

Volume 13, issue 1, March 2002 | Papier court

The effect of interleukin-1beta (IL-1beta) and tumor necrosis factor-alpha (TNF-alpha) on granulocyte macrophage-colony stimulating factor (GM-CSF) production by neuronal precursor cells

Abstract

Aims: To determine whether granulocyte macrophage-colony stimulating factor (GM-CSF) production by neuronal precursor (NT2) cells can be regulated by IL-

1beta and TNF-alpha. Background: We have previously demonstrated GM-CSF expression by neurons of the developing human brain, as well as by NT2 cells. IL-1beta and TNF-alpha upregulate GM-CSF production in glial cells, but GM-CSF regulation in neurons is as yet undefined. We hypothesized that IL-1beta and TNF-alpha would increase GM-CSF mRNA and protein production in NT2 cells. Methods: The effect of IL-1beta and TNF-alpha on GM-CSF production was assessed by dose response (0 to 2,000 U/ml), and time course (0 to 48 hours incubation) experiments. GM-CSF mRNA and protein production were assessed by quantitative RT-PCR and by ELISA. The effect of these cytokines on cell turnover was determined by BrdU incorporation. Results: IL-1beta increased GM-CSF mRNA and protein expression by NT2 cells. This effect was time and dose dependent, and the effective dose ranging from (20-200 U/ml). TNF-alpha increased GM-CSF mRNA expression to a lessor extent than did IL-1beta (maximal stimulation at 200 U/ml), and a minimal increase in net protein accumulation was noted. Neither cytokine increased NT2 cell turnover. Conclusions: IL-1beta and TNF-alpha both increase GM-CSF mRNA expression by NT2 cells, but only IL-1beta increases net GM-CSF protein accumulation.

Full text

INTRODUCTION

The role of cytokines in the development and homeostasis of the central nervous system (CNS) is an area of intense research. Granulocyte macrophage-colony stimulating factor (GM-CSF), originally discovered for its role in stimulating clonal production of granulocytes and macrophages, has been among the cytokines studied. Like many other hematopoietic cytokines, GM-CSF acts by interacting with its specific cell surface receptor (GM-CSF-R), and has important non-hematopoietic effects [1-4]. Neurons, microglia, astrocytes, and oligodendrocytes all express GM- CSF-R mRNA [5], and GM-CSF production has been demonstrated in astrocytes stimulated by inflammatory cytokines IL-1beta and TNF-alpha, and by microglia stimulated with LPS [6]. Another possible source of GM-CSF in the CNS may be systemic circulating GM-CSF, as it can cross the blood-brain barrier [7].

Some of the non-hematopoietic functions of GM-CSF have been demonstrated in differentiated cell lines. For example, GM-CSF stimulates proliferation of microglia [6] and astrocytes [8]. GM-CSF also increases choline

acetyltransferase in SN6.10.2.2 and septal neurons. In combination with IL-3, GM-CSF increases neurite outgrowth of cholinergic neurons [3]. *In vivo*, GM-CSF and erythropoietin promote survival of septal cholinergic neurons of adult rats which have undergone fimbria-fornix transections [1].

While GM-CSF production has been documented in mature cells of the CNS, little is known about GM-CSF expression or function in cell in the developing CNS. We have recently shown that many cell types (neurons, astrocytes, and glial cells) in the developing CNS express GM-CSF and its receptor [9]. We postulated that GM-CSF might play an important role in neurodevelopment, and furthermore, that GM-CSF is expressed by neurons and neuronal precursors in a regulated manner. The present experiments were designed to test the second postulate. Specifically, we sought to determine whether the inflammatory cytokines IL-1beta and TNF-alpha regulate GM-CSF expression by NT2 cells, a human committed neuronal precursor cell line.

