

# ANNOUNCEMENTS

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**Liver Cancer Stem Cells . . .** *Stewart Sell and Hyam L. Leffert* pp 2800-2805

In an effort to review the evidence that liver cancer stem cells exist, two fundamental questions must be addressed. First, do hepatocellular carcinomas (HCC) arise from liver stem cells? Second, do HCCs contain cells that possess properties of cancer stem cells? For many years the finding of preneoplastic nodules in the liver during experimental induction of HCCs by chemicals was interpreted to support the hypothesis that HCC arose by dedifferentiation of mature liver cells. More recently, recognition of the role of small oval cells in the carcinogenic process led to a new hypothesis that HCC arises by maturation arrest of liver stem cells. Analysis of the cells in HCC supports the presence of cells with stem-cell properties (ie, immortality, transplantability, and resistance to therapy). However, definitive markers for these putative cancer stem cells have not yet been found and a liver cancer stem cell has not been isolated.

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**Pancreatic Cancer Stem Cells . . .** *Cheong J. Lee, Joseph Dosch, and Diane M. Simeone* pp 2806-2812

Cellular heterogeneity in cancer was observed decades ago by studies in mice which showed that distinct subpopulations of cells within a tumor mass are capable of driving tumorigenesis. Conceptualized from this finding was the stem-cell hypothesis for cancer, which suggests that only a specific subset of cancer cells within each tumor is responsible for tumor initiation and propagation, termed tumor initiating cells or cancer stem cells (CSCs). Recent data has been provided to support the existence of CSCs in human blood cell-derived cancers and solid organ tumors of the breast, brain, prostate, colon, and skin. Study of human pancreatic cancers has also revealed a specific subpopulation of cancer cells that possess the characteristics of CSCs. These pancreatic cancer stem cells express the cell surface markers CD44, CD24, and epithelial-specific antigen, and represent 0.5% to 1.0% of all pancreatic cancer cells. Along with the properties of self-renewal and multilineage differentiation, pancreatic CSCs display upregulation of important developmental genes that maintain self-renewal in normal stem cells, including Sonic hedgehog (*SHH*) and *BMI-1*. Signaling cascades that are integral in tumor metastasis are also upregulated in the pancreatic CSC. Understanding the biologic behavior and the molecular pathways that regulate growth, survival, and metastasis of pancreatic CSCs will help to identify novel therapeutic approaches to treat this dismal disease.

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**Implications of the Cancer Stem-Cell Hypothesis for Breast Cancer Prevention and Therapy . . .** *Madhuri Kakarala and*

*Max S. Wicha* pp 2813-2820

Recent research in breast biology has provided support for the cancer stem-cell hypothesis. Two important components of this hypothesis are that tumors originate in mammary stem or progenitor cells as a result of dysregulation of the normally tightly regulated process of self-renewal. As a result, tumors contain and are driven by a cellular subcomponent that retains key stem-cell properties including self-renewal, which drives tumorigenesis and differentiation that contributes to cellular heterogeneity. Advances in stem-cell technology have led to the identification of stem cells in normal and malignant breast tissue. The study of these stem cells has helped to elucidate the origin of the molecular complexity of human breast cancer. The cancer stem-cell hypothesis has important implications for early detection, prevention, and treatment of breast cancer. Both hereditary and sporadic breast cancers may develop through dysregulation of stem-cell self-renewal pathways. These aberrant stem cells may provide targets for the development of cancer prevention strategies. Furthermore, because breast cancer stem cells may be highly resistant to radiation and chemotherapy, the development of more effective therapies for this disease may require the effective targeting of this cell population.

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**Medulloblastoma Stem Cells . . .** *Xing Fan and Charles G. Eberhart* pp 2821-2827

Medulloblastoma and other embryonal brain tumors are similar in appearance and differentiation potential to neural stem and progenitor cells. Expression studies performed using human tumor samples, as well as the analysis of murine transgenic models, suggest that both multipotent cerebellar stem cells and lineage-restricted progenitors of the external germinal layer can be transformed into medulloblastoma by genetic alterations. These molecular changes frequently involve constitutive activation of signaling pathways such as Wnt, Hedgehog, and Notch, which play a key role in non-neoplastic neural stem cells. Pharmacologic blockade of the Hedgehog and Notch pathways suppresses the growth of medulloblastoma in culture and in vivo and may prove effective in targeting the small cancer stem-cell subpopulation required for tumor initiation and long-term propagation.

