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Chapter 1 : melanoma techniques and protocols - TÃ i liá»‡u text

In Melanoma Techniques and Protocols: Molecular Diagnosis, Treatment, and Monitoring, a broadly diverse group of researchers and clinicians offer not only reviews of the most important recent advances in melanoma oncology, tumor immunology, and pathology, but also state-of-the-art molecular techniques for probing melanoma's basic biology.

Please click button to get melanoma techniques and protocols book now. This site is like a library, you could find million book here by using search box in the widget. From the simple discovery in that resorbing tadpole tail expressed an enzyme MMP that could degrade collagen gels, matrix metalloproteinase MMP research has advanced to discover more than twenty distinct vertebrate MMPs and four specific inhibitors TIMPS , a veritable family of enzymes involved in many physiological and pathological processes. Each method includes step-by-step instructions and notes on variant applications and pitfalls to avoid. A selective overview of the MMP arena spells out where the field has been, where it is, and where it is going. Comprehensive and highly practical, Matrix Metalloproteinase Protocols brings together the long and hard-earned experience of master experimentalists that will allow not only novices to get up to speed quickly, but also add to the repertoire of successful techniques in expert laboratories. Despite considerable scientific and medical effort over the past decades, malaria remains the most important human parasitic disease. It is responsible for up to 3 million deaths and another million new cases each year, and is becoming resistant to the current chemoprophylactic and chemotherapeutic agents. In Malaria Methods and Protocols, internationally respected scientists and clinicians describe in step-by-step detail their most useful conventional and cutting-edge techniques for the study of malaria. Areas covered include clinical and laboratory diagnosis and typing, animal models, molecular biology, immunology, cell biology, vaccinology, laboratory models, and field applications. Each readily reproducible protocol has been tested, standardized, and optimized for experimental success, and includes many laboratory notes on troubleshooting, avoiding pitfalls, and interpreting results. Several of the most widely used methods are either described here in detail for the first time or have been thoroughly updated since their original publication e. This book not only surveys the whole arena of novel anticancer drug targets, but also presents a wide-ranging selection of cuttingedge techniques currently being applied throughout novel antitumor drug discovery and development. The methods are applied to experiments involving such topics as immunotherapy, angiogenesis, cancer metastasis, the cell cycle, signal transduction inhibitors, apoptosis, antibodies, antisense molecules, microarray gene expression, flow cytometry, and PET imaging for cancer target validation. There are also proven methods for the preclinical identification of drug targets. Validate new drug targets both preclinically and clinically Identify novel anticancer drug targets in preclinical stages Follow proven instructions to obtain successful results and avoid failure. Although ninety percent of fatal cancer cases involve the spread of a primary tumor, the formation of metastases is still a poorly understood, complex process and a significant problem in the treatment of cancer patients. In Metastasis Research Protocols, leading international investigators describe the key methods needed to investigate why and how metastasis occurs. Volume I of this two-volume set, Analysis of Cells and Tissues, presents a comprehensive collection of established and leading-edge techniques for analyzing the expression of key molecules and for examining their production at the genetic level. The work focuses on the analysis and mapping of molecules produced by cells and tissues, and on the molecular biology underlying their expression. The second volume of this set, Analysis of Cell Behavior In Vitro and In Vivo, moves to the level of living cells and tissues to present methodologies applicable to examining metastatic behavior in vitro and in the whole animal. Comprehensive and authoritative, the two volumes of Metastasis Research Protocols constitute a gold-standard collection of readily reproducible methods for understanding the metastatic cascade-first at the cellular and molecular levels, then at the level of the whole organism-responsible for the spread of cancer and for developing novel strategies to combat its spread.

Chapter 2 : Online Melanoma Techniques And Protocols

In Melanoma Techniques and Protocols: Molecular Diagnosis, Treatment, and Monitoring, a broadly diverse group of researchers and clinicians offer not only reviews of the most important recent advances in melanoma oncology, tumor immunology, and pathology, but also state-of-the-art molecular techniques for probing its basic biology.

