the Danish Twin Registry showed that the age–adjusted risk of asthma was significantly increased in obese individuals of both sexes; this correlation was higher in women for whom there was also a statistical correlation with genetic predisposition with respect to candidate genes for obesity and asthma (9). The main explanation for an association between asthma and obesity suggested so far is based on the possible action of adipocyte-derived cytokines (e.g. IL-10) to decrease immunological tolerance by inhibiting the activity of regulatory T cells (9).

Adipocytes are well known to release hormones, such as leptin and adiponectin (10). Adipocytes were first reported by Spiegelman and colleagues to make TNF-α (11). They have since been shown to secrete a surprisingly large number of cytokines including IL-6 and TNF-α, which are important in inflammation (10, 12-13). It was also recently reported that induction of intestinal inflammation stimulated preadipocytes to release inflammatory cytokines, while exposure of human mesenteric preadipocytes to substance P increased NK-1R expression and stimulated IL-8 secretion (14). Moreover, the type of adipocyte innervation may also affect their function (15).

An alternative, but not mutually exclusive, hypothesis to explain an association between inflammation and obesity could be based on the role of mast cells. We recently showed that mast cells are located among adipocytes (Fig. 1) and can be activated by allergic and non-allergic triggers to release molecules that stimulate adipocyte cytokine production directly or indirectly (Fig. 2). Such mast cell action could only be explained if they have the ability to release mediators selectively without

Key words: allergic inflammation, adipocytokines

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0394-6320 (2008)

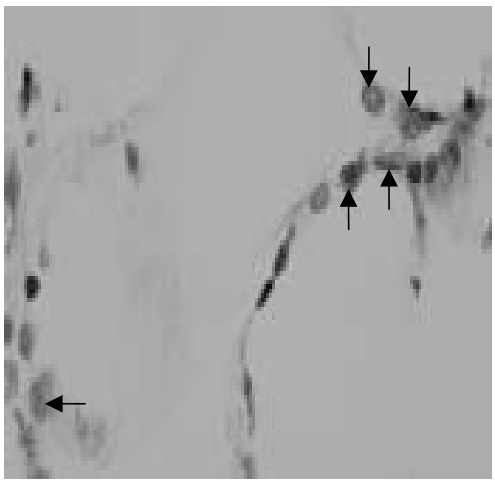

Fig. 1. *Photomicrograph of white fat stained with toluidine blue (1%, pH 2) showing metachromatic mast cells (arrows) among adipocytes (magnification = x 400).*

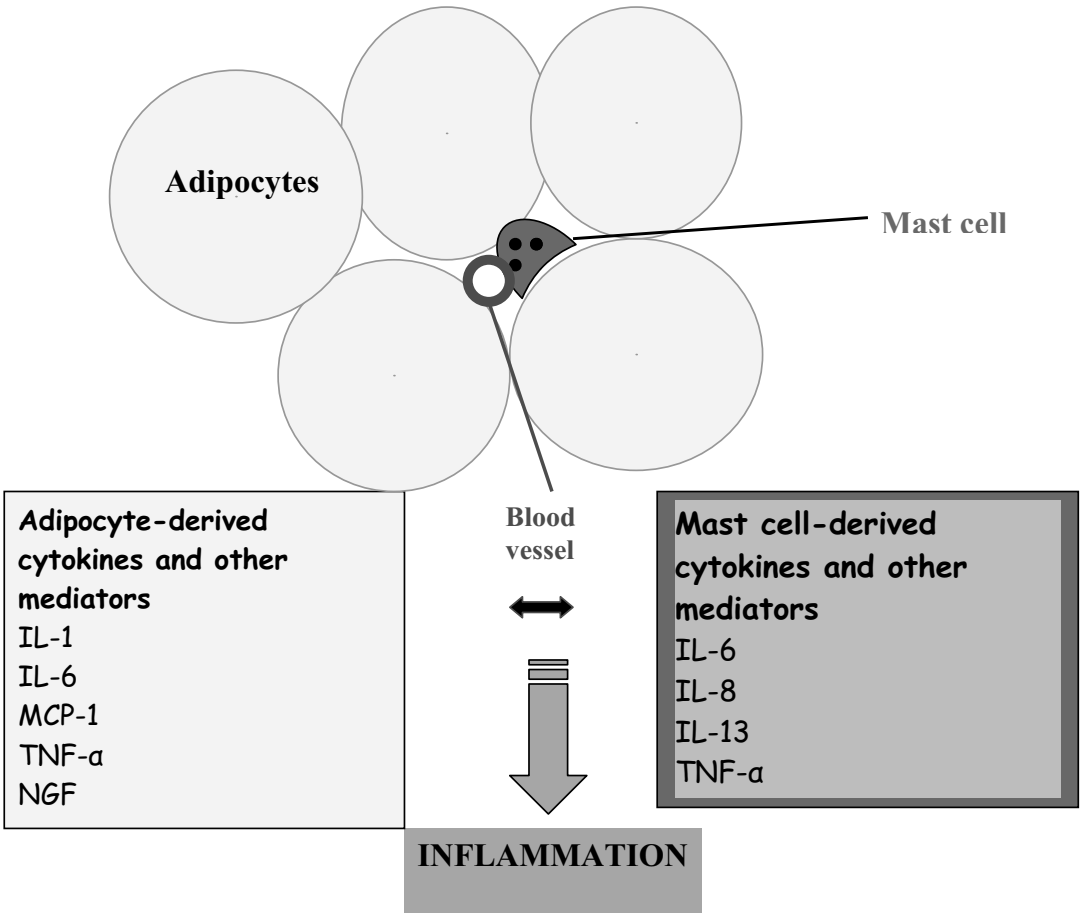

Fig. 2. *Schematic representation of the proposed interactions between mast cells, adipocytes and blood vessels in promoting inflammation.*

degranulation (16). TGF-β and IL-6 released from mast cells, as well as IL-6 and IL-22 released from adipocytes, could stimulate maturation and proliferation of T17 cells, which have recently been shown to be critical in autoimmune and inflammatory processes (17). Adipocytes can also release MCP-1, which is a strong mast cell chemoattractant (18), and IL-1 which can stimulate selective mast cell secretion of IL-6 (6), suggesting that there may be a reciprocal relationship between mast cells and fat depots.

These implications are particularly important given the alarming increase in obese individuals that is reaching epidemic proportions. New therapeutic approaches may target mast cell inhibition as a way of breaking the cycle between atopy-inflammation-obesity.

ACKNOWLEDGEMENTS

Some of our research was supported by US NIAMSD 2 R01 AR47652-06 to TCT. We thank Dr. Andrew Greenberg (USCDA, Boston, MA) for some of the histological images.

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