MATERIALS AND METHODS

NT2 cells

A human committed neuronal precursor cell line, NT2, is derived from teratocarcinoma (Stratagene, LaJolla, CA) and can be induced to differentiate *in vitro* into postmitotic neurons by retinoic acid [10, 11]. NT2 cell were plated in 100 mm dishes and grown in 50:50 mixture of Dulbecco's modified Eagle's medium-high glucose (DMEM-HG) and F12 (Gibco, Gaithersburg, MD) to which 5% fetal bovine serum (FBS), 2 mM L-Glutamine, 100 U penicillin, and 100 mug streptomycin were added. At approximately 75-80% confluence, cells were treated with IL-1beta or TNF-alpha as follows.

Dose response curve. IL-1beta or TNF-alpha were added in triplicate at doses of 0.2. 2.0, 20.0, 200, and 2,000 U/ml to 100 mm plates of NT2 cells. Cells were incubated for 8 hours, after which the media was collected and total RNA extracted.

Time course. Triplicate cultures of NT2 cells were treated with 200 U/ml IL-1beta or TNF-alpha, then incubated for 0, 0.5, 1, 2, 4, 8, 12, 24, and 48 hours. Media were collected after each time point, and cells were harvested for total RNA

extraction. Spent media and harvested cell lysates were stored at - 70° C until the ELISA or RNA isolation was performed.

BrdU incorporation. To detect possible differences in cell proliferation associated with either IL-1beta or TNF-alpha, BrdU incorporation (2 hours) was evaluated in NT2 cells at 50-60% confluence following overnight incubation with either agent, in the presence and absence of 5% FBS. A colorimetric cell proliferation BrdU ELISA (Roche, Molecular Biochemicals, Mannheim, Germany) was used according to manufactures instructions. BrdU incorporation was quantified by measuring the absorbance at a wavelength of 490 nm.

Quantitative RT-PCR (QRT-PCR)

Total RNA isolation. Total RNA was isolated from the cells utilizing the RNeasy elution kit (Quiagen, Santa Clarita, CA) [9]. Total RNA was frozen at - 70° C.

cRNA template. cRNA was transcribed from a template plasmid containing sequences homologous to the GM-CSF primers [13, 14]. This plasmid contains a T7 promoter region and a polyA tail. The concentration and purity of the cRNA was determined by UV spectroscopy, and diluted to a stock solution containing 10^{15} molecules/mul. Copy numbers from 10^{14} to 10^{7} were used per reaction as internal competing standards to determine the quantity of GM-CSF mRNA in each 2 mug of total RNA.

Reverse transcription. Two mug of total RNA from each culture condition was reverse transcribed along with the competing template cRNA at copy numbers ranging from 10^{14} to 10^{7}. The reactions were set up as follows: 2 mug total RNA, template cRNA, as explained above, 20 mM Tris-HCl (pH 8.4), 50 mM KCl, 6 mM $MgCl_2$, 2 mM dNTP, 0.015 mug/mul oligo dT, 0.25 Units/mul RNase Inhibitor (Sigma, St. Louis, MO), 6 U/mul Superscript II reverse transcriptase (Gibco). This mixture was incubated at 25° C for 10 min followed by 60 min at 37° C and ending with 5 min at 94° C. Incubations were performed with a Perkin Elmer Cetus Thermal Cycler (Perkin Elmer).

Polymerase chain reactions (PCR). Ten percent of the RT reaction was added to 20 mM Tris-HCl (pH 8.4), 50 mM KCl, 1.5 mM $MgCl_2$, 0.2 mM dNTP, 0.4 muM of each primer, 25 mU/mul Taq polymerase (Gibco). This mixture was incubated for 35 cycles (1 min 94° C; 1 min 59° C; 1.5 min 72° C).

Scion image software (Scion Corp, Fredrick, MD) was utilized to determine band intensities. Ratios of band intensities were calculated and normalized for molecular weight using Microsoft Excel (Microsoft, USA). The normalized ratios were plotted on a log-log scale versus copy number and a best-fit curve and the equation for the line [log(y) = A + B*log(x)] were determined using Sigma Plot (SPSS Inc, Chicago, IL). The slope and the y intercept were used to solve for x. Where the band intensity ratios equal one (or Y = 1) indicates the copy number present in the 2 mug of total RNA (or X = copy number).