Methods and Protocols Edited by: Nickoloff Melanoma of the skin is one of the most rapidly increasing malignancies in both young and old patients 1,2. Not only is the incidence increasing, but the number of annual deaths from melanoma is also on the rise worldwide 3. In the United States, melanoma will be diagnosed in 43, new patients each year and be responsible for deaths 1 death every 72 min. The capacity of melanoma to develop in young patients is reflected by the rather alarming statistic that it has become one of the top causes of death in both men and women between the ages of 25 and 40 3. Indeed, among Caucasian females, melanoma is the leading cause of death from malignancy between the ages of 25 and 29 3. It is expected that by , 1 in 70 Americans will develop melanoma during their lifetime 2. Also, melanoma is second only to adult leukemia as the leader in the number of potential years of life lost, which is significantly greater than for patients with cervical, breast, and colon malig- nancies 4. Despite the frequent presence of melanoma and major associated health problems around the globe, only recently have clinicians and labora- tory-based researchers begun to unravel some of the molecular mysteries of melanoma 5,6. The purpose of Melanoma: Although the bad news is that the incidence as well as morbidity and mortal- ity rates for melanoma are on the rise, the good news is that our knowledge has tremendously increased across many clinical and scientific disciplines 5â€”7. The challenge for compiling a valuable multiauthored text containing contem- 4 Nickoloff porary viewpoints, scientific facts, clinical treatment protocols, and other dis- coveries is to select authors who can contribute their ideas and present the state-of-the art techniques from a rather broad-ranging set of perspectives. Thus, this book is written by a quite diverse group of individuals who share several unifying characteristics. First, the authors all are involved in the clini- cal practice of medicine either directly as surgeons, oncologists, tumor immu- nologists, or pathologists, or have decided to focus their investigative talents on working closely with these clinicians. Second, and perhaps most relevant for their selection to contribute a chapter in this book, is that they focus on the molecular basis of melanoma. Third, the authors have agreed to include in their respective chapters all relevant literature citations with an emphasis on the most recent available data. Fourth, the authors were encouraged to reduce their experimental procedures to a practical level so that others not familiar with specific techniques could use these important approaches in their own laboratories, hospitals, and cancer centers. Finally, despite the difficulty in translating scientific discoveries into clinical practice, each author was encouraged to select the most medically important advances in their respective areas and highlight the relevance of such findings for clinicians caring for patients with melanoma. This book provides a rich admixture of clinical perspectives, cutting-edge technological advances, including narrative overviews, as well as specific and detailed laboratory-based protocols. The emphasis on molecular biology throughout reflects the progress made in delineating the genetic basis for mela- noma, a forward-thinking approach to rendering molecular-based diagnostic reports, understanding the immunobiology of melanoma, initiating vaccine- based gene therapy to treat patients with melanomas, and using the tools of genomics i. From the Microscope to the Molecular Diagnosis of Melanoma During the past 15 yr as a practicing dermatopathologist, I have witnessed many changes in the field, particularly regarding pigmented skin lesions. Dur- ing my initial training in Boston, pathology reports of melanoma focused pri- marily on the Clark level and Breslow measurements of depths of invasion of the primary cutaneous lesion. In the early and mids, many academic der- matopathology units were struggling with delineation of accurate and repro- ducible criteria for potential precursor lesions of melanoma including dysplastic nevi and congenital nevi 8. By examining relatively large data- bases and using computer-generated multivariant analysis, numerous indepen- dent prognostic indicators were put forward to assist the clinician in the management of patients with melanoma 9. Thus, our current pathology Molecular Medicine of Melanoma 5 reports include the Clark level defined as level I for in situ, Level II for mela- nomas partially infiltrating papillary dermis, Level III for

