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CIRCULATING NGF ANTIBODY ALTERS THE DISTRIBUTION OF NG2 AND CD56 POSITIVE CELLS IN THE BRAIN OF AN ANIMAL MODEL OF INFLAMMATORY DISORDER

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INTRODUCTION

One important limiting factor in the replacement of damaged cells and in promoting mechanisms of repair is the difficulty to identify and stimulate resident immature cells of the central nervous system (CNS). Undifferentiated cells able to give rise to glial cells and neurones have been detected in specific regions of developing and adult brain (40). The knowledge of the events and molecules involved in stem cell proliferation and differentiation could be helpful to develop repair strategies for brain disorders where damage and/or loss of cells occurs. A number of extracellular signals and growth factors (17, 23, 33) regulate stem cell proliferation, cell fate determination, progenitor migration and differentiation, including Nerve Growth Factor (NGF) (29).

NGF is the first and best-characterised member of the family of structurally and functionally related neurotrophins (22, 27), which include brain-derived neurotrophic factor (BDNF) and neurotrophins 3/5 (NT-3/5) (7, 8). NGF is produced and released by a variety of tissues within and outside the central nervous system (CNS) of mammals and plays a crucial role during neuronal development and after injury (27). In addition to its neurotrophic activity, NGF exerts broad biological activities on other cell types, including cells of the innate and adaptive immune responses, such as mast cells, basophils and lymphocytes (2). The biological effect of NGF is mediated by binding to two classes of receptors: trkA, the tyrosine kinase receptor, and p75, which lack intrinsic kinase activity (7, 16). NGF seems to participate to the compensatory mechanisms intervening in response to inflammation in the central nervous system (CNS) of EAE rats (13, 30, 31), the experimental model of the human disease Multiple Sclerosis (MS) (18).

We have previously shown that the levels of NGF in the cerebrospinal fluid (CSF) of patients affected by MS significantly increase during the acute phase of the disease (11). Moreover we observed that NGF injected into the brain ventricle of rats with Experimental Allergic Encephalomyelitis (EAE) is taken up by SVZ cells and transported into brain parenchyma (3, 13). Indeed, neuroepithelial cells lying in the subventricular zone (SVZ) of amphibians (26) and rodents express NGF-receptors and are responsive to the action of NGF (3).

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