



Molecular neuropathology: an essential and evolving toolbox for the diagnosis and clinical management of central nervous system tumors

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Abstract

Molecular profiling has transformed the diagnostic workflow of CNS tumors during the last years. The latest WHO classification of CNS tumors (5th edition), published in 2021, pushed forward the integration between histopathological features and molecular hallmarks to achieve reproducible and clinically relevant diagnoses. To address these demands, pathologists have to appropriately deal with multiple molecular assays mainly including DNA methylation profiling and DNA/RNA next generation sequencing. Tumor classification by DNA methylation profiling is now a critical tool for many diagnostic tasks in neuropathology including the assessment of complex cases, to evaluate novel tumor types and to perform tumor subgrouping in heterogeneous entities like medulloblastoma or ependymoma. DNA/RNA NGS allow the detection of multiple molecular alterations including single nucleotide variations, small insertions/deletions (InDel), and gene fusions. These molecular markers can provide key insights for diagnosis, for example, if a tumor-specific mutation is detected, but also for treatment since targeted therapies are progressively entering the clinical practice. In the present review, a brief, but comprehensive overview of these tools will be provided, discussing their technical specifications, diagnostic value, and potential limitations. Moreover, the importance of molecular profiling will be shown in a representative series of CNS neoplasms including both the most frequent tumor types and other selected entities for which molecular characterization plays a critical role.

Keywords Neuropathology · Molecular pathology · DNA methylation profiling · NGS · CNS tumors

Introduction

The evaluation of specific molecular hallmarks has become a mandatory step for diagnosing central nervous system (CNS) tumors since multiple years. Thanks to the publication of the 4th revised edition of the World Health Organization (WHO) classification of CNS tumors in 2016 [1], the concept of an

integrated histopathological and molecular diagnosis has become a cornerstone of oncological neuropathology.

The integrated diagnosis is a diagnosis based on multiple layers which, starting from the conventional histopathological features, is enriched by molecular information. Molecular profiling can help or even provide by itself the diagnostic classification of a tumor type and/or improve the prognostic stratification by complementing histology-based tumor grading and/or help tailor treatment by disclosing potential therapeutic targets. These layers are frequently intertwined and a solid background knowledge about the interpretation of each molecular marker in the relevant diagnostic context is required for their correct translation into diagnostic practice and clinical management.

The latest 2021 WHO classification of CNS tumors (5th edition) [2] has further expanded the significance of molecular profiling in this setting and to date, all the most frequent CNS tumor types envisage the evaluation of a subset of molecular markers in their diagnostic workflow. Additionally, many novel tumor types were

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Molecular Neuropathology

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Molecular Neuropathology:

Molecular Neuropathology Gareth W. Roberts, Julia M. Polak, 1995-06-08 This volume provides an introduction to the essential techniques required for studying the molecular biology of brain disease The approaches and strategies for investigations of gene structure and regulation are described with reference to the molecular genetics of prion and Alzheimer's disease The effects of aberrant gene regulation can also be examined at the protein level by immunocytochemistry and autoradiography Improved understanding of basic biology has resulted in new approaches to animal models using transgenic techniques and new therapeutic approaches The volume is structured to illustrate all these approaches and demonstrate the practice and promise of molecular neuropathology [Biomedical Index to PHS-supported Research: pt. A. Subject access A-H](#) ,1992

Neurology 19 Edenilson Brandl, 2025-05-03 Neurological science has entered an era of unprecedented innovation and discovery From cutting edge imaging technologies to groundbreaking genetic therapies the field is revolutionizing how we diagnose treat and understand disorders of the brain and nervous system This book serves as a comprehensive guide for both professionals and enthusiasts offering deep insights into the mechanisms and therapeutic strategies that shape modern neurology The journey of compiling this work was fueled by the ever growing intersection of technology genetics and medicine Each chapter explores a pivotal aspect of neurological health blending foundational science with emerging applications that promise to redefine treatment paradigms As you delve into these pages you will find both depth and clarity in understanding the complexity of the human brain In sharing this work my hope is to inspire curiosity foster learning and contribute to the global dialogue on improving neurological health Let this book be a beacon for those seeking knowledge and a call to action for continued innovation in this vital field **Biomedical Index to PHS-supported Research** , [Biomedical Index to PHS-supported Research: Project number listing, investigator listing](#) ,1989