GM-CSF ELISA

GM-CSF concentrations in spent media were determined by specific ELISA (R&D Systems, Minneapolis, MN). Duplicate samples of spent media were collected from each plate during the time course for IL-1beta and TNF-alpha. Fresh cell culture media containing 10% FBS, and spent control media spiked with GM-CSF were tested to determine if any components of the media or growth factors would effect the recovery of GM-CSF.

RESULTS

IL-1beta increased NT2 cell GM-CSF mRNA expression by 2 logs at lower concentrations (0.2 and 2 U/ml), with expression increasing 3 logs from baseline at higher concentrations (20 to 2,000 U/ml, Figure 1A). The pattern of GM-CSF expression resulting from TNF-alpha stimulation was different, with no increase in expression noted at 0.2 U/ml, a single log increase noted at 2 and 20 U/ml, increasing by 3 logs from baseline at 200 U/ml, with a subsequent small decrease in expression at the highest dose (Figure 1B).

Using 200 U/ml, NT2 cells were stimulated with IL-1beta for up to 48 hours. Figure 2 shows a representative set of gels done to determine the number of mRNA copies per mug total RNA expressed by NT2 cells following IL-1beta stimulation. Baseline GM-CSF expression was 2.2×10^8 molecules/mug total RNA. Maximal GM-CSF mRNA production (2.0×10^{12} molecules/mug total RNA) was noted at 4 hours, with a gradual tapering of expression thereafter (Figure 3A). TNF-alpha (200 U/ml) increased GM-CSF mRNA expression rapidly, with maximal expression (4.9×10^{11} molecules/mug total RNA) noted at 1 and 2 hours. Unlike with IL-1beta stimulation, TNF-alpha stimulation did not persist, but rather decreased at 12 hours (Figure 3B).

GM-CSF was present in the spent media at all time points tested, however, a marked increase was noted after incubation with IL-1beta for 48 hours (Figure 4). GM-CSF concentrations in fresh media containing 10% FBS were below the detectable limit of the ELISA. When recombinant GM-CSF was "spiked" into such media, full recovery was measured. GM-CSF concentration in spent media collected from NT2 cells treated with 200 U/ml of TNF-alpha for up to 48 hours did not change significantly (Figure 4).

Stimulation of NT2 cells with IL-1beta or TNF-alpha did not affect cell turnover when compared to unstimulated cells, as determined by BrdU incorporation ($p = 0.394$, and 0.9, respectively). The presence or absence of FBS in the cultures did not affect these results.

DISCUSSION

GM-CSF is a 23 kD glycoprotein first identified for its role in hematopoiesis, as it stimulates clonal maturation of a broad range of hematopoietic precursor cells [15-17]. GM-CSF is produced by T cells, monocytes, fibroblasts, and endothelial cells, and is also produced within the CNS by stimulated astrocytes [18-20]. We previously demonstrated that GM-CSF and its receptor are present in the CNS during fetal development, but its role in development is not clear [9]. GM-CSF has several demonstrated effects in the CNS including growth and activation of astrocytes, oligodendrocytes, and microglia [8, 21, 22]. In addition, GM-CSF has a trophic effect on certain types of neurons, promoting the survival and enhancing neurite outgrowth of such cells *in vitro* and *in vivo* [1-3, 23]. These findings suggest an important role for GM-CSF in the development and homeostasis of the CNS.

IL-1beta is an inflammatory cytokine produced by mononuclear cells and macrophages in response to infection. It is a classic "alarm peptide" synthesized by macrophages and other cells in response to infection, and stimulates a reaction cascade known as the "acute phase response". This response includes eicosanoid production, T cell activation, and results in increased vascular permeability. In physiologic systems IL-1 is usually balanced by IL-1 receptor antagonist (IL-1Ra). In the CNS, astrocytes and glial cells are sources of IL-1 [4, 24, 25]. IL-1beta acts *via* the IL-1 receptor that is shared by IL-1alpha. IL-1R has been identified in many regions of the brain in specific subpopulations of neurons and glial cells, suggesting a role for IL-1 in the CNS [26-32].

