Ashfaq A. Marghoob *Editor*

Nevogenesis

Mechanisms and Clinical Implications of Nevus Development



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Scott C. Dulebohn

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clinical photographs from the authors private collections histopathologic microphotographs imaging studies crisp illustrations and videos Clinical Ophthalmic Oncology s clinically focused and user friendly format allows for rapid retrieval of information in daily practice and is written for residents fellows and any physician involved in the care of patients with ocular or orbital malignancies Additionally this edition adds several hundred new images to improve comprehension of procedures and techniques This volume is devoted solely to uveal tumors explaining various diagnostic and biopsy techniques videos and describing the therapeutic options for different types of uveal tumors and their simulating conditions clinical evaluation of senescence-associated markers to distinguish melanocytic nevi from melanomas Kyriakos Orfanidis, 2019-12-19 Melanoma is a form of cancer that develops in melanocytes While it represents only 5% of skin malignancies it is the most aggressive and lethal Benign proliferation of these cells form the melanocytic nevi The definitive diagnosis of melanocytic nevi or melanoma lesions is histopathologic However it is estimated that a correct diagnosis is established by means of standard skin biopsy in only 83% of the melanocytic lesions of the remaining cases 8% and 9% are overinterpreted false positives and under interpreted false negatives respectively This underscores the importance of additional diagnostic tests Since cellular senescence is considered to be a tumor suppressive mechanism immuno histochemistry using senescence markers has been suggested for the evaluation of difficult melanocytic lesions however the routinely used senescence markers lack the ability to distinguish nevi from melanoma The general aim of this thesis is therefore to identify novel senescence markers that may aid in melanoma diagnosis In study I we established a cellular model with nevus mimicking characteristics consisting in primary melanocytes that become senescent Transcriptomic analysis allowed expanding the set of senescence associated markers that could distinguish nevi from melanoma and identifying tubulin 3 as a potential diagnostic marker Depletion of tubulin 3 and pretreatment with tubulin destabilizing drugs in melanocytes and melanoma cells induced a senescence like phenotype in vitro In particular reduced migration capacity and induction of cell cycle arrest in G2 M phase of the cell cycle was demonstrated In study II a potential inter cellular signaling pathway between melanoma cells and stromal fibroblasts that might facilitate melanoma invasion was investigated Ultraviolet UV radiation was shown both in melanoma cells and fibroblasts to promote the release and activation of TGF 1 and subsequent increase in expression of the serine protease FAP a protein that plays role in extracellular matrix degradation and therefore facilitates the invasion of melanoma cells Such mechanism was not functional in senescent melanocytes In study III it was shown that tubulin 3 immunostaining aids in the diagnosis of nevi and melanomas The diagnostic criterium was the tubulin 3 gradient within the melanocytic nevi that was no longer apparent in melanoma Different patterns of tubulin 3 immunostaining in melanoma were described dermoscopy immunohistochemistry associations were found specific dermoscopic features highlighted and the prognostic value of this tubulin 3 marker was examined The progression rate in patients whose melanomas had areas with loss of tubulin 3 was 4 times higher than in patients without