lesions filling the papillary dermis, Level IV for melanomas extending into reticular dermis, and Level V for melanomas extending into sc fatty tissue , Breslow depth of inva- sion expressed in millimeters of thickness from the granular-cell layer in the epidermis to the deepest portion in the dermis , presence or absence of regres- sion, surface ulceration, and microscopic satellitosis, to name a few Although these rather objective measurements provide valuable prognostic information for the patient and physician, there is still a growing awareness and appreciation of the phenotypic complexity and capricious behavior of melanoma. Initially, it appeared that one of the most important determinants of the biologic behavior of melanoma was primary tumor thickness. However, it has become clear that many other molecular determinants are important to the biologic behavior of melanoma, and the remainder of this chap- ter is devoted to a brief review of such molecules and the pathways they regu- late. Indeed, despite a National Institutes of Health Consensus Panel meeting, and numerous attempts to define suitable histologic criteria, pathologists still are not able to agree con- sistently on these problematic pigmented legions Given the limitations in rendering meaningful diagnosis when such an element of subjectivity is present, it becomes clear that moving from the microscope to a more mole- cular-based analysis of melanoma Fig. One of the most important new advances in this area has been the use of molecular staging of the sentinel lymph node in melanoma patients Importance of Sentinel Lymph Node Assessment As described in more detail in Chapter 17, surgical techniques have greatly advanced in the last decade and provide an opportunity to perform clinical staging of melanoma using the sentinel lymph node SLN biopsy It is 6 Nickoloff based on the principle that the sentinel node is the first lymph node a metasta- sis encounters before entering into other lymph nodes Because SLN biopsy can be performed under local anesthesia, and because it can detect sub- clinical metastatic disease when assessed using molecular-based techniques, it provides a new method to stage a patient without a period of clinical observa- tion previously requiring a certain period of time to elapse before the detection of palpable lymph nodes could be appreciated by the physician 19â€” A pathologist can generally detect 1 malignant melanoma cell in a back- ground of 10, lymphocytes in a lymph node using routine light microscopy Fig. However, using reverse transcriptase polymerase chain reaction RT-PCR to detect a simple transcriptâ€”e. This is not just an academic exercise, because data clearly demonstrate the superior clinical correlation using molecular-based i. For example, if an SLN is upstaged i. Moving from a morphologic to a molecular-based diagnostic approach in melanoma. Molecular Medicine of Melanoma 7 increased chance of recurrence. The rate of recurrence and overall survival for patients based on SLN analysis was as follows: Biologic Determinants of Melanoma Behavior This section provides an analysis of the critical biologic determinants that can supplement the light microscopic and molecular viewpoint, as previously mentioned, with an emphasis on those characteristics that are associated with metastasis. The focus on metastasis is important because despite improvement in clinical diagnosis, surgical techniques, and the use of novel treatments and adjuvant approaches, most melanoma deaths result from metastasis. Indeed, while considerable debate raged for years regarding the appro- Fig. As already mentioned, significant advances have been made so that we can rou- tinely assess, by molecular techniques, the status of the SLN. After all, most patients do not succumb to local recurrence of their melanoma, but they do experience significant morbidity and mortality when their melanoma moves from the skin to extracutaneous sites. None of the randomized double-blind clinical studies of the width of surgical resection of melanoma ever pointed to a statistical significance on long-term survivalâ€”only rates of local recurrence. Having covered these histologic, surgical, and clinical perspectives, we now review some of the molecular determinants that can be useful in understanding and, it is hoped, predicting more reliably the progression of melanoma, includ- ing its metastasis beyond the confines of the epidermis and dermis. Before covering melanoma, it may be instructive first to review the biologic behavior of nevi, because many melanomas develop from such preexisting nevi. As documented by dermatologists, the num- Fig. Molecular staging of melanoma. Molecular Medicine of Melanoma 9 ber of nevi or moles on each individual actually change over a lifetime, with many nevi coming and going with the passage of time. The molecular factors that prompt a single melanocyte in the basal cell layer of the epidermis in a teenager to change phenotypically into a nevus cell, and then initially prolifer- ate largely in a relatively tightly nested or clustered group to produce a junc- tional nevus, are not known. Neither is it clear as to the nature of the stimulus that triggers an exodus of