TNF-alpha is an inflammatory cytokine produced by endotoxin-activated macrophages, activated T cells, NK cells, and mast cells. Endotoxin-stimulated microglia and astrocytes in the CNS produce TNT-alpha, with microglia being the major producer [33]. TNF-alpha in turn can induce GM-CSF production by astrocytes, although less than IL-1beta [6]. TNF-alpha stimulates the proliferation of simian astrocytes [8].

NT2 cells are a committed human neuronal precursor cell line which retain some stem cell characteristics and which are capable only of terminal differentiation into neurons [11]. In the present study, we showed that these cells produce a small amount of GM-CSF under baseline culture conditions, but when stimulated by IL-1beta, GM-CSF expression is greatly increased. This upregulation of GM-CSF suggests a local function for GM-CSF in the injured or developing CNS. GM-CSF causes the proliferation of microglia [4, 34] and astrocytes [8], and may be an important component of the response to injury.

IL-1beta induction of GM-CSF mRNA and protein has been demonstrated in several cell lines, including endothelial cells. In these and other cells the mechanism of GM-CSF mRNA upregulation is due, in part, to mRNA stabilization *via* the AU rich motif in the 3' untranslated region of the GM-CSF mRNA [35]. Two nuclear factors NF-kappa B and NF-GM2 may also play a role in the upregulation induced by IL-1beta stimulation [36, 37].

To determine whether IL-1beta or TNF-alpha might increase the expansion of "neuronal precursors", thereby potentially giving rise to more differentiated neurons by increasing the pool of potential neurons, we evaluated BrdU incorporation in the presence and absence of these cytokines. No difference was observed between conditions.

In contrast to IL-1beta effects, TNF-alpha up-regulates GM-CSF mRNA, but does not induce protein secretion. This suggests an inhibitory mechanism that is not present in IL-1beta stimulated NT2 cells. This could possibly include ribosome binding proteins that activate translation of the message that are induced with IL-1beta stimulation and not with TNF-alpha. Alternatively, inhibition of secretory vesicle formation or protein degradation prior to excretion could be the cause.

CONCLUSION

We conclude that IL-1beta (but not TNF-alpha) is a potent inducer of GM-CSF production by NT2 cells and that the response is dose and time dependent. Further, we speculate that this ability of neuronal precursors to produce GM-CSF may indicate a role for GM-CSF in CNS development.

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References

1. Konishi Y, Chui D H, Hirose H, Kunishita T, Tabira T. 1993. Trophic effect of erythropoietin and other hematopoietic factors on central cholinergic neurons *in vitro* and *in vivo. Brain Res.* 609: 29.

2. Tabira T, Konishi Y, Gallyas F, Jr. 1995. Neurotrophic effect of hematopoietic cytokines on cholinergic and other neurons *in vitro. Int. J. Dev. Neurosci.* 13: 241.

3. Kamegai M, Konishi Y, Tabira T. 1990. Trophic effect of granulocyte-macrophage colony-stimulating factor on central cholinergic neurons *in vitro. Brain Res.* 532: 323.

4. Giulian D, Li J, Li X, George J, Rutecki P A. 1994. The impact of microglia-derived cytokines upon gliosis in the CNS. *Dev. Neurosci.* 16: 128.

5. Sawada M, Itoh Y, Suzumura A, Marunouchi T. 1993. Expression of cytokine receptors in cultured neuronal and glial cells. *Neurosci. Lett.* 160: 131.

6. Lee S C, Liu W, Brosnan C F, Dickson D W. 1994. GM-CSF promotes proliferation of human fetal and adult microglia in primary cultures. *Glia.* 12: 309.