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**Human Colon Cancer Stem Cells: A New Paradigm in Gastrointestinal Oncology . . . Bruce M. Boman and Emina Huang**  
pp 2828-2838

For the past half century, oncologists have had systemic drugs available, agents that are able to induce tumor responses in patients with colorectal cancer. However, in cases of advanced colorectal cancer, these regimens are almost never curative. The recently introduced concept that cancer stem cells (SCs) drive tumor growth suggests a reason for these therapeutic failures—current chemotherapeutics target rapidly dividing cells but cancer SCs divide only slowly, and, they are relatively resistant to cytotoxic systemic therapies. It also suggests a solution—development of therapeutics that target cancer SCs. However, there is a paucity of information about the mechanisms by which SC populations are maintained and about the mechanisms by which tumor SCs are involved in colon cancer development. In this article, we discuss these mechanisms and recent developments in the identification and isolation of colon cancer SCs using new SC markers. We then discuss the role of SCs in homeostasis of normal colonic epithelium, and mechanisms by which dysregulation of crypt mechanisms can lead to initiation and progression of colon cancer. Our hypothesis, which has received recent experimental support, is that the mechanism that links abnormalities at the gene level (eg, *APC* mutations) and abnormalities at the tissue level (eg, proliferative shift, dysplasia, carcinoma) from cancer initiation to metastasis is SC overpopulation. Finally, we discuss the concept that symmetric cancer SC division is an essential mechanism that drives tumor growth, and that development of a new generation of therapeutics that target colon cancer SCs by inhibiting symmetric SC division holds promise for truly curative approaches for patients with advanced colorectal cancers.

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**Survival of the Fittest: Cancer Stem Cells in Therapeutic Resistance and Angiogenesis . . . Christine E. Eyler and Jeremy N. Rich** pp 2839-2845

In an increasing number of cancers, tumor populations called cancer stem cells (CSCs), or tumor-initiating cells, have been defined in functional assays of self-renewal and tumor initiation. Moreover, recent work in several different cancers has suggested the CSC population as a source of chemotherapy and radiation-therapy resistance within tumors. Work in glioblastoma and breast cancers supports the idea that CSCs may possess innate resistance mechanisms against radiation- and chemotherapy-induced cancer cell death, allowing them to survive and initiate tumor recurrence. Several resistance mechanisms have been proposed, including amplified checkpoint activation and DNA damage repair as well as increased Wnt/ $\beta$ -catenin and Notch signaling. Novel targeted therapies against the DNA damage checkpoint or stem-cell maintenance pathways may sensitize CSCs to radiation or other therapies. Another important category of cancer therapies are antiangiogenic and vascular targeting agents, which are also becoming integrated in the treatment paradigm of an increasing number of cancers. Recent results from our laboratory and others support a role for CSCs in the angiogenic drive as well as the mechanism of antiangiogenic agents. Identifying and targeting the molecular mechanisms responsible for CSC therapeutic resistance may improve the efficacy of current cancer therapies.

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**“Stemness” Genomics Law Governs Clinical Behavior of Human Cancer: Implications for Decision Making in Disease Management . . . Gennadi V. Glinsky** pp 2846-2853

One of the most significant accomplishments of translational oncogenomics is a realistic promise of efficient diagnostic tests that would facilitate implementation of the concept of individualized cancer therapies. Recent discovery of the *BMI1* pathway rule indicates that gene expression signatures (GESs) associated with the “stemness” state of a cell might be informative as molecular predictors of cancer therapy outcome. We illustrate a potential clinical utility of this concept using GESs derived from genomic analysis of embryonic stem cells (ESCs) during transition from self-renewing, pluripotent state to differentiated phenotypes. Signatures of multiple stemness pathways (signatures of *BMI1*, *Nanog/Sox2/Oct4*, *EED*, and *Suz12* pathways; transposon exclusion zones and ESC pattern 3 signatures; signatures of Polycomb-bound and bivalent chromatin domain transcription factors) seem informative in stratification of cancer patients into low- and high-intensity treatment groups on the basis of prediction of the long-term therapy outcome. A stemness cancer therapy outcome predictor (CTOP) algorithm combining scores of nine stemness signatures outperforms individual signatures and demonstrates a superior prognostic accuracy in retrospective supervised analysis of large cohorts of breast, prostate, lung, and ovarian cancer patients. Our analysis suggests that stemness genomics law governs clinical behavior of human malignancies and defines epigenetic boundaries of therapy-resistant and -sensitive tumors within distinct stemness/differentiation programs. One of the main conclusions of our analysis is that near-term progress in practical implementation of the concept of personalized cancer therapies would depend on timely delivery to practicing physicians of relevant scientific information regarding the outcome of prospective trials validating prognostic performance of CTOP tests in a clinical setting.

