SHORT COMMUNICATION:
NGF, BDNF, Leptin, and Mast Cells in Human Coronary Atherosclerosis and Metabolic Syndrome

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Abstract
While multiple growth factor, cytokines, and immune cells are identified in atherosclerotic lesions, as well as an essential nonneuronal function of neurotrophins implicated in cardiovascular tissue development and in lipid and glucose metabolism, the role of the neurotrophins NGF and BDNF and also the adipokine leptin in human coronary atherosclerosis and related disorders, such as metabolic syndrome, remains unclear. Here we report that (i) both the amount and the immunoreactivity of NGF was reduced and the expression of p75NGF receptor and the number of mast cell increased in human atherosclerotic coronary arteries (n = 12) compared with control specimens (n = 9) obtained from autopsy cases, and (ii) NGF and BDNF plasma levels were reduced in patients with metabolic syndrome (n = 23) compared with control subjects (n = 10). Also, in metabolic syndrome patients, a positive correlation between the plasma leptin levels and the number of adipose tissue mast cells was found, suggesting that leptin may be a novel adipoinimmune mediator. Altogether, the results provide the first correlative evidence for the potential involvement of NGF, BDNF, leptin, and mast cells in human coronary atherosclerosis and metabolic syndrome, implying neuroimmune and adipoinimmune pathways in the pathobiology of these cardiovascular disorders.

Keywords: NGF, BDNF, leptin, mast cells, coronary atherosclerosis, metabolic syndrome, human.

Introduction
Atherosclerosis, an inflammatory disease (Ross, 1999; Chaldakov et al., 2000a), with its manifestation coronary artery disease, is the major cause of morbidity and mortality worldwide, while metabolic syndrome (MS) (Zimmer et al., 1999; Groop, 2000) demonstrates a population with extreme high risk for myocardial infarction, a major complication of advanced atherosclerotic lesions. Neurotrophins (Donovan et al., 1995; Abe et al., 1997; Nagtegaal et al., 1998; Bu et al., 1998; Aloe & Micera 1999; Ono et al., 2000; Wang et al., 2000) and adipokines (adipose tissue-secreted molecules) (Yokata et al., 2000; Chaldakov et al., 2000b) constitute a complex network of multifunctional mediators increasingly implicated in various neuroimmune, adipoinimmune, inflammatory, vascular, and metabolic events. However, there are no correlative studies available, to our knowledge, describing whether the constitutive presence of neurotrophins, leptin, and mast cells is altered in human coronary atherosclerosis and in patients with MS. The aim of the present study was therefore to investigate the possible involvement of nerve growth factor (NGF), brain-derived neurotrophic factor (BDNF), leptin, and mast cells in the pathogenesis of human coronary atherosclerosis and MS.

Subjects and methods
Coronary atherosclerosis
The specimens of human coronary arteries were obtained from 21 autopsy cases. The mean interval between death and the beginning of specimen processing was 11 hours, range: 3 to 22 hours. We examined the proximal 15–20mm of the left anterior descending coronary artery of men without atherosclerotic lesions (n = 9), and subjects with atherosclerotic lesions (n = 12), including type II lesions (n = 1), type V lesions (n = 4), and type VI lesions (n = 7), according to Stary