7. McLay R N, Kimura M, Banks W A, Kastin A J. 1997. Granulocyte-macrophage colony-stimulating factor crosses the blood-brain and blood-spinal cord barriers. *Brain* 120: 2083.

8. Guillemin G, Boussin F D, Le Grand R, Croitoru J, Coffigny H, Dormont D. 1996. Granulocyte macrophage colony stimulating factor stimulates *in vitro* proliferation of astrocytes derived from simian mature brains. *Glia.* 16: 71.

9. Dame J B, Christensen R D, Juul S E. 1999. The distribution of granulocyte/macrophage colony-stimulating factor and its receptor in the developing human fetus. *Pediatr. Res.* 46: 358.

10. Lee V M, Andrews P W. 1986. Differentiation of NTERA-2 clonal human embryonal carcinoma cells into neurons involves the induction of all three neurofilament proteins. *J. Neurosci.* 6: 514.

11. Pleasure S J, Lee V M. 1993. NTERA 2 cells: a human cell line which displays characteristics expected of a human committed neuronal progenitor cell. *J. Neurosci. Res.* 35: 585.

12. Greene L A, Tischler A S. 1976. Establishment of a noradrenergic clonal line of rat adrenal pheochromocytoma cells which respond to nerve growth factor. *Proc. Natl. Acad. Sci. USA* 73: 2424.

13. Chegini N, Tang X M, Dou Q. 1999. The expression, activity and regulation of granulocyte macrophage-colony stimulating factor in human endometrial epithelial and stromal cells. *Mol. Hum. Reprod.* 5: 459.

14. Zhao Y, Chegini N. 1999. The expression of granulocyte- macrophagecolony stimulating factor (GM-CSF) and receptors in human endometrium. *Am. J. Reprod. Immunol.* 42: 303.

15. Ruef C, Coleman D L. 1990. Granulocyte-macrophage colony-stimulating factor: pleiotropic cytokine with potential clinical usefulness. (Review) *Rev. Infect. Dis.* 12: 41.

16. Metcalf D. 1991. Lineage commitment of hemopoietic progenitor cells in developing blast cell colonies: influence of colony-stimulating factors. *Proc. Natl. Acad. Sci. USA* 88: 11310.

17. Metcalf D, Nicola N A. 1992. The clonal proliferation of normal mouse hematopoietic cells: enhancement and suppression by colony-stimulating

factor combinations. *Blood* 79: 2861.

18. Malipiero U V, Frei K, Fontana A. 1990. Production of hemopoietic colony-stimulating factors by astrocytes. *J. Immunol.* 144: 3816.

19. Raivich G, Gehrmann J, Kreutzberg G W. 1991. Increase of macrophage colony-stimulating factor and granulocyte-macrophage colony-stimulating factor receptors in the regenerating rat facial nucleus. *J. Neurosci. Res.* 30: 682.

20. Tweardy D J, Glazer E W, Mott P L, Anderson K. 1991. Modulation by tumor necrosis factor-alpha of human astroglial cell production of granulocyte-macrophage, colony-stimulating factor (GM-CSF) and granulocyte colony-stimulating factor (G-CSF). *J. Neuroimmunol.* 32: 269.

21. Baldwin G C, Benveniste E N, Chung G Y, Gasson J C, Golde D W. 1993. Identification and characterization of a high-affinity granulocyte-macrophage colony-stimulating factor receptor on primary rat oligodendrocytes. *Blood* 82: 3279.

22. Fischer H G, Bielinsky A K, Nitzgen B, Daubener W, Hadding U. 1993. Functional dichotomy of mouse microglia developed *in vitro:* differential effects of macrophage and granulocyte/macrophage colony-stimulating factor on cytokine secretion and antitoxoplasmic activity. *J. Neuroimmunol.* 45: 193.

23. Kannan Y, Bienenstock J, Ohta M, Stanisz A M, Stead R H. 1996. Nerve growth factor and cytokines mediate lymphoid tissue-induced neurite outgrowth from mouse superior cervical ganglia *in vitro. J. Immunol.* 157: 313.