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**Mathematical Models of Cancer Stem Cells . . . Franziska Michor** pp 2854-2861

Human cancers are thought to be sustained in their growth by a pathologic counterpart of normal adult stem cells: cancer stem cells. This concept was first developed in human myeloid leukemias and is today being extended to solid tumors such as breast and brain cancers. A quantitative understanding of cancer stem cells requires a mathematical framework to describe the dynamics of cancer initiation and progression, the response to treatment, and the evolution of resistance. In this review, I use chronic myeloid leukemia as an example to discuss how mathematical and computational techniques have been used to gain insights into the biology of cancer stem cells.

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**Prostate Cancer Stem Cells: A New Target for Therapy . . .** Norman J. Maitland and Anne T. Collins **pp 2862-2870**

The existence of prostate cancer stem cells offers a theoretical explanation for many of the enduring uncertainties surrounding the etiology and treatment of the most commonly diagnosed tumor in US males. The study of cancer stem cells in prostate, as in other complex tissues, is critically dependent on the availability of pure cell populations, a situation complicated by the heterogeneity of prostate tumors. However, selection of cells with a CD133<sup>+</sup>/α2β1 integrin/CD44<sup>+</sup> phenotype enriches for a tumor-initiating population from human prostate cancers. Among the most pressing needs is for enduring therapy in patients who have experienced failure of hormonal treatments. Because the putative cancer stem cell does not express androgen receptor, it is likely to be immune from most androgen-based therapies, and an inherent genetic instability would enable the tumor to develop the new variants present in hormone-refractory disease. Prostate cancer stem cells have a unique gene expression signature that can also be related to Gleason grade and patient outcome. The scarcity of cancer stem cells in a prostate tumor will probably limit their usefulness in cancer diagnosis and prognosis. However, the emergence of new stem-cell therapeutic targets not only will require new assays for efficacy (because of their relatively quiescent nature), but also holds real promise of more lasting treatments to augment those currently directed against the remaining tumor cells, which comprise 99.9% of tumor mass, but paradoxically have a poor tumor-initiating capacity.

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**Cancer Stem Cells in Head and Neck Squamous Cell Cancer . . .** Mark E.P. Prince and Laurie E. Ailles **pp 2871-2875**

Appropriate treatment of head and neck squamous cell cancer (HNSCC) remains one of the most difficult challenges in head and neck oncology. Overall survival of patients with HNSCC remains at approximately 50% at 5 years. Surgical therapy can be mutilating and often has significant effects on swallowing, speech, and physical appearance. The addition of chemotherapy to radiation treatment has shown efficacy in organ preservation in some sites in the head and neck, but has resulted in limited improvement in survival rates. HNSCC resistance to chemotherapy has limited the usefulness of chemotherapy in the treatment of this disease. We have recently demonstrated that human head and neck squamous cell cancers contain a tumorigenic, so-called cancer stem cell, subpopulation of cells that can self-renew and produce differentiated cells that form the bulk of the tumor. These tumorigenic HNSCC cells have a distinct phenotype and can be identified by a surface marker. Current treatment for HNSCC regimens may selectively kill the differentiated cancer cells, producing tumor regression while sparing the cancer stem cells, leading to tumor regrowth and relapse. It is important for us to understand why HNSCC does not respond to chemotherapy and to identify new targeted treatments that can overcome resistance and improve patient outcomes. Further study of HNSCC stem cells will increase our knowledge of this devastating disease and allow us to develop novel treatments.

