

# The Molecular Genetics of Gastroenteropancreatic Neuroendocrine Tumors

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The pathobiology of neuroendocrine tumors (NETs) is hampered by the lack of scientific tools that define their mechanisms of secretion, proliferation, and metastasis and, currently, there are no accurate means to assess tumor behavior and disease prognosis. Molecular biologic techniques and genetic analysis may facilitate the delineation of the molecular pathology of NETs and provide novel insights into their cellular mechanisms. The current status and recent advances in assessment of the molecular basis of tumorigenesis of gastroenteropancreatic neuroendocrine tumors (GEP-NETs) were reviewed (1981–2004). The objectives of this retrospective study were to provide a cohesive overview of the current state of knowledge and to develop a molecular understanding of these rare tumor entities to facilitate the establishment of therapeutic targets and rational management strategies. Multiple differences in chromosomal aberration patterns were noted between gastrointestinal (GI) neuroendocrine and pancreatic endocrine tumors (PETs). Divergence in gene expression patterns in the development of GI carcinoids and PETs was identified, whereas examination of the PET and GI carcinoid data demonstrated only few areas of overlap in the accumulation of genetic aberrations. These data suggest that the recent World Health Organization classification of GEP-NETs may require updating. In addition, previous assumptions of tumor similarity (pancreatic vs. GI) may be unfounded when they are examined at a molecular level. On the basis of the evolution of genetic information, enteric neuroendocrine lesions (carcinoids) and PETs may need to be classified as two distinct entities rather than grouped together as the single entity “GEP-NETs.” *Cancer* 2005;104:2292–309. © 2005 American Cancer Society.

**KEYWORDS:** carcinoid, DNA, genetics, gastroenteropancreatic neuroendocrine tumor, methylation, neuroendocrine, pancreatic endocrine tumor, comparative genomic hybridization.

**G**astroenteropancreatic neuroendocrine tumors (GEP-NETs) are a poorly understood group of lesions that encompass a broad category of neoplasms derived from neuroendocrine cells of the gastrointestinal (GI) mucosa and the pancreas (for review, see Solcia et al.<sup>1</sup>). The lesions are grouped based on the acceptance that they have a common cell lineage and produce similar secretory products: chromogranin A (CgA),<sup>2</sup> synaptophysin,<sup>3</sup> and neuron-specific enolase (NSE).<sup>4</sup> The GEP-NET classification includes carcinoids, insulinomas, gastrinomas, tumors that secrete vasoactive intestinal peptide, glucagonomas, somatostatinomas, and nonfunctional pancreatic endocrine tumors (PETs). Although they are rarer than adenocarcinomas, the estimated incidence of PETs is ~ 5 per 1,000,000 population, whereas carcinoids (bronchopulmonary and GI) comprise ~ 0.46% of all malignancies.<sup>5</sup> Although they are categorized together, their clinical behaviors are strikingly divergent in terms of both symptoms and

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# Molecular And Cell Biological Aspects Of Gastroenteropancreatic Neuroendocrine Tumor Disease