the nevus cells from the epidermal compartment into the papillary dermis. However, a few recent molecular clues have emerged that point to the role of basic fibroblast growth factor bFGF and its receptor. Thus, when nevus cells are in the dermis, they acquire the capacity to produce their own bFGF in an autocrine fashion to ensure their independence of the epidermal-based constraints. As recently discussed, this autocrine switch may represent a double-edged sword, because the acquisition of the ability to produce a potent mitogen, coupled with the constitutive expression of the growth factor receptor, has been demonstrated in several oncologic models to represent an early event in the transformation process Indeed, it has been documented that early stage melanoma cells cannot produce bFGF in abun- dance compared with late-stage melanoma cells Another relevant molecular change controlling the migration of nevus cells from the epidermis to the dermis are the cadherin-mediated adhesive interactions A large number of molecular markers have been documented to be corre- lated to the progression of melanoma. In general, it is possible to classify these changes as resulting from either an increase in the levels relative to normal keratinocytes or nevus cells, or a relative decrease in their expression. In addition, melanoma cells express intercellular adhesion molecule-1, MUC, integrins i. To escape immunosurveillance, melanoma cells may also cease to express other molecules such as class I major histocompatibility complex anti- gens and CD95 antigen. Because monoclonal antibodies MAbs are available that can detect the presence or absence of many of these molecular markers, one wonders whether pathology reports that include semiqualitative assessments of such molecules could enhance the predictive value of our otherwise routine histologic analysis of primary cutaneous melanomas. After all, we have all had patients with a relatively thin melanoma i. Another important diagnostic dilemma for dermatopathologists is the iden- tification of a metastatic infiltrate in the lymph node or other extracutaneous sites when no primary cutaneous lesion is present. If the meta- static cells are producing melanin, there is no difficulty in recognizing the malignancy as melanoma. However, in amelanotic malignant infiltrates, it is necessary to use immunohistochemical analysis to determine whether the tumor is related to melanoma. While ultrastructural studies using electron micros- copy can yield insight into the diagnosis by identifying melanomas or premelanomas, several MAbs have permitted assignment of metastatic lesions to the melanoma category Fig. These diagnostic reagents include use of detection of S highly sensitive, relatively nonspecific , gp i. Forward-looking depiction of sampling a pigmented lesion by needle biopsy followed by array analysis using microchip technology to assess thousands of mRNA transcripts. Molecular Medicine of Melanoma 11 5. Future Directions Given the limitations in rendering precise and prognostically relevant pathology reports based solely on light microscopic criteria, it is likely that a more molecular-based approach will be forthcoming as the immunobiology and genetic basis of melanoma is better understood. Indeed, the Human Genome Project is revolutionizing the practice of biology and medicine in several respects Cancers such as melanoma can be viewed as a systems problem, and using global tools of genomics, the information pathway responsible for conversion of a benign melanocyte to a melanoma cell can be understood As has been shown elegantly by Duggan et al. Not only can this technology assist the pathologist in better cataloguing of various phenotypes of melanoma, but with more experience this approach will also facilitate more customized treatment protocols. For example, there may be considerably greater heterogeneity in the behavior of melanomas besides the current distinc- tion of radial vs vertical growth phases of melanoma. A more prognostically sophisticated classification scheme based on differential transcription profiles may yield several distinctive phenotypes. Within each tumor classification, further distinctions may be made with clinical experience based on therapeutic responsiveness, so that not only will new diagnostic categories be created but also therapeutic decisions based on such molecular analysis will be forthcom- ing. It is probable that the next few years will highlight the concomitant use of conventional pathologic analysis with gene assay technology Fig. More rapid progress in defining highly accurate and prognostic molecular reports will occur by the active participation of derma- topathologists with our molecular biologyâ€”based scientific colleagues. This transitional period will be difficult for classically trained diagnostic pathologists, but it is our obligation to not only support this technological revo- lution, but to provide the necessary quality assurance and critically important correlative light microscopic descriptions to ensure a rapid transition. Perhaps most important we need to prepare the current pathology residents in-training with an appreciation of not only important