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**Gastric Cancer Stem Cells . . .** Shigeo Takaishi, Tomoyuki Okumura, and Timothy C. Wang **pp 2876-2882**

Cancer stem cells are defined as the unique subpopulation in the tumors that possess the ability to initiate tumor growth and sustain self-renewal as well as metastatic potential. Accumulating evidence in recent years strongly indicate the existence of cancer stem cells in solid tumors of a wide variety of organs. In this review, we will discuss the possible existence of a gastric cancer stem cell. Our recent data suggest that a subpopulation with a defined marker shows spheroid colony formation in serum-free media in vitro, as well as tumorigenic ability in immunodeficient mice in vivo. We will also discuss the possible origins of the gastric cancer stem cell from an organ-specific stem cell versus a recently recognized new candidate bone marrow-derived cell (BMDC). We have previously shown that BMDC contributed to malignant epithelial cells in the mouse model of *Helicobacter*-associated gastric cancer. On the basis of these findings from animal model, we propose that a similar phenomenon may also occur in human cancer biology, particularly in the cancer origin of other inflammation-associated cancers. The expanding research field of cancer stem-cell biology may offer a novel clinical apparatus to the diagnosis and treatment of cancer.

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**Cancer Stem Cells and the Ontogeny of Lung Cancer . . .** Craig D. Peacock and D. Neil Watkins **pp 2883-2889**

Lung cancer is the leading cause of cancer death in the world today and is poised to claim approximately 1 billion lives during the 21st century. A major challenge in treating this and other cancers is the intrinsic resistance to conventional therapies demonstrated by the stem/progenitor cell that is responsible for the sustained growth, survival, and invasion of the tumor. Identifying these stem cells in lung cancer and defining the biologic processes necessary for their existence is paramount in developing new clinical approaches with the goal of preventing disease recurrence. This review summarizes our understanding of the cellular and molecular mechanisms operating within the putative cancer-initiating cell at the core of lung neoplasia.

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**Melanoma Stem Cells: The Dark Seed of Melanoma . . .** Susan E. Zabierowski and Meenhard Herlyn **pp 2890-2894**

Cells with stem-cell markers and features have recently been identified in melanoma tissues and cell lines. Melanoma stem-like cells possess many traits of tumor-initiating or tumor stem cells including self-renewal capacity, high tumorigenicity, and differentiation into various mesenchymal lineages, including melanocytic cells. Four subpopulations of melanoma-initiating cells have been distinguished: CD20<sup>+</sup>, CD133<sup>+</sup>, label-retaining or slow-cycling cells, and side-population cells with high efflux activities. Whether these are distinct or overlapping populations is currently under investigation. Ongoing studies are dissecting and characterizing the hierarchy of these subpopulations within a malignant lesion. Understanding these and the dynamics of clonal dominance will aid in the development of novel therapeutic strategies.

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**Multiple Myeloma Cancer Stem Cells . . . Carol Ann Huff and William Matsui pp 2895-2900**

Multiple myeloma is characterized by the clonal expansion of neoplastic plasma cells within the bone marrow, elevated serum immunoglobulin, and osteolytic bone disease. The disease is highly responsive to a wide variety of anticancer treatments including conventional cytotoxic chemotherapy, corticosteroids, radiation therapy, and a growing number of agents with novel mechanisms of action. However, few if any patients are cured with these modalities and relapse remains a critical issue. A better understanding of clonogenic multiple myeloma cells is essential to ultimately improving long-term outcomes, but the nature of the cells responsible for myeloma regrowth and disease relapse is unclear. We review evidence that functional heterogeneity exists in multiple myeloma and discuss potential strategies and clinical implications of the stem-cell model of cancer in this disease.

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**Invincible, but Not Invisible: Imaging Approaches Toward In Vivo Detection of Cancer Stem Cells . . . Lori S. Hart and Wafik S. El-Deiry pp 2901-2910**