**Bertram Wiedenmann**



## **Molecular And Cell Biological Aspects Of Gastroenteropancreatic Neuroendocrine Tumor Disease:**

*Molecular and Cell Biological Aspects of Gastroenteropancreatic Neuroendocrine Tumor Disease* Bertram Wiedenmann, 1994 New molecular and cell biological approaches in the fields of neurobiology and neuroendocrinology have identified a large number of molecules that can be assigned structurally and functionally to various subcellular structures such as secretory vesicles the Golgi complex the trans Golgi network and endosomes It has become evident that neurons and neuroendocrine cells share many properties such as the expression of very similar secretory vesicles and molecules including cell adhesion molecules neurotransmitters hormones neurotransmitter receptors and hormone receptors Various molecules discovered and characterised in basic research have been found to be increasingly applicable for improved diagnosis and therapy of neuroendocrine tumour disease This volume reviews current research in both basic science and clinical research from the viewpoint of its direct applicability to clinical medicine Gastroenteropancreatic Neuroendocrine Tumor Disease Bertram Wiedenmann, 2004 At the beginning of the last century the development of the Neuroendocrine Concept sparked intensive and worldwide research efforts leading to fascinating insights into the complex and diverse system of neuroendocrine cells and its importance in human physiology and disease Recent developments in new and expanding research areas including developmental biology regulation of angiogenesis cellular signaling and transcription and impressive results obtained by application of genomics and proteomics warranted a reevaluation of the neuroendocrine concept impact of the current understanding of neuroendocrine biology and pathobiology in these research areas In particular new discoveries are presented in neuroendocrine developmental biology with special emphasis on transcription factors controlling neuroendocrine differentiation of endodermal stem cells controlling formation and proliferation of blood and lymphatic vessels and molecular determinants of hematogenous and lymphatic tumor dissemination Given their central importance for the establishment and maintenance of the neuroendocrine phenotype signal transduction cascades and their cellular targets related to the regulation of adhesion processes receptor mediated endocytosis and cell cycle events as well as secretory activation and membrane trafficking are discussed in the context of neuroendocrine physiology and neuroendocrine tumor disease Since many of the recent discoveries made in basic research can be directly linked to clinical applications this volume summarizes and discusses innovative treatment and or diagnostic approaches for neuroendocrine tumor disease

*Endocrine Neoplasms* Andrew Arnold, 2012-12-06 Andrew Arnold The past several years have been a time of intense excitement and have brought major advances in the understanding and treatment of endocrine neoplasms This is therefore an excellent point at which to undertake a broad based overview of the state of the art in endocrine neoplasia for the Cancer Treatment and Research series Because of the wide and interdisciplinary readership of this series our aim for each chapter has been to provide ample background for those not highly familiar with the topic while emphasizing the most recent advances Furthermore the chapters have been written with the clinician in mind whether she or he is an oncologist

endocrinologist surgeon generalist pathologist or radiologist As such the authors mission has been to focus on clinically relevant issues and to present the scientific basis of current or potential future advances in a manner easily digestible to the nonexpert Endocrine tumors often cause problems for the patient by virtue of their hormonal activity which may frequently but certainly not always overshadow the adverse consequences related to their mass per se In fact it is important to keep in mind that endocrine tumors can manifest two biologically separable but often intertwined properties namely increased cell mass and abnormal hormonal function These need not go hand in hand and their distinction has definite clinical relevance in for example the increasingly recognized problem of incidentally discovered adrenal or pituitary masses

Radiotherapy in practice - radioisotope therapy Peter J Hoskin,2007-02-08 Radioisotope therapy is an internal form of radiation used to treat cancer it may be administered orally or intravenously and represents the nearest treatment option to the magic bullet specifically targeting sites of disease whilst sparing surrounding normal tissues Radioisotope therapy has an important role to play in modern medicine particularly in the treatment of thyroid disease neuroendocrine tumours bone metastasis and non Hodgkin s lymphoma It is found in both the diagnostic setting and in therapy but recently there has been a renaissance in the application of radioisotope unsealed sources in therapeutic indications It is an active area of research with the quest for new compounds that will be specific for therapeutic targets This book is an essential practical guide to the use of radioisotope therapy and also includes the background and developmental biology which underpins its use Individual tumours and diseases are explored with specific focus given to radioisotope treatment options The barriers to radioisotope therapy such as ease of access acquisition of radioisotopes radiation protection regulations and cost are also discussed

ABOUT THE SERIES Radiotherapy remains the major non surgical treatment modality for the management of malignant disease with over 50% of patients receiving treatment at some time during the management of their malignant disease It is based on the application of the principles of applied physics radiobiology and tumour biology to clinical practice Each volume in this series takes the reader through the basic principles of different types of radiotherapy and then develops these by individual sites This series of practical handbooks are aimed at physicians both training and practising in radiotherapy as well as medical physicists dosimetrists radiographers and senior nurses