this feature although statistical significance could not be reached p 0 06 In conclusion transcriptomic analysis expanded the set of senescence associated markers that could distinguish nevi from melanoma and identified tubulin 3 as novel immunohistochemistry marker shown to have diagnostic and probably prognostic value From a mechanistical point of view ultraviolet radiation was shown to promote not only the formation of melanoma but also its progression by increasing a cathepsin TGF 1 FAP pathway resulting in extracellular matrix degradation Malignt melanom r en form av cancer som utvecklas i melanocyter de celler i huden som bildar pigmentet melanin ven om malignt melanom endast utg r 5% av alla hudcancrar r den den mest aggressiva och d dliga Godartad ansamling av melanocyter bildar en leverfl ck eller ett sk nevus Vid minsta misstanke om melanom opereras nevuset bort och analyseras i mikroskop Det uppskattas dock att en korrekt diagnos fastst lls endast i 83% av de bortopererade lesionerna Av de terst ende fallen r 8% vertolkade och 9% undertolkade Detta understryker vikten av att f rb ttra melanomdiagnostik Melanocyter i nevi anses i motsats till melanom ha avtagande f rm ga att fr ka sig efter ett visst antal celldelningar p grund av cell ldrande P visande av cell ldrande mark rer skulle d rf r kunna f rb ttra diagnostiken av sv rbed mda lesioner De idag rutinm ssigt anv nda cell ldrande mark rerna saknar dock f rm ga att skilja nevi fr n melanom Det vergripande syftet med denna avhandling var d rf r att f rs ka identifiera nya cell ldrande mark rer f r att f rb ttra melanom diagnostiken I studie I etablerade vi en cellmodell med nevus efterliknande egenskaper best ende av melanocyter som ldras Med genuttryck analys studerades cell ldrande mark rer som kunde skilja nevi fr n melanom Proteinet tubulin 3 identifierades som en potentiell diagnostisk mark r Minskning av tubulin 3 och f rbehandling med tubulin destabiliserande l kemedel i melanocyter visade sig inducera ett tillst nd som liknar cell ldrandet I studie II unders ktes en signalv g mellan melanomceller och fibroblaster som kan underl tta melanomcellers f rm ga att infiltrera och aktivt f rst ra omgivande v vnad Fibroblaster r en typ av bindv vsceller i l derhuden som tillverkar mnen som finns mellan celler s k extracellul r matrix Ultraviolett UV str lning visade sig b de i melanomceller och fibroblaster fr mja signalv gen som resulterar i kat proteinuttryck av FAP ett protein som bidrar till nedbrytning av extracellul r matrix vilket kan underl tta infiltration av melanomceller En s dan signalv g var inte funktionell i ldrande melanocyter I studie III visade vi att proteinet tubulin 3 r en mark r som underl ttar diagnostik av nevi respektive melanom Det diagnostiska kriteriet var tubulin 3 gradienten som kunde ses i nevi men som ej var synligt i melanom Olika m nster av tubulin 3 analys i melanom beskrevs kliniska associationer hittades och v rdet av denna mark r f r att f ruts ga sjukdomens f rlopp unders ktes Melanompatienter vars melanom hade omr den med f rlust av tubulin 3 hade fyra g nger h gre progressionstakt av sjukdomen j mf rt med patienter utan detta m nster Sammanfattningsvis studerade vi cell ldrande mark rer som kunde skilja nevi fr n melanom och vi identifierade proteinet tubulin 3 som en mark r med diagnostiskt och f rmodligen prognostiskt v rde Vi visade att ultraviolett str lning inte bara fr mjar melanombildning utan ocks dess progression genom att ka en signalv g mellan melanomceller och fibroblaster som resulterar i extracellul r matrixnedbrytning Pathology of Melanocytic Nevi and