With evidence emerging in support of a cancer stem-cell model of carcinogenesis, it is of paramount importance to identify and image these elusive cells in their natural environment. The cancer stem-cell hypothesis has the potential to explain unresolved questions of tumorigenesis, tumor heterogeneity, chemotherapeutic and radiation resistance, and even the metastatic phenotype. Intravital imaging of cancer stem cells could be of great value for determining prognosis, as well as monitoring therapeutic efficacy and influencing therapeutic protocols. Cancer stem cells represent a rare population of cells, as low as 0.1% of cells within a human tumor, and the phenotype of isolated cancer stem cells is easily altered when placed under in vitro conditions. This represents a challenge in studying cancer stem cells without manipulation or extraction from their natural environment. Advanced imaging techniques allow for the in vivo observation of physiological events at cellular resolution. Cancer stem-cell studies must take advantage of such technology to promote a better understanding of the cancer stem-cell model in relation to tumor growth and metastasis, as well as to potentially improve on the principles by which cancers are treated. This review examines the opportunities for in vivo imaging of putative cancer stem cells with regard to currently accepted cancer stem-cell characteristics and advanced imaging technologies.

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**Chronic Myeloid Leukemia Stem Cells . . . Edward Kavalchik, Daniel Goff, and Catriona H.M. Jamieson pp 2911-2915**

Although rare, chronic myeloid leukemia (CML) represents an important paradigm for understanding the molecular events leading to malignant transformation of primitive hematopoietic progenitors. CML was the first cancer to be associated with a defined genetic abnormality, *BCR-ABL*, that is necessary and sufficient for initiating chronic phase disease as well as the first cancer to be treated with molecular targeted therapy. Malignant progenitors or leukemia stem cells (LSCs) evolve as a result of both epigenetic and genetic events that alter hematopoietic progenitor differentiation, proliferation, survival, and self-renewal. LSCs are rare and divide less frequently, and thus, represent a reservoir for relapse and resistance to a molecularly targeted single agent. On subverting developmental processes normally responsible for maintaining robust life-long hematopoiesis, the LSCs are able to evade the majority of current cancer treatments that target rapidly dividing cells. Enthusiasm for the enormous success of tyrosine kinase inhibitors at controlling the chronic phase disease is tempered somewhat by the persistence of the LSC pool in the majority of the patients. Combined therapies targeting aberrant properties of LSC may obviate therapeutic resistance and relapse in advanced phase and therapeutically recalcitrant CML.

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**Brain Tumor Stem Cells: Bringing Order to the Chaos of Brain Cancer . . . Peter B. Dirks pp 2916-2924**

Brain tumors are generally incurable cancers. Work from a number of laboratories strongly suggests that they are organized as a hierarchy based on a subset of cancer cells that have stem-cell properties. These cells have now been shown to be resistant to conventional therapy and responsive to differentiation therapy. New in vitro and in vivo models for interrogating brain tumor cells in stem-cell conditions have been developed that provide important new opportunities for elucidating the key pathways responsible for driving the proliferation of these cells. Continued application of the principles of stem-cell biology to the study of brain cancers is likely to continue to bring further important insight into these aggressive cancers, bringing new treatments and understanding of the origins.

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# JOURNAL OF CLINICAL ONCOLOGY

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**Identical Outcome After Autologous or Allogeneic Genoidentical Hematopoietic Stem-Cell Transplantation in First Remission of Acute Myelocytic Leukemia Carrying Inversion 16 or t(8;21): A Retrospective Study From the European Cooperative Group for Blood and Marrow Transplantation**

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**Impact of Intensity-Modulated Radiation Therapy on Local Control in Primary Soft Tissue Sarcoma of the Extremity**

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**Doxorubicin, Cardiac Risk Factors, and Cardiac Toxicity in Elderly Patients With Diffuse B-Cell Non-Hodgkin's Lymphoma**

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# CALENDAR OF ONCOLOGY EVENTS