Cumulated Index Medicus ,1995 Oxford Textbook of Endocrinology and Diabetes John A.H. Wass,Paul M. Stewart,2011-07-28 Now in its second edition the Oxford Textbook of Endocrinology and Diabetes is a fully comprehensive evidence based and highly valued reference work combining basic science with clinical guidance and providing first rate advice on diagnosis and treatment

Oxford Textbook of Oncology David J. Kerr,Daniel G. Haller,Cornelis J. H. van de Velde,Michael Baumann,Nagahiro Saijo,2016 Written by internationally recognized key opinion leaders in all of the oncology sub disciplines and covering all aspects of the field the Oxford Textbook of Oncology Third Edition reflects current best practice and represents a modern approach to managing the cancer patient This is a definitive resource for oncologists of all varieties

Functional Neuroendocrine Tumors Bojana Popovic,Aviral Singh,Francesca

Spada,Karin Zibar Tomsic,2025-09-10 One of authentic features of neuroendocrine tumors NETs is a potential to synthesize and secrete biogenic peptides and hormones Typically arising from tumors originating from the pancreas lungs and intestine these products can cause recognizable clinical hormone syndromes Even rarer among the rare functional NETs are in the minority compared to nonfunctional tumors i e 10 40% in a group of pancreatic NETs but they represent great diagnostic and therapeutic challenges For any case of functional NET hormonal hypersecretion syndrome causes excess morbidity sometimes even more threatening than the cancer itself This makes control of hormonal hypersecretion not only additional but sometimes in fact a primary therapeutic goal On the other hand secretory products can be useful as tumor markers and facilitate monitoring of treatment response Unfortunately many of these tumors become refractory to treatment over time and new modalities are required Annals of the New York Academy of Sciences Thomas Lincoln Casey,Gilbert Van Ingen,Charles Lane Poor,Edmund Otis Hovey,Ralph Winfred Tower,2003 Records of meetings 1808 1916 in v 11 27

Theranostics, Gallium-68, and Other Radionuclides Richard P. Baum, Frank Rösch, 2012-08-23 This book is based on contributions presented at the 1st World Congress on Gallium 68 and Peptide Receptor Radionuclide Therapy which examined recent developments in theranostics the emerging field of molecular targeting of vectors that can be used for both diagnosis and therapy when modified accordingly The focus of this book is on the rapidly developing research into and clinical applications of gallium 68 and other generator produced PET radionuclides in the personalized diagnosis and treatment of neuroendocrine tumors and other diseases In addition new PET radiopharmaceuticals are considered and the latest ideas and concepts presented Theranostics embodies both molecular and personalized medicine It is at the cutting edge of medicine and the contents of this volume will be of interest to chemists physicians and investigators dealing with generators PET radiochemistry molecular imaging and radionuclide therapy Endocrine Pathology with Online Resource Ozgur Mete, Sylvia L. Asa, 2016-07-14 A much needed comprehensive resource Endocrine Pathology covers clinical radiologic biochemical molecular cytogenetic immunologic and histopathologic aspects of endocrine disorders including the full spectrum of both neoplastic and non neoplastic lesions The first section of the book provides an overview of the clinical presentations of endocrine diseases while the second section reviews the wide variety of investigative techniques used in their diagnosis The third and largest section provides a comprehensive tissue and organ based approach to the diagnosis of endocrine disorders including morphologic genetic and proteomic features with clinicopathologic correlations All chapters are richly illustrated with numerous color images tables and algorithms and the book is packaged with a password giving the user online access to all text and images Written and edited by the world's leading experts this comprehensive and up to date book is the definitive resource on endocrine pathology for all pathologists endocrinologists and researchers **Journal of the National Cancer Institute**, 2008-07 **Hybrid SPECT/CT Imaging in Clinical Practice** Ora Israel, Stanley J. Goldsmith, 2006 Exploring a technology that is significantly impacting the noninvasive evaluation of the physiology and