anatomic-based pattern recognition skills, but the appropriate mentoring and educational experiences and knowledge to facilitate their role in rendering molecular diagnostic profiles of melanoma. Analysis of the melanoma epidemic, both apparent and real. Molecular biology of human melanoma development and progression. The immunotherapy and gene therapy of cancer. Molecular Medicine of Melanoma 13 NIH consensus development panel on early melanoma. Su and Jeffrey M. Introduction The multistep genetic alterations thought to involve both oncogenes and tumor suppressor genes that are causally related to melanocytic transformation remain largely undetermined 1. Mapping of alterations to chromosome 6 indicates that multiple genetic loci on 6q contribute causally to the develop- ment and progression of malignant melanoma 1. This notion is also supported by the introduction of chromosome 6 in malignant melanoma cell lines suppressing either their tumorigenicity 2 or metastasis 3,4. However, the suppressor genes involved have yet to be identified. Specifically, the parental malignant melanoma cell line UACC was derived from a primary mela- noma specimen and displays anchorage-independent growth and rapid popula- tion doubling in plastic culture 2. These three cell lines are genetically linked and phenotypically display readily distinguishable growth features. They pro- vide us with the unique cellular resource for the successful identification of tumor suppressor genes by DNA microarrays 6. Briefly, cDNA templates for genes of interest are amplified from plasmid clones carrying human genes by polymerase chain reaction PCR using the vector sequence-specific primers. Following purifi- cation and quality control, aliquots of cDNA 1â€”16 ng are printed on poly- lysine-coated glass microscope slides using a computer-controlled, high-speed robot.

Chapter 3 : Melanoma Techniques & Protocols Molecular Diagnosis | Cancer Forum

This is an unusual book: unusual not because it is a methods "recipe" book for molecular and cell biologic aspects of melanoma, but because the editor has (sensibly) broadened the topics covered to include more translational work.

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Chapter 4 : Melanoma Chemotherapy: Chemo Treatments & Options | CTCA

This book is about melanomaâ€"its biology, immunology, and pathology, as well as the initial use of powerful genomic tools to study its fundamental molecu- lar and genetic characteristics.

Introduction Melanoma of the skin is one of the most rapidly increasing malignancies in both young and old patients 1,2. Not only is the incidence increasing, but the number of annual deaths from melanoma is also on the rise worldwide 3. In the United States, melanoma will be diagnosed in 43, new patients each year and be responsible for deaths 1 death every 72 min. The capacity of melanoma to develop in young patients is reflected by the rather alarming statistic that it has become one of the top causes of death in both men and women between the ages of 25 and 40 3. Indeed, among Caucasian females, melanoma is the leading cause of death from malignancy between the ages of 25 and 29 3. It is expected that by , 1 in 70 Americans will develop melanoma during their lifetime 2. Also, melanoma is second only to adult leukemia as the leader in the number of potential years of life lost, which is significantly greater than for patients with cervical, breast, and colon malignancies 4. Despite the frequent presence of melanoma and major associated health problems around the globe, only recently have clinicians and laboratory-based researchers begun to unravel some of the molecular mysteries of melanoma 5,6. The purpose of Melanoma: Although the bad news is that the incidence as well as morbidity and mortality rates for melanoma are on the rise, the good news is that our knowledge has tremendously increased across many clinical and scientific disciplines 5â€"7. The challenge for compiling a valuable multiauthored text containing contemFrom: Methods in Molecular Medicine, Vol. Methods and Protocols Edited by: Thus, this book is written by a quite diverse group of individuals who share several unifying characteristics. First, the authors all are involved in the clinical practice of medicine either directly as surgeons, oncologists, tumor immunologists, or pathologists, or have decided to focus their investigative talents on working closely with these clinicians. Second, and perhaps most relevant for their selection to contribute a chapter in this book, is that they focus on the molecular basis of melanoma. Third, the authors have agreed to include in their respective chapters all relevant literature citations with an emphasis on the most recent available data. Fourth, the authors were encouraged to reduce their experimental procedures to a practical level so that others not familiar with specific techniques could use these important approaches in their own laboratories, hospitals, and cancer centers. Finally, despite the difficulty in translating scientific discoveries into clinical practice, each author was encouraged to select the most medically important advances in their respective areas and highlight the relevance of such findings for clinicians caring for patients with melanoma. This book provides a rich admixture of clinical perspectives, cutting-edge technological advances, including narrative overviews, as well as specific and detailed laboratory-based protocols. The emphasis on molecular biology throughout reflects the progress made in delineating the genetic basis for melanoma, a forward-thinking approach to rendering molecular-based diagnostic reports, understanding the immunobiology of melanoma, initiating vaccinebased gene therapy to treat patients with melanomas, and using the tools of genomics i. From the Microscope to the Molecular Diagnosis of Melanoma During the past 15 yr as a practicing dermatopathologist, I have witnessed many changes in the field, particularly regarding pigmented skin lesions. During my initial training in Boston, pathology reports of melanoma focused primarily on the Clark level and Breslow measurements of depths of invasion of the primary cutaneous lesion. In the early and mids, many academic dermatopathology units were struggling with delineation of accurate and reproducible criteria for potential precursor lesions of melanoma including dysplastic nevi and congenital nevi 8. By examining relatively large databases and using computer-generated multivariant analysis, numerous independent prognostic indicators were put forward to assist the clinician in the management of patients with melanoma 9. Thus, our current pathology Molecular Medicine of Melanoma 5 reports include the Clark level defined as level I for in situ, Level II for melanomas partially infiltrating papillary dermis, Level III for lesions filling the papillary dermis, Level IV for melanomas extending into reticular dermis, and Level V for melanomas extending into sc fatty tissue , Breslow depth of invasion expressed in millimeters of thickness from the granular-cell layer in the epidermis to the deepest portion in the dermis , presence or absence of