Fluorescent Proteins Mayank Sharma, 2022-09-15 This volume brings together cutting edge laboratory protocols to characterize the novel fluorescent proteins FPs and approaches based on fluorescent proteins that aim to answer some of the key cell biological questions The book covers topics ranging from the database of fluorescent proteins to their characterization and adaptation to a wide range of biological systems Written for the highly successful Methods in Molecular Biology series chapters include introductions to their respective topics lists of the necessary materials and reagents step by step and readily reproducible laboratory protocols and tips on troubleshooting and avoiding known pitfalls Authoritative and practical **Fluorescent Proteins Methods and Protocols** serves as an ideal guide for students and academicians enthusiastic about the recent progress in the practical application of fluorescent protein technology [The Unsung Heroes of Paediatric Medicine](#) Ernest Cutz, David Wencer, 2020 Within the world of medicine the work the pathologist does is integral to positive patient outcomes but it is rare for the pathologist to actually have any interaction with their patients Thus their work can often go unrecognized and uncelebrated **The Unsung Heroes of Paediatric Medicine** paints a broad portrait of the myriad

facets that go into the making of a superb department of paediatric pathology Not only is it the science but it is also the people that helped to make a department such as this grow and flourish becoming one of the best if not the best in North America Within these pages Dr Cutz walks the reader through a century of pediatric pathology at Sick Kids Hospital in Toronto Ontario Building on both personal experience and archival material Dr Cutz s memoir touches on the history of pathology and the evolution of pediatric pathology then moves into a detailed overview of both the leadership and staff of the Department of Pathology at Sick Kids Hospital In addition readers can follow Dr Cutz s personal journey from his research fellowship to his beginnings as a staff pathologist ending with his research advances and breakthroughs all made whilst a pathologist at Sick kids *Unsung Heroes* also touches on controversies tragedies and challenging events from the hospital s history including digoxin the Olivieri affair the rise and fall of Charles Smith and the Mother Risk controversy among others

Society And Structures, Proceedings Of The International Seminar On Nuclear War And Planetary Emergencies - 27th Session Richard C Ragaini, 2003-04-29 This was the first of a number of seminars dealing with one of the most complex of the new challenges in the 21st century which call for the participation of a broad range of experts Eminent economists decision makers defence specialists political analysts and sociologists presented their views and participated in the debates In the wake of the dramatic event of 11 September 2001 the Afghanistan war and the resurgence of terrorist acts on all the continents a host of issues were reconsidered and the role of science and technology was reassessed The 27th Session was primarily oriented toward the definition of the new types of confrontation and the identification of various factors and issues that gave rise to them and global trends The proceedings have been selected for coverage in Index to Scientific Technical Proceedings ISTP CDROM version ISI Proceedings Index to Social Sciences Humanities Proceedings ISSHP ISI Proceedings Index to Social Sciences Humanities Proceedings ISSHP CDROM version ISI Proceedings **Recent Progress in**

Alzheimer's and Parkinson's Diseases Israel Hanin, Ramon Cacabelos, Abraham Fisher, 2005-06-03 This book brings together the proceedings of Alzheimer s and Parkinson s Diseases New Perspectives the Sixth International Conference on Alzheimer s Disease and Parkinson s Disease held recently in Seville Spain and discusses the latest developments in the basic science and therapy of Alzheimer s and Parkinson s diseases by leading specialists *Neuronal Degeneration and Regeneration: From Basic Mechanisms to Prospects for Therapy* F.W. Van Leeuwen, A. Salehi, R.J. Giger, A.J.G.D. Holtmaat, J. Verhaagen, 1998-11-09 This book is the result of the 20th International Summer School in Brain Research organized in August 1997 in Amsterdam by the Netherlands Institute for Brain Research at the Royal Netherlands Academy of Sciences It is the first book that provides a complete overview of the field of neurodegeneration and regeneration including spinal cord injury neurodegenerative diseases and therapy Divided into five sections the first two sections give an overview of fundamental research on nerve cell death neuronal survival neurite outgrowth and guidance Extensive attention is given to the role of neurotrophins their receptor tyrosine kinases and cell adhesion molecules in development and regeneration of the

nervous system The third section of the book is devoted to research involving human neurodegenerative diseases and emerging treatment strategies Section four focusses on recent advances in the understanding of pathophysiological mechanisms underlying neurodegenerative diseases including Alzheimer s Parkinson s and Huntington s diseases along with prion diseases Novel insights into the neuropathological hallmarks of these diseases as well as into transgenic animal models the involvement of environmental factors and genomic and mRNA changes that can cause neurodegeneration The final section of this volume reveals recent developments in the use of cell and gene therapy to treat neurodegenerative disease and lesion related deficits Implantation of genetically modified cells direct gene transfer with viral vectors and the first clinical trials with encapsulated genetically modified cells in patients suffering from amyotrophic lateral sclerosis are examples of new therapeutic strategies treating neurodegenerative diseases The book is of particular interest to departments of neuroscience neurological clinics and departments the pharmacological industry and medical libraries