anatomy of tumors as well as the diagnosis of infectious processes and cardiac diseases this source presents recent advances and clinical applications of sequential single session single photon emission computed tomography and computed tomography imaging This source is written by pioneers in hybrid imaging and offers authoritative sections on state of the art breakthroughs in sentinel lymph node identification cardiac imaging and the study and treatment of a variety of disorders including lymphoma thyroid and parathyroid tumors neuroendocrine tumors prostatic cancer and bone metastases

Endocrine Pathology, An Issue of Surgical Pathology Clinics Justine A Barletta,2019-11-06 This issue of Surgical Pathology Clinics Guest Edited by Dr Justine A Barletta will focus on Endocrine Pathology Topics include but are not limited to Pitfalls in Thyroid Cytology Prognostic Parameters in Differentiated Thyroid Carcinomas Thyroid Tumors You Don t Want to Miss Molecular Alterations in Thyroid Carcinomas Treatment of Differentiated Thyroid Carcinomas Treatment of Aggressive Thyroid Carcinomas A Guide to Pheochromocytomas and Paragangliomas A Diagnostic Approach to Adrenocortical Tumors Treatment of Adrenocortical Carcinoma and Pheochromocytomas Parathyroid Pathology Neuroendocrine Tumors of the GI Tract and Pancreas Treatment of GI Neuroendocrine Tumors and Neuroendocrine Tumors of the Lung *Molecular Anatomic Imaging* Gustav Konrad von Schulthess,2007 This fully updated Second Edition focuses sharply on clinical PET CT and SPECT CT examinations omitting lengthy physics discussions The book is now strictly disease oriented and integrates PET CT and SPECT CT applications completely When both techniques are relevant for a disease they are discussed together when only one is relevant it is discussed alone More than 1 200 illustrations are included A bound in DVD contains over 80 cases to be viewed in three orthogonal planes and different CT windows organized as reference and self assessment files The cases provide excellent training and allow readers to test their abilities in making diagnoses on their own Endocrine Tumors Orlo H. Clark,2003 ACS American Cancer Society Atlas of Clinical Oncology Surgical endocrinology or endocrine surgical oncology is an important component of general surgery and of some areas of head and neck surgery Endocrine Tumors proves the latest information regarding the management of endocrine cancers of the thyroid parathyroid adrenal *Atlas of Thyroid and Neuroendocrine Tumor Markers* Luca Giovanella,2018-01-22 This book highlights the increase in thyroid tumors and NET and demonstrates the growing importance of circulating markers in diagnosis as well as treatment and follow up Dramatic technical improvements have heightened the clinical impact of well established conventional biochemical markers In addition more recent genetic and molecular approaches have provided innovative molecular markers In this context effective communication between clinicians and laboratory physicians scientists is essential in allowing all those involved to fully profit from these exciting advances In this comprehensive up to date book authors from different laboratory and clinical areas link laboratory and clinical topics Analytical problems such as interferences false negative and false positive results are discussed in depth and flow charts offer insights into identifying and avoiding them Illustrated clinical cases detail the clinical role and limitations of different tumor markers Lastly it

explores health technology assessment and economic issues This is a valuable resource for endocrinologists oncologists nuclear medicine physicians scientists and technologists who want to keep abreast of the latest developments