24. Yao J, Keri J E, Taffs R E, Colton C A. 1992. Characterization of interleukin-1 production by microglia in culture. *Brain Res.* 591: 88.

25. Romero L I, Tatro J B, Field J A, Reichlin S. 1996. Roles of IL-1 and TNF-alpha in endotoxin-induced activation of nitric oxide synthase in cultured rat brain cells. *Am. J. Physiol.* 270: R326.

26. Ban E, Milon G, Prudhomme N, Fillion G, Haour F. 1991. Receptors for interleukin-1 (alpha and beta) in mouse brain: mapping and neuronal localization in hippocampus. *Neuroscience* 43: 21.

27. Cunningham E T Jr, Wada E, Carter D B, Tracey D E, Battey J F, De Souza E B. 1992. *In situ* histochemical localization of type 1 interleukin-1 receptor messenger RNA in the central nervous system, pituitary, and adrenal gland of the mouse. *J. Neurosci.* 12: 1101.

28. Haour F, Marquette C, Tsiang H, Ban E, Crumeyrolle-Arias M, Rostene W, Fillion G. 1994. Interleukin-1 receptors in brain and pituitary. Characterization and modulation during infection and stress. (Review) *Ann. N.Y. Acad. Sci.* 741: 324.

29. Parnet P, Amindari S, Wu C, Brunke-Reese D, Goujon E, Weyhenmeyer J A, Dantzer R, Kelley K W. 1994. Expression of type I and type II interleukin-1 receptors in mouse brain. *Brain Res. Mol. Brain Res.* 27: 63.

30. Takao T, Tracey D E, Mitchell W M, De Souza E B. 1990. Interleukin-1 receptors in mouse brain: characterization and neuronal localization. *Endocrinology* 127: 3070.

31. Yabuuchi K, Minami M, Katsumata S, Satoh M. 1994. Localization of type I interleukin-1 receptor mRNA in the rat brain. *Brain Res. Mol. Brain Res.* 27: 27.

32. Cunningham E T Jr, Wada E, Carter D B, Tracey D E, Battey J F, De Souza E B. 1991. Localization of interleukin-1 receptor messenger RNA in murine hippocampus. *Endocrinology* 128: 2666.

33. Sawada M, Kondo N, Suzumura A, Marunouchi T. 1989. Production of tumor necrosis factor-alpha by microglia and astrocytes in culture. *Brain Res.* 491: 394.

34. Giulian D, Ingeman J E. 1988. Colony-stimulating factors as promoters of ameboid microglia. *J. Neurosci.* 8: 4707.

35. Bagby G C, Shaw G, Heinrich M C, Hefeneider S, Brown M A, De Loughery T G, Segal G M, Band L. 1990. Interleukin-1 stimulation stabilizes GM-CSF mRNA in human vascular endothelial cells: preliminary studies on the role of the 3'AU rich motif. *Prog. Clin. Biol. Res.* 352: 233.

36. Tsuboi A, Sugimoto K, Yodoi J, Miyatake S, Arai K, Arai N. 1991. A nuclear factor NF-GM2 that interacts with a regulatory region of the GM-CSF gene essential for

its induction in responses to T cell activation: purification from human T cell leukemia line Jurkat cells and similarity to NF-kappa B. *Int. Immunol.* 3: 807.

37. Adcock I M, Newton R, Barnes P J. 1997. NF-kappa B involvement in IL-1 beta-induction of GM-CSF and COX-2: inhibition by glucocorticoids does not require I-kappa B. *Biochern. Soc. Trans.* 25: 154S.