MEETING/LOCATION	DATES	CONTACT
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<b>Ninth International Lung Cancer Congress</b> <i>Koloa, Hawaii</i>	June 18-21, 2008	<a href="http://www.cancerconferences.com/thoracic/9th_lcc/index.php">www.cancerconferences.com/thoracic/9th_lcc/index.php</a>
<b>RTOC Semi-Annual Meeting</b> <i>Philadelphia, Pennsylvania</i>	June 19-20, 2008	<a href="https://registrations.acr.org/rtog/">https://registrations.acr.org/rtog/</a>
<b>7th ICATMM and 4th EADO Joint Meeting</b> <i>Marseille, France</i>	June 19-21, 2008	<a href="http://www.icatmm-eado2008.com">www.icatmm-eado2008.com</a>
<b>Disparities in Health in America: Working Toward Social Justice 6th Annual Workshop</b> <i>Houston, Texas</i>	June 21-28, 2008	<a href="http://www.mdanderson.org/conferences">www.mdanderson.org/conferences</a>
<b>World Conference on Interventional Oncology and Best of ASCO Annual Meeting</b> <i>Los Angeles, California</i>	June 22-28, 2008	<a href="http://www.asco.org/ASCO/Meetings/Calendar+of+Events">http://www.asco.org/ASCO/Meetings/Calendar+of+Events</a>
<b>5th Annual Meeting on the NCI's Cancer Biomedical Informatics Grid (caBIG Initiative (Annual Meeting))</b> <i>Washington, DC</i>	Jun 23-25, 2008	<a href="https://cabig.nci.nih.gov/2008AnnualMeeting/">https://cabig.nci.nih.gov/2008AnnualMeeting/</a>
<b>5th European Spring Oncology Conference</b> <i>Marbella, Spain</i>	June 25-27, 2008	<a href="http://www.bnyco.com/webbnyco/bnyco/index.asp?lang=UK">www.bnyco.com/webbnyco/bnyco/index.asp?lang=UK</a>
<b>Multinational Association of Supportive Care in Cancer</b> <i>Houston, TX</i>	June 26-28, 2008	<a href="http://www.mdanderson.org/prof_education">http://www.mdanderson.org/prof_education</a>
<b>2008 International Symposium of Supportive Care in Cancer: Multinational Association of Supportive Care of Cancer/International Society for Oral Oncology</b> <i>Houston, Texas</i>	June 26-28, 2008	<a href="http://www.mdanderson.org/conferences">www.mdanderson.org/conferences</a>

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<b>MEETING/LOCATION</b>	<b>DATES</b>	<b>CONTACT</b>
<b>CALGB 2008 Summer Group Meeting</b> <i>Chicago, Illinois</i>	June 26-29, 2008	<a href="http://www.calgb.org/Public/meetings/meetings.php">www.calgb.org/Public/meetings/meetings.php</a>
<b>Best of ASCO – East Coast</b> <i>Boston, Massachusetts</i>	June 27-28, 2008	<a href="http://www.asco.org/ASCO/Meetings/Calendar+of+Events">http://www.asco.org/ASCO/Meetings/Calendar+of+Events</a>
<b>ESMO Conference Lugano 2008</b> <i>Lugano, Switzerland</i>	Jul 3-6, 2008	<a href="http://www.esmo.org/activities/ecluconference">http://www.esmo.org/activities/ecluconference</a>
<b>Best of ASCO Japan</b> <i>Tokyo, Japan</i>	Jul 5-6, 2008	<a href="http://jsmo.umin.jp">http://jsmo.umin.jp</a>
<b>Best of ASCO Lebanon</b> <i>Beirut, Lebanon</i>	Jul 10-11, 2008	<a href="http://www.infomedweb.com/boa2008lebanon">http://www.infomedweb.com/boa2008lebanon</a>
<b>Eighth International Congress on Genitourinary Malignancies</b> <i>Washington, DC</i>	Jul 17-19, 2008	<a href="http://www.cancerconferences.com/genitourinary/8th_gu/index.php">http://www.cancerconferences.com/genitourinary/8th_gu/index.php</a>
<b>GOG Semi-Annual Meeting</b> <i>Chicago, IL</i>	Jul 17-20, 2008	<a href="http://www.gog.org/meetinginformation.html">http://www.gog.org/meetinginformation.html</a>
<b>Advances in Long-Term Management of Adult Patients Undergoing Hematopoietic Stem Cell Transplantation</b> <i>San Francisco, CA</i>	Jul 18-20, 2008	<a href="http://www.cancerconferences.com/hematologic/heme_stemcell_0708/index.php">http://www.cancerconferences.com/hematologic/heme_stemcell_0708/index.php</a>
<b>7th International Conference on Head and Neck Cancer</b> <i>San Francisco, California</i>	July 19-23, 2008	<a href="http://www.ahns.info/meetings/intnlconference.php">www.ahns.info/meetings/intnlconference.php</a>
<b>Seventh Annual International Congress on the Future of Breast Cancer</b> <i>Koloa, Hawaii</i>	July 23-26, 2008	<a href="http://www.cancerconferences.com/breast_cancer/7th_bcc/index.php">www.cancerconferences.com/breast_cancer/7th_bcc/index.php</a>
<b>Denali Oncology Group (Alaska)</b> <i>Coldfoot, AK</i>	Jul 24-24, 2008	<a href="http://www.asco.org/ASCO/State+Affiliates/State+and+Regional+Affiliates">http://www.asco.org/ASCO/State+Affiliates/State+and+Regional+Affiliates</a>
<b>Mayo Clinic's 18<sup>th</sup> Annual Hematology/Oncology Reviews</b> <i>Amelia Island, FL</i>	Aug 4-8, 2008	<a href="http://www.mayo.edu/cme/">http://www.mayo.edu/cme/</a>
<b>South Carolina Oncology Society</b> <i>Charleston, SC</i>	Aug 8-9, 2008	<a href="http://www.scosonline.com/">http://www.scosonline.com/</a>
<b>Best of ASCO Singapore</b> <i>Singapore</i>	Aug 15-16, 2008	<a href="http://www.singaporeoncology.org.sg/">http://www.singaporeoncology.org.sg/</a>