**Peptides in Oncology III** K. Höffken,R. Kath,2012-12-06 Interference with protein mediated intra and intercellular pathways has become a major goal of preclinical and clinical research A rapidly increasing number of peptides are known to be responsible for endo para and autocrine signal transduction These peptides and their receptors have been studied with regard to their cell growth stimulatory action and their impact on differentiation In parallel peptide antagonists are being investigated in terms of their potential role in preclinical and clinical application Thus biotherapy might improve the clinical outcome of patients with tumors that respond to the respective hormonal manipulation Among the numerous peptides of interest somatostatin somatotropin release inhibitory factor and the luteinizing hormone releasing hormone LH RH have been the topic of intensive research during recent years In this third volume of peptides in oncology experts in the field extensively review and update the mechanisms of action of somatostatin and LH RH analogues in oncology Somatostatin and its various short and long acting analogues have the unique feature of suppressing and inhibiting a wide range of cellular processes including cell proliferation Receptors for these peptides which belong to the family of neuropeptides or neurotransmitters are widely distributed a feature which is not in keeping with the general view of a growth hormone regulatory system LH RH analogues play an established role in curative adjuvant and palliative treatment of hormone sensitive tumors

**Practical Medical Oncology Textbook** Antonio Russo,Marc Peeters,Lorena Incorvaia,Christian Rolfo,2021-10-06 This textbook combines essential information on clinical cancer medicine with a guide to the latest advances in molecular oncology and tumor biology Providing a systematic overview of all types of solid tumors including epidemiology and cancer prevention genetic aspects of hereditary cancers differential diagnosis typical signs and symptoms diagnostic strategies and staging and treatment modalities it also discusses new and innovative cancer treatments particularly targeted therapy and immunotherapy Expert commentaries at the end of each chapter highlight key points offer insights suggest further reading and discuss clinical application using case descriptions This textbook is an invaluable practice oriented tool for medical students just beginning their clinical oncology studies as well as for medical oncology residents and young professionals

**Handbook of Neuroendocrinology** George Fink,Donald W. Pfaff,Jon Levine,2011-08-31 Neuroendocrinology the discipline concerned with how the nervous system controls hormonal secretion and how hormones control the brain is pivotal to physiology and medicine Neuroendocrinology has disclosed and underpins fundamental physiological molecular biological and genetic principles such as the regulation of gene transcription and translation the mechanisms of chemical neurotransmission and intracellular and systemic feedback control systems Reproduction growth stress aggression metabolism birth feeding and drinking and blood pressure are some of the bodily functions that are triggered and or controlled by neuroendocrine systems In turn neuroendocrine dysfunction due to genetic or other deficits can lead for

example to infertility impotence precocious or delayed puberty defective or excessive growth obesity and anorexia Cushing's Syndrome hypertension or thyroid disorders These as well as neuroendocrine tumors are some of the themes covered in the 36 chapters of the Handbook Drafted by internationally acknowledged experts in the field the Handbook chapters feature detailed up to date bibliographies as well as how do we know call out sections that highlight the experimental or technical foundations for major concepts principles or methodological advances in each area Aimed at senior undergraduate and graduate students post doctoral fellows and faculty in neuroscience medicine endocrinology psychiatry psychology and cognate disciplines the Handbook of Neuroendocrinology satisfies an unmet need that will prove useful at the laboratory bench as well as in the office The most comprehensive up to date source covering basic principles neural regulation hormone brain function and behavior and neuroendocrine pathology How do we know callout sections highlight core concepts Heavily illustrated with over 350 figures 4 color throughout



## **Molecular And Cell Biological Aspects Of Gastroenteropancreatic Neuroendocrine Tumor Disease** Book Review: Unveiling the Power of Words

In some sort of driven by information and connectivity, the energy of words has be more evident than ever. They have the capability to inspire, provoke, and ignite change. Such may be the essence of the book **Molecular And Cell Biological Aspects Of Gastroenteropancreatic Neuroendocrine Tumor Disease**, a literary masterpiece that delves deep to the significance of words and their affect our lives. Written by a renowned author, this captivating work takes readers on a transformative journey, unraveling the secrets and potential behind every word. In this review, we will explore the book is key themes, examine its writing style, and analyze its overall effect on readers.

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