Melanoma Raymond L. Barnhill, Michael W. Piepkorn, Klaus J. Busam, 2014-02-18 Highly acclaimed and considered the leading reference in the field Pathology of Melanocytic Nevi and Malignant Melanoma has once again been fully revised and updated to reflect the most recent advances and techniques in the field of melanoma pathology. The successful focus and format of the previous editions have been preserved Each lesion and diagnosis is clearly illustrated with the aid of a wealth of digitally enhanced full color photomicrographs A concise description of the clinical features histopathology differential diagnosis and the most important characteristics of each lesion provides readers with a quick yet comprehensive overview of each topic covered Pathology of Melanocytic Nevi and Malignant Melanoma is the essential reference for every practicing dermatopathologist pathologist dermatologist and cancer research scientist today **Reflectance Confocal Microscopy** for Skin Diseases Rainer Hofmann-Wellenhof, Giovanni Pellacani, Joseph Malvehy, H. Peter Soyer, 2012-03-01 This book focuses on the use and significance of in vivo reflectance confocal microscopy RCM for non invasive high resolution imaging of the skin All of the chapters in this hands on guide are generously illustrated with numerous confocal images and structured in a reader friendly way The contents include detailed information on the most relevant and up to date aspects of RCM schematic drawings summarizing and explaining the most important RCM criteria and a chapter specifically devoted to bridging the gap between dermoscopy RCM and histopathology At the end of each chapter core messages recapitulate the most pertinent aspects Reflectance Confocal Microscopy for Skin Diseases will be a valuable resource for all physicians involved in the diagnosis and treatment of neoplastic and inflammatory skin diseases Precision Molecular Pathology of Dermatologic Diseases Victor G. Prieto, 2015-08-10 This volume is a concise yet comprehensive resource for physicians dealing with and interested in the field of molecular pathology in dermatopathology. The book includes descriptions of the techniques and their application to cutaneous diseases and describes possible future techniques and their use in dermatopathology Special emphasis is also given to the practical application of these techniques to particular situations illustrated by demonstrative cases Written by experts in their fields Precision Molecular Pathology of Dermatologic Diseases is of great value to pathologists dermatologists resident and fellows internists and general practitioners who deal with dermatologic diseases The Pigmentary System James J. Nordlund, Raymond E. Boissy, Vincent J. Hearing, Richard A. King, William S. Oetting, Jean-Paul Ortonne, 2008-04-15 The most comprehensive and integrated book on pigmentation The Pigmentary System Second Edition gathers into one convenient all inclusive volume a wealth of information about the science of pigmentation and all the common and rare clinical disorders that affect skin color The two parts physiology science and pathophysiology clinical disorders are complementary and annotated so that those reading one part can easily refer to relevant sections in the other For the clinician interested in common or rare pigment disorders or the principles of teaching about such disorders this book provides an immediate and complete resource on the biologic bases for these disorders For the scientist studying the biology of melanocyte function the book provides a list of disorders that are related to

basic biological functions of melanocytes New features of this Second Edition include Completely new section on the basic science of pigmentation explaining the integration of melanocyte functions with other epidermal cells and with various organ systems like the immune system New chapters on pigmentary disorders related to intestinal diseases the malignant melanocyte benign proliferations of melanocytes nevi and phototherapy with narrow band UV All clinical chapters include the latest genetic findings and advances in therapy More than 400 color images of virtually all clinical disorders The book is ideal for all dermatologists and especially those interested in disorders of pigmentation It is of particular use for pediatric dermatologists and medical geneticists caring for patients with congenital and genetic pigmentary disorders This authoritative volume will fill the gap for dermatology training programs that do not have local experts on pigmentation Basic and cosmetic scientists studying pigmentation and melanocytes will find the science and clinical correlations very useful in showing human significance and relevance to the results of their studies Cutaneous Oncology, An Issue of Hematology/Oncology Clinics of North America, E-Book David E. Fisher, 2024-09-05 In this issue of Hematology Oncology Clinics guest editor Dr David E Fisher brings his considerable expertise to the topic of Cutaneous Oncology Top experts first provide information on skin structure function and immunology then offer overviews of the therapeutic state of the art for both melanoma and non melanoma skin cancers Discussions focus on unique clinical challenges and biological breakthroughs which have come to light in recent studies of cutaneous malignancies Contains 16 relevant practice oriented topics including high risk non melanoma skin cancers progress in immune checkpoints for melanoma therapy targeted therapy innovations for melanoma advances in vaccines for melanoma microbiome and immunotherapy Merkel cell carcinoma and more Provides in depth clinical reviews on cutaneous oncology offering actionable insights for clinical practice Presents the latest information on this timely focused topic under the leadership of experienced editors in the field Authors synthesize and distill the latest research and practice guidelines to create clinically significant topic based reviews