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<b>Seventh International Congress on Targeted Therapies in Cancer</b> <i>Washington, DC</i>	Aug 22-24, 2008	<a href="http://www.cancerconferences.com/other_solid_tumors/7th_targeted_therapies_2032/index.php">http://www.cancerconferences.com/other_solid_tumors/7th_targeted_therapies_2032/index.php</a>
<b>Best of ASCO Brazil</b> <i>Porto Alegre, Brazil</i>	Aug 22-23	<a href="http://www.slacom.org/">http://www.slacom.org/</a>
<b>4th Physicians Network Conferences</b> <i>Boston, Massachusetts</i>	August 23-27, 2008	<a href="http://www.mdanderson.org/conferences">www.mdanderson.org/conferences</a>
<b>International Union Against Cancer (UICC) World Cancer Congress</b> <i>Geneva, Switzerland</i>	August 27-31, 2008	<a href="http://www.uicc.org">www.uicc.org</a>
<b>Australia and Asia Pacific Clinical Oncology Research Development (ACORD) Workshop</b> <i>Queensland, Australia</i>	Aug 31-Sept 6, 2008	<a href="http://www.acordworkshop.org.au/">http://www.acordworkshop.org.au/</a>
<b>Living Fully Conference</b> <i>Houston, Texas</i>	September 4-6, 2008	<a href="http://www.mdanderson.org/conferences">www.mdanderson.org/conferences</a>
<b>2008 Breast Cancer Symposium</b> <i>Washington, DC</i>	September 5-7, 2008	<a href="http://www.breastcasymposium.org/breastcasymposium">www.breastcasymposium.org/breastcasymposium</a>
<b>33rd ESMO Congress</b> <i>Stockholm, Sweden</i>	September 12-16, 2008	
<b>Palliative Care Leadership Center Training</b> <i>Richmond, Virginia</i>	September 15-16, 2008	<a href="http://www.capc.org/palliative-care-leadership-initiative">http://www.capc.org/palliative-care-leadership-initiative</a>
<b>9th Annual Perspectives in Colorectal Cancer</b> <i>Miami, Florida</i>	September 19-20, 2008	<a href="mailto:meetings@imedex.com">meetings@imedex.com</a>
<b>50th ASTRO Annual Meeting</b> <i>Boston, Massachusetts</i>	September 21-25, 2008	<a href="http://www.astro.org/Meetings/AnnualMeetings/">www.astro.org/Meetings/AnnualMeetings/</a>

# JOURNAL OF CLINICAL ONCOLOGY

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##### **Phase III Trial Comparing Retroperitoneal Lymph Node Dissection With One Course of Bleomycin, Etoposide, Plus Cisplatin Chemotherapy in the Adjuvant Treatment of Clinical Stage I Nonseminomatous Testicular Germ Cell Tumors: AUO Trial AH 01/94 by the German Testicular Cancer Study Group**

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### **The 38th David A. Karnofsky Lecture: The Paradoxical Actions of Estrogen in Breast Cancer—Survival or Death?**

V. Craig Jordan

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### **Don’t Mention It**

David P. Steensma