Perspectives in Brain Research ,2011-09-22 Perspectives in Brain Research Cancer of the Nervous System Peter McL. Black,Jay S. Loeffler,2005 Thoroughly revised to reflect the latest advances in neurosurgery radiation oncology chemotherapy biological therapy and the basic sciences the Second Edition of this highly acclaimed volume is the most comprehensive current reference on tumors of the central and peripheral nervous system More than 100 of the foremost authorities present multimodality treatment strategies for specific tumor types and examine the mechanisms of tumorigenesis Coverage includes state of the art information on image guided surgery local delivery systems intraoperative imaging proton beam therapy conformal systems radiosurgery new drugs and biological agents and cell cycle deregulation and chromosomal abnormalities in tumorigenesis This edition contains over 400 illustrations

Charney and Nestler's Neurobiology of Mental Illness Dennis Charney,Eric Nestler,Joseph D. Buxbaum,Elisabeth B. Binder,Joshua A. Gordon,Marina R. Picciotto,2025-01-03 The genetic investigation into mental illnesses has progressed rapidly since the mapping of the human genome Driven by advances in genomic profiling technology massive genomic datasets are powering the discovery of genetic variation associated to complex traits including mental illness From severe neurodevelopmental disorders to schizophrenia and depression genetic variation plays some role in risk Critically most mental illnesses are complex multifactorial and the consequence of a combination of genetic and environmental influences This chapter will introduce the genome its variation and the methods used to identify what variants and genes matter for mental illnesses

Neuro-oncology, An Issue of Neurologic Clinics Patrick Y Wen,Eudocia Quant Lee,2018-08-07 This issue of Neurologic Clinics edited by Drs Patrick Y Wen and Eudocia Quant Lee will focus on Neuro oncology Topics include but are not limited to Epidemiology of brain tumors Molecular pathogenesis of brain tumors Changes in WHO classification of brain tumors Neurologic and medical management of brain tumors Grade 2 and 3 Gliomas Glioblastoma Benign brain tumors Primary CNS lymphoma and neurologic complications of systemic lymphoma Pediatric brain tumors Brain metastases Metastatic complications of cancer

Neurologic complications of radiation therapy Neurologic complications of systemic anticancer therapies Neurocognitive complaints in cancer patients and Paraneoplastic syndromes **Motor Neuron Disease in Adults** Mark B. Bromberg, 2015 Motor Neuron Disease reviews new information from 1998 as it applies to all aspects of motor neuron disease Articles included use evidence based methods to ensure that the new information is solid and advances the topic The book can be used by anyone who provides any type of care to ALS patients **Neurobiology of Ischemic Brain Damage** K. Kogure, K.-A. Hossmann, B. Siesjö, 1993-05-10 In the eight years since the publication of Volume 63 of Progress in Brain Research on this subject developments in the research field have been very fast For example receptor physiology and pharmacology is now an intensively studied field and the excitotoxic hypothesis of cell death is commonly accepted Furthermore it is recognized that ischemia and other insults give rise to a sustained depression of overall protein synthesis yet lead to the expression of dormant genes and to synthesis of new proteins In view of this development this volume focusses on the cellular and molecular aspects of ischemic brain damage The book will be of great value to all those interested in the pathophysiology of ischemic and traumatic brain damage **The Neuroscience of Dementia** Colin R Martin, Victor R Preedy, 2020-12-23 The Neuroscience of Dementia brings together different fields of dementia research into a single book covering a wide range of subjects including Alzheimer s disease Lewy body dementia mixed dementia vascular dementia physical activity risk factors mortality biomarkers SPECT CT MRI questionnaires nutrition sleep delirium hearing loss agitation aggression delusions anxiety depression hallucinations psychosis senile plaques tau and amyloid beta neuroinflammation molecular biology and more This foundational comprehensive book compiles the latest understanding on all forms of dementia and their common features in a single source It is an invaluable resource for neuroscientists neurologists and anyone in the field Offers comprehensive coverage of a broad range of topics related to dementia Contains in each chapter an abstract key facts mini dictionary of terms and summary points to aid in understanding Provides unique sections on specific subareas intellectual components and knowledge based niches that will help readers navigate key areas for research and further clinical recommendations Features preclinical and clinical studies to help researchers map out key areas for research and further clinical recommendations Serves as a one stop source for everything you need to know about dementia Genetics, Neurology, Behavior, and Diet in Dementia Colin R Martin, Victor R Preedy, 2020-08-11 Genetics Neurology Behavior and Diet in Dementia The Neuroscience of Dementia Volume 2 consolidates different fields of dementia research into a single book covering a range of subjects including Alzheimer s disease Lewy body dementia mixed dementia vascular dementia physical activity risk factors mortality biomarkers SPECT CT MRI questionnaires nutrition sleep delirium hearing loss agitation aggression delusions anxiety depression hallucinations psychosis senile plaques tau and amyloid beta neuroinflammation and molecular biology This foundational comprehensive book assembles the latest understanding on all dementias and their common features in a single source It is an invaluable resource for neuroscientists neurologists and

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Cumulated Index Medicus ,1999

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