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Alpha/Beta Interferon Is a Neuronal Growth Factor

Audrius V. Plioplys[a,b]
Nicolas Massimini[a]

[a] Division of Neurology, Mercy Hospital and Medical Center, and
[b] Department of Neurology, University of Illinois, Chicago, Ill., USA

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Abstract
We investigated the effect of alpha/beta interferon on neuronal survivability. E16 murine telencephalic vesicles were dissected aseptically and grown on collagen-coated coverslips. After 2 weeks of culturing, the media was supplemented with mouse alpha/beta interferon (1,500 U/ml). After an additional 2 weeks of culturing, all of the control cultures demonstrated significant neuronal death. In the 16 interferon-treated cultures, neuronal death took place only in 1 culture, baseline survivability occurred in 2 and proliferation in 13 cultures ($p < 0.005$). Thus, alpha/beta interferon sustains neuronal growth.

Introduction

The effects of alpha/beta interferon on cultured fibroblasts and leukocytes have been well investigated. These include decreased rates of mitosis, locomotion, membrane ruffling and staltatory movements of intracellular granules [1, 2]. Interferon treatment also changes the amount and cellular distribution of actin and fibronectin [2, 3] and produces defective lymphocyte capping following concanavalin A administration [4].

Alpha/beta interferon may play a physiologic role in the mature central nervous system (CNS). Interferon is present in the cerebrospinal fluid [5]. In monkeys the CNS can produce interferon-dependent RNA following intrathecal administration of interferon [6]. Neurons in vivo and in culture are sensitive to interferon, thus suggesting the possibility of functional interferon receptors in the CNS [7].

There have been few investigations of the effect of alpha/beta interferon on the developing nervous system. Fetal and newborn human fibroblasts and mononuclear cells can produce adult levels of virus-induced interferon [8, 9]. If the effect of alpha/beta interferon on the developing CNS is similar to that on fibroblasts and leukocytes, one would expect the interferons to be neuronal growth inhibitors. Forty-eight hours of alpha/beta interferon treatment of cultured fetal murine CNS increases the immunohistochemical expression of the 210-kD neurofilament subunit [10]. This observation does not answer the question of what effects interferon exposure may have on neuronal growth and survival.

We decided to investigate the effect of prolonged (2 weeks) exposure of interferon on neuronal growth and survival using cultured fetal murine CNS neurons.

Materials and Methods

Pregnant mice were sacrificed by cervical dislocation. Using sterile techniques, E16 normal fetuses were removed from the uterine sacks. Their telencephalic vesicles were dissected and homogenized through a coarse stainless steel sieve into a trypsin-EDTA solution for 2 min. The homogenates were washed several times in Dulbecco's modified Eagle's medium supplemented with 10% fetal calf serum and plated onto 32 separate collagen-coated coverslips at plating density of 10^6 cells/ml. The cultures were incubated at 37°C in a 94% air/6% CO_2 atmosphere. The media was replaced every 4 days. After 2 weeks, the media of 16 cultures was supplemented with mouse

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Dr. A.V. Plioplys
Division of Neurology
Mercy Hospital and Medical Center
Stevenson Expressway at King Drive
Chicago, IL 60616 (USA)

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