Reflectance Confocal Microscopy of Cutaneous Tumors Salvador Gonzalez,2017-07-06 Reflectance confocal microscopy enables lesions in skin to be examined without excision but with improved diagnostic accuracy assessment of dermoscopic histologic correlation assessment of surgical margins as well as speed and convenience for the physician and patient This extensively enlarged and updated text reviews the current and future state of the art for those involved with the diagnosis and treatment of skin tumors with a greatly increased amount of material on the expected normal patterns of skin throughout life and on non melanocytic tumors

Color Atlas of Dermoscopy Horacio Cabo,2017-07-17 Dermoscopy is a non invasive widely used diagnostic tool that aids the diagnosis of skin lesions and is proven to increase the accuracy of melanoma diagnosis This colour atlas is a comprehensive guide to the diagnosis of skin lesions and melanomas using a dermoscope Beginning with an introduction to the use of the dermascope the following chapters teach clinicians how to recognise dermoscopic criteria colours and patterns how to diagnose different types of lesions and calculate diagnostic algorithms The

finals sections cover related topics including entomodermatoscopy inflammatoscopy trichoscopy and capilaroscopy This highly useful resource is enhanced by more than 1000 clinical images and illustrations Key points Comprehensive guide to diagnosis of skin lesions and melanomas using a dermoscope Teaches clinicians how to recognise dermoscopic criteria Covers related dermatoscopic topics Includes more than 1000 images and illustrations An Atlas of Dermoscopy Ashfag Marghoob, Ralph Braun, 2012-07-26 Building on a successful first edition this revised and extended Atlas of Dermoscopy demonstrates the state of the art of how to use dermoscopy to detect and diagnose lesions of the skin with a special emphasis on malignant skin tumours With well over 1 500 photographs drawings and tables the book has extensive clinical correlation **Dermatology for Advanced Practice Clinicians** Margaret Bobonich, Mary Nolen, Jeremy Honaker, Douglas DiRuggiero, 2021-05-14 The newly updated abundantly illustrated Dermatology for Advanced Practice Clinicians A Comprehensive Guide to Diagnosis and Treatment 2nd Edition is your complete evidence based guide to accurate and successful assessment diagnosis and treatment of cutaneous diseases Focusing on the most common and most critical skin conditions this expertly written guide offers essential dermatology knowledge for diagnosing and managing a broad range of skin hair and nail conditions Whether in primary care or full time dermatology this comprehensive text is both an ideal foundation for new practitioners and an essential companion to experienced clinicians **Essentials of Surgical Pediatric Pathology** Marta C. Cohen, Irene Scheimberg, 2015-02-05 Essentials of Surgical Pediatric Pathology is a clear and practical yet comprehensive guide for trainee pediatric pathologists and non pediatric pathologists Each chapter corresponds to one of the main subspecialties such as dermatopathology head and neck pathology and system pathology Practical guidance is given on handling pediatric specimens and the authors highlight the ways in which common conditions present differently in adults and children Other chapters cover conditions typical of childhood including soft tissue tumors and blue round cell tumors The chapters begin with a brief clinical presentation followed by a clear macroscopical and histological description of the principal pathologies seen in children Up to date genetic and immunohistochemical information is provided and the book includes hundreds of high quality color images Written and edited by leading international experts in the field this is an essential resource for trainee pediatric pathologists as well as general pathologists who may encounter pediatric cases

Essentials of Ophthalmic Oncology Arun D. Singh,2009 The first edition of this text offers guidance and advice on the diagnosis and management of the complete spectrum of ophthalmic tumors including the eyelid conjunctival intraocular and orbital tumors The editors are joined by over 120 international contributors to present a broad perspective from a multidisciplinary team that will offer a diverse and balanced view of ophthalmic oncology clinical practice This is a comprehensive book that includes over 100 chapters organized into 7 sections that provide a wealth of information for the management of patients with ophthalmic tumors from examination techniques to classification to surgical techniques

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