regression, surface ulceration, and microscopic satellitosis, to name a few Although these rather objective measurements provide valuable prognostic information for the patient and physician, there is still a growing awareness and appreciation of the phenotypic complexity and capricious behavior of melanoma. Initially, it appeared that one of the most important determinants of the biologic behavior of melanoma was primary tumor thickness. However, it has become clear that many other molecular determinants are important to the biologic behavior of melanoma, and the remainder of this chapter is devoted to a brief review of such molecules and the pathways they regulate. Indeed, despite a National Institutes of Health Consensus Panel meeting, and numerous attempts to define suitable histologic criteria, pathologists still are not able to agree consistently on these problematic pigmented legions Given the limitations in rendering meaningful diagnosis when such an element of subjectivity is present, it becomes clear that moving from the microscope to a more molecular-based analysis of melanoma Fig. One of the most important new advances in this area has been the use of molecular staging of the sentinel lymph node in melanoma patients Importance of Sentinel Lymph Node Assessment As described in more detail in Chapter 17, surgical techniques have greatly advanced in the last decade and provide an opportunity to perform clinical staging of melanoma using the sentinel lymph node SLN biopsy It is 6 Nickoloff Fig. Moving from a morphologic to a molecular-based diagnostic approach in melanoma. Because SLN biopsy can be performed under local anesthesia, and because it can detect subclinical metastatic disease when assessed using molecular-based techniques, it provides a new method to stage a patient without a period of clinical observation previously requiring a certain period of time to elapse before the detection of palpable lymph nodes could be appreciated by the physician 19â€” A pathologist can generally detect 1 malignant melanoma cell in a background of 10, lymphocytes in a lymph node using routine light microscopy Fig. However, using reverse transcriptase polymerase chain reaction RT-PCR to detect a simple transcriptâ€”e. This is not just an academic exercise, because data clearly demonstrate the superior clinical correlation using molecular-based i. For example, if an SLN is upstaged i. The rate of recurrence and overall survival for patients based on SLN analysis was as follows: Biologic Determinants of Melanoma Behavior This section provides an analysis of the critical biologic determinants that can supplement the light microscopic and molecular viewpoint, as previously mentioned, with an emphasis on those characteristics that are associated with metastasis. The focus on metastasis is important because despite improvement in clinical diagnosis, surgical techniques, and the use of novel treatments and adjuvant approaches, most melanoma deaths result from metastasis. Indeed, while considerable debate raged for years regarding the appro- 8 Nickoloff Fig. Molecular staging of melanoma. As already mentioned, significant advances have been made so that we can routinely assess, by molecular techniques, the status of the SLN. After all, most patients do not succumb to local recurrence of their melanoma, but they do experience significant morbidity and mortality when their melanoma moves from the skin to extracutaneous sites. None of the randomized double-blind clinical studies of the width of surgical resection of melanoma ever pointed to a statistical significance on long-term survivalâ€”only rates of local recurrence. Having covered these histologic, surgical, and clinical perspectives, we now review some of the molecular determinants that can be useful in understanding and, it is hoped, predicting more reliably the progression of melanoma, including its metastasis beyond the confines of the epidermis and dermis. Before covering melanoma, it may be instructive first to review the biologic behavior of nevi, because many melanomas develop from such preexisting nevi. As documented by dermatologists, the num- Molecular Medicine of Melanoma 9 ber of nevi or moles on each individual actually change over a lifetime, with many nevi coming and going with the passage of time. The molecular factors that prompt a single melanocyte in the basal cell layer of the epidermis in a teenager to change phenotypically into a nevus cell, and then initially proliferate largely in a relatively tightly nested or clustered group to produce a junctional nevus, are not known. Neither is it clear as to the nature of the stimulus that triggers an exodus of the nevus cells from the epidermal compartment into the papillary dermis. However, a few recent molecular clues have emerged that point to the role of basic fibroblast growth factor bFGF and its receptor. Thus, when nevus cells are in the dermis, they acquire the capacity to produce their own bFGF in an autocrine fashion to ensure their independence of the epidermal-based constraints. As recently discussed, this autocrine switch may represent a double-edged sword, because the acquisition of the ability to produce a potent mitogen, coupled

