

## Trophic factors and central nervous system metastasis

Garth L. Nicolson and David G. Menter

*Department of Tumor Biology (108), The University of Texas M.D. Anderson Cancer Center, 1515 Holcombe Blvd., Houston, Texas 77030, USA*

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### Abstract

To metastasize to the central nervous system (CNS) malignant cells must attach to brain microvessel endothelial cells, respond to brain endothelial cell-derived motility factors, respond to CNS-derived invasion factors and invade the blood-brain barrier (BBB), and finally, respond to CNS survival and growth factors. Trophic factors such as the neurotrophins play an important role in tumor cell invasion into the CNS and in the survival of small numbers of malignant cells under stress conditions. Trophic factors promote BBB invasion by enhancing the production of basement membrane-degrading enzymes in neurotrophin-responsive cells. The expression of certain neurotrophin receptors on brain-metastatic neuroendocrine cells occurs in relation to their invasive and survival properties. For example, CNS-metastatic melanoma cells respond to particular neurotrophins (nerve growth factor, neurotrophin-2) that can be secreted by normal cells within the CNS. In addition, a paracrine form of transferrin is important in CNS metastasis, and brain-metastatic cells respond to low levels of transferrin and express high levels of transferrin receptors. CNS-metastatic tumor cells can also produce autocrine factors and inhibitors that influence their growth, invasion and survival in the brain. Synthesis of paracrine factors and cytokines may influence the production of trophic factors by normal brain cells adjacent to tumor cells. Moreover, we found increased amounts of neurotrophins in brain tissue at the invasion front of human melanoma tumors in CNS biopsies. Thus the ability to form metastatic colonies in the CNS is dependent on tumor cell responses to trophic factors as well as autocrine and paracrine growth factors and probably other underdescribed factors.

### 1. Introduction-prevalence of CNS metastases

The central nervous system (CNS) is a unique organ for metastatic colonization [1–3]. It is highly sensitive to the slightest change in the local microenvironment, and it is surrounded by a formidable blood-brain barrier (BBB, Fig. 1) that must be penetrated by brain-metastatic tumor cells. Moreover, the CNS lacks lymphatic drainage and cannot remove fluid that accompanies tumor growth in the brain. This results in cerebral edema which represents a major complication resulting from CNS tu-

ors [4]. Therapy of CNS metastases is usually only palliative and is often accompanied by clinical complications. Thus CNS tumor formation and metastasis to the CNS are extremely difficult clinical problems.

Metastatic lesions in the CNS and spinal cord commonly occur in certain types of cancers, such as disseminated malignant melanoma, breast cancer, lung cancer and others. When these cancers metastasize to the CNS, they frequently result in severe and debilitating neurological complications. Even small metastasis in the CNS can cause severe symp-

# Trophic Factors And The Nervous System

**Patrick R. Hof, Charles V. Mobbs**



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*Trophic Factors and the Nervous System* Lloyd A. Horrocks, Ohio State University. Neuroscience Program, 1990

*Neurotrophic Factors* Sandra E. Loughlin, James H. Fallon, 2012-12-02 This volume clearly synthesizes current information on defined neurotrophic factors emphasizing their localization and molecular cellular function in the central nervous system Brain development and aging neurodegenerative disorders plasticity and memory all are closely examined within the context of this rapidly expanding field Researchers in neurobiology cell biology and molecular biology will find Neurotrophic Factors an invaluable reference for their research libraries Offers the most up to date synthesis of concepts on neurotrophic factors in the nervous system Integrates molecular cellular and neuroanatomical concepts of neurotrophic factor function Includes special chapters on primary secondary and tertiary messenger systems Examines brain development differentiation neurodegenerative disorders and adult plasticity *Noback's Human Nervous System, Seventh Edition*

Norman L. Strominger, Robert J. Demarest, Lois B. Laemle, 2012-06-07 With this seventh edition Noback's Human Nervous System Structure and Function continues to combine clear prose with exceptional original illustrations that provide a concise lucid depiction of the human nervous system The book incorporates recent advances in neurobiology and molecular biology Several chapters have been substantially revised These include Development and Growth Blood Circulation and Imaging Cranial Nerves and Chemical Senses Auditory and Vestibular Systems Visual System and Cerebral Cortex Topics such as neural regeneration plasticity and brain imaging are discussed Each edition of The Human Nervous System has featured a set of outstanding illustrations drawn by premier medical artist Robert J Demarest Many of the figures from past editions have been modified and or enhanced by the addition of color which provides a more detailed visualization of the nervous system Highly praised in its earlier versions this new edition offers medical dental allied health science and psychology students a readily understandable and organized view of the bewilderingly complex awe inspiring human nervous system Its explanatory power and visual insight make this book an indispensable source of quick understanding that readers will consult gratefully again and again [The Human Nervous System](#) Charles R. Noback, David A. Ruggiero, Norman L.

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reproductive functions changes in body weight and sleeplessness As the average age of our society increases diseases of aging become more common and conditions associated with aging need more attention by doctors and researchers This book offers an overview of topics related to neurobiological impairments which are related to the aging brain and nervous system Coverage ranges from animal models to human imaging fundamentals of age related neural changes and pathological neurodegeneration and offers an overview of structural and functional changes at the molecular systems and cognitive levels Key pathologies such as memory disorders Alzheimer s dementia Down syndrome Parkinson s and stroke are discussed as are cutting edge interventions such as cell replacement therapy and deep brain stimulation There is no other current single volume reference with such a comprehensive coverage and depth Authors selected are the internationally renowned experts for the particular topics on which they write and the volume is richly illustrated with over 100 color figures A collection of articles reviewing our fundamental knowledge of neural aging the book provides an essential affordable reference for scientists in all areas of Neuroscience Neuropsychology and Gerontology The most comprehensive source of up to date data on the neurobiology of aging review articles cover normal sensory and cognitive aging neuroendocrine structural and molecular factors and fully address both pathology and intervention Chapters represent an authoritative selection of relevant material from the most comprehensive source of information about neuroscience ever assembled Encyclopedia of Neuroscience synthesizing information otherwise dispersed across a number of journal articles and book chapters and saving researchers the time consuming process of finding and integrating this information themselves Offering outstanding scholarship each chapter is written by an expert in the topic area and over 20% of chapters feature international contributors representing 11 countries Provides more fully vetted expert knowledge than any existing work with broad appeal for the US UK and Europe accurately crediting the contributions to research in those regions Fully explores various pathologies associated with the aging brain Alzheimer s dementia Parkinson s memory disorders stroke Down s syndrome etc Coverage of disorders and key interventions makes the volume relevant to clinicians as well as researchers Heavily illustrated with over 100 color figures

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