Figures

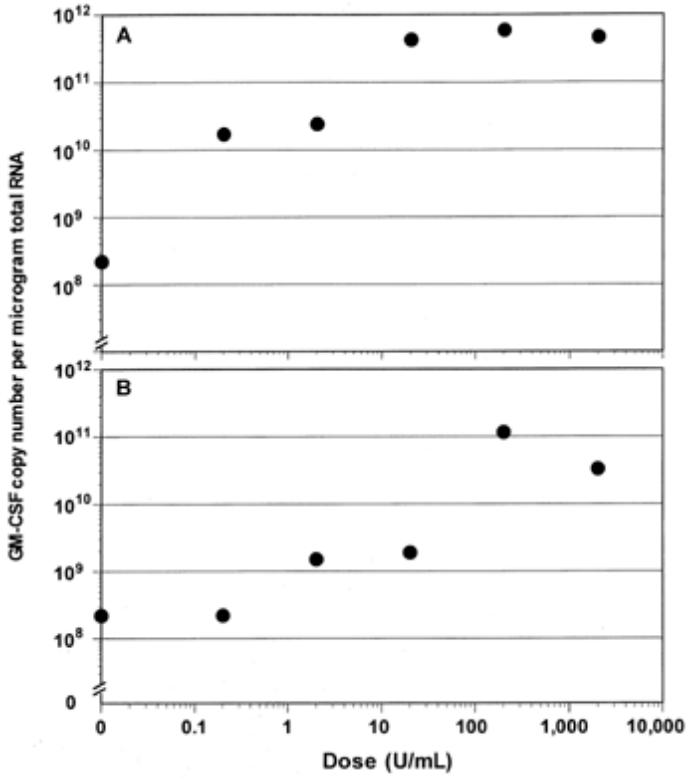


Figure 1 Dose-response curves for IL-1beta and TNF-alpha stimulation of NT2 cells. Panel A shows the dose response results for IL-1beta stimulation of NT2 cells. The dose used ranged from 0 to 2,000 U/ml. Data are shown on a log-log scale, with GM-CSF mRNA copy number per microgram total RNA on the Y axis, and study drug concentration shown on the X axis. **Panel B** shows the comparable results for TNF-alpha stimulation.

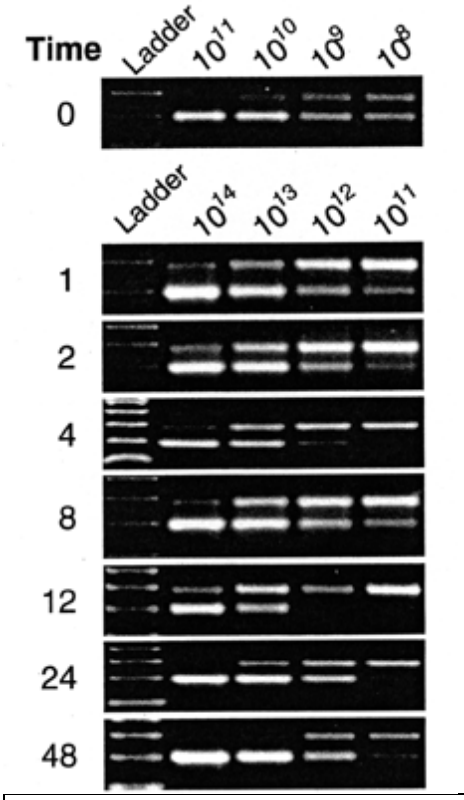


Figure 2 GM-CSF quantitative RT-PCR. Representative quantitative RT-PCR gels are shown for GM-CSF expression at timed intervals following IL-1beta stimulation. Time points range from 0 to 48 hours. Each gel shows 4 lanes, with template cRNA copy numbers ranging from 10^{14} to 10^{8}, as denoted in the legend. The lane in which the band intensity of the competitive template and the sample RNA are the same, indicates the copy number present in the 2 mug of total RNA.