with the constitutive expression of the growth factor receptor, has been demonstrated in several oncologic models to represent an early event in the transformation process Indeed, it has been documented that early stage melanoma cells cannot produce bFGF in abundance compared with late-stage melanoma cells Another relevant molecular change controlling the migration of nevus cells from the epidermis to the dermis are the cadherin-mediated adhesive interactions A large number of molecular markers have been documented to be correlated to the progression of melanoma. In general, it is possible to classify these changes as resulting from either an increase in the levels relative to normal keratinocytes or nevus cells, or a relative decrease in their expression. In addition, melanoma cells express intercellular adhesion molecule-1, MUC, integrins i. 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If the metastatic cells are producing melanin, there is no difficulty in recognizing the malignancy as melanoma. However, in amelanotic malignant infiltrates, it is necessary to use immunohistochemical analysis to determine whether the tumor is related to melanoma. While ultrastructural studies using electron microscopy can yield insight into the diagnosis by identifying melanomas or premelanomas, several MAbs have permitted assignment of metastatic lesions to the melanoma category Fig. These diagnostic reagents include use of detection of S highly sensitive, relatively nonspecific , gp i. Molecular Medicine of Melanoma 11 5. Future Directions Given the limitations in rendering precise and prognostically relevant pathology reports based solely on light microscopic criteria, it is likely that a more molecular-based approach will be forthcoming as the immunobiology and genetic basis of melanoma is better understood. Indeed, the Human Genome Project is revolutionizing the practice of biology and medicine in several respects Cancers such as melanoma can be viewed as a systems problem, and using global tools of genomics, the information pathway responsible for conversion of a benign melanocyte to a melanoma cell can be understood As has been shown elegantly by Duggan et al. Not only can this technology assist the pathologist in better cataloguing of various phenotypes of melanoma, but with more experience this approach will also facilitate more customized treatment protocols. For example, there may be considerably greater heterogeneity in the behavior of melanomas besides the current distinction of radial vs vertical growth phases of melanoma. A more prognostically sophisticated classification scheme based on differential transcription profiles may yield several distinctive phenotypes. Within each tumor classification, further distinctions may be made with clinical experience based on therapeutic responsiveness, so that not only will new diagnostic categories be created but also therapeutic decisions based on such molecular analysis will be forthcoming. More rapid progress in defining highly accurate and prognostic molecular reports will occur by the active participation of dermatopathologists with our molecular biologyâ€”based scientific colleagues. This transitional period will be difficult for classically trained diagnostic pathologists, but it is our obligation to not only support this technological revolution, but to provide the necessary quality assurance and critically important correlative light microscopic descriptions to ensure a rapid transition. Perhaps most important we need to prepare the current pathology residents in-training with an appreciation of not only important anatomic-based pattern recognition skills, but the appropriate mentoring and educational experiences and knowledge to facilitate their role in rendering molecular diagnostic profiles of melanoma. Analysis of the melanoma epidemic, both apparent and real. Molecular biology of human melanoma development and progression. The immunotherapy and gene therapy of cancer. Molecular Medicine of Melanoma 13 NIH consensus development panel on early melanoma. Su and Jeffrey M. Introduction The multistep genetic alterations thought to involve both oncogenes and tumor suppressor genes that are causally related to melanocytic transformation remain largely undetermined 1.