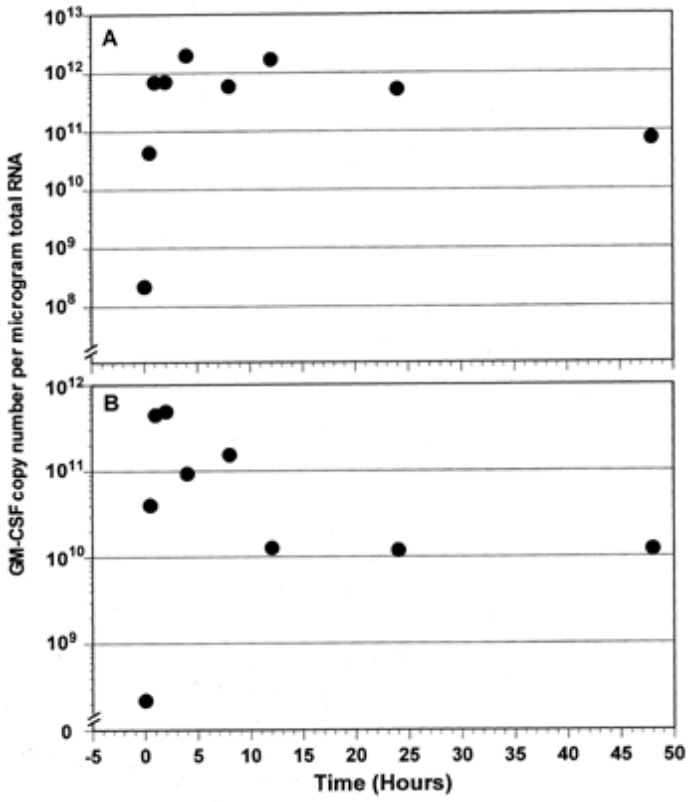


Figure 3 Time curves for IL-1beta and TNF-alpha stimulation of NT2 cells. Panel A shows the upregulation of GM-CSF mRNA expression resulting from IL-1beta stimulation of NT2 cells (200 U/ml). GM-CSF mRNA copy number per microgram total RNA on the Y axis, with time in hours on the X axis. **Panel B** shows timed GM-CSF mRNA expression following TNF-alpha stimulation.

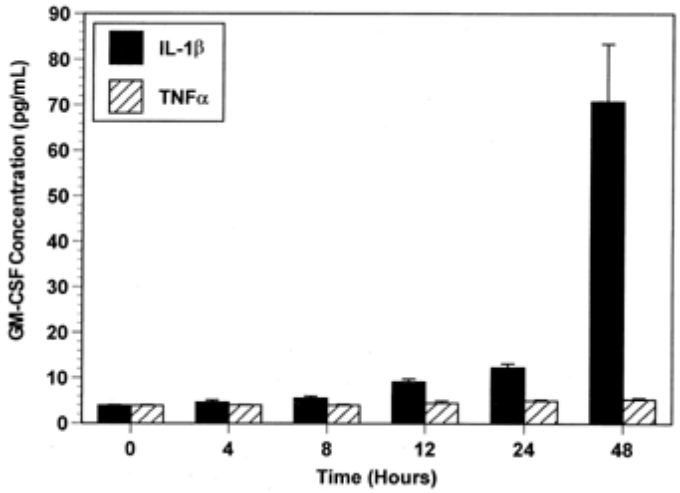


Figure 4 The effect of IL-1beta and TNF-alpha stimulation on GM-CSF secretion by NT2 cells. GM-CSF secreted into the media by NT2 cells after IL-1beta or TNF-alpha stimulation was measured by specific ELISA. Net GM-CSF concentration is shown on the Y axis, with the time of measurement shown on the X-axis.

Authors

J. Benjamin Dame, Nasser Chegini, Robert D. Christensen, Sandra E. Juul

872 East Nicholls Road, Fruit Heights, UT 84037.

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CSF-1, tumour progression, metastasis, de-differentiation.

The effect of interleukin-1beta (IL-1beta) and tumor necrosis factor-alpha (TNF-alpha) on granulocyte macrophage-colony stimulating factor (GM-CSF) production by neuronal precursor cells

J. Benjamin Dame, Nasser Chegini, Robert D. Christensen, Sandra E. Juul
IL-1beta, TNF-alpha, GM-CSF, neuron, mRNA, protein.

Les éditions JLE

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