Mapping of alterations to chromosome 6 indicates that multiple genetic loci on 6q contribute causally to the development and progression of malignant melanoma 1. This notion is also supported by the introduction of chromosome 6 in malignant melanoma cell lines suppressing either their tumorigenicity 2 or metastasis 3,4. However, the suppressor genes involved have yet to be identified. Specifically, the parental malignant melanoma cell line UACC was derived from a primary melanoma specimen and displays anchorage-independent growth and rapid population doubling in plastic culture 2. These three cell lines are genetically linked and phenotypically display readily distinguishable growth features. They provide us with the unique cellular resource for the successful identification of tumor suppressor genes by DNA microarrays 6. Briefly, cDNA templates for genes of interest are amplified from plasmid clones carrying human genes by polymerase chain reaction PCR using the vector sequence-specific primers. Following purification and quality control, aliquots of cDNA 1â€”16 ng are printed on polylysine-coated glass microscope slides using a computer-controlled, high-speed robot. Equal amounts of the labeled DNA are combined and allowed to hybridize under stringent conditions to the probes on the array. Laser excitation of the incorporated fluorescence yields an emission with characteristic spectra, which are measured using a laser scanner.

Chapter 5 : Full text of "Protocols_molecular_biology"

This book on the biology, immunology, pathology and microbiology of melanoma deserves a place in the library of all units with a specific interest in melanoma research and management.

The study of cancer will be profoundly impacted by the Human Genome Project. I would like to discuss some of these changes. The first draft of the human genome sequence was announced in June , and we have just scratched the surface of the changes it will engender in medicine. A relevant question is what are the long-term effects of the Human Genome Project for medicine? I would argue that there are three, and each of these three point toward the view that systems biology will dominate biology and medicine of the 21st century. First, the Human Genome Project introduced a new type of s- ence-discovery science. Discovery science takes a biological system e. Thus, it creates a rich infrastructure from which the classical hypo- esis-driven science can be done more effectively. The effective integration of discovery- and hypothesis-driven science is a key for systems approaches to bi- ogy and medicine. Second, the Human Genome Project has provided a "periodic table of life. Texte du rabat In Melanoma Techniques and Protocols: Molecular Diagnosis, Treatment, and Monitoring, a broadly diverse group of researchers and clinicians offer not only reviews of the most important recent advances in melanoma oncology, tumor immunology, and pathology, but also state-of-the-art molecular techniques for probing its basic biology. These readily reproducible methods can be used to develop new diagnostic approaches, therapeutics, and status monitoring of patients suffering both early- and late-stage melanoma. With emphasis on the experimental details critical to experimental success, each method is described in step-by-step fahion by hands-on masters, often those who have developed hem in their own laboratories. Comprehensive and highly instructive, Melanoma Techniques and Protocols: Molecular Diagnosis, Treatment, and Monitoring offers both clinicians and basic scientists concerned with malignant melanoma both new clinical perspectives and the wide ranging experimental protocols essential for achieving more rapid breakthroughs in this near-epidemic disease. Su and Jeffrey M. Ullrich and David A. Cooper, and Nicholas M. Diagnosis Genetic Testing in Familial Melanoma: Caroline Le Poole and Thomas L. Chang, Keishi Tanigawa, Joel C. Goydos and Douglas S. Lee Informations sur le produit.

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It is very comprehensive in its scope and has 20 chapters written by different authors starting with general aspects of melanoma molecular biology, ranging through tumour suppressor genes, tumour specific antigens, and genetic testing, going on to diagnostic aspects, treatment, and monitoring of residual disease.

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