Printed and Published by
Rajiv Gandhi Cancer Institute
and Research Centre, Sector - V
Rohini, Delhi - 110085

From the Desk of Director Research

The "Special Feature" in this issue reports on the Molecular Markers of Cancer which help to detect cancers at an early stage, determine prognosis and monitor disease progression or therapeutic response.

Natural Orifice Transluminal Endoscopic Surgery, the minimally invasive surgery, is highlighted under "Perspective," whereas "In Focus" gives an insight into the Antioxidants and Cancer. MD Anderson Cancer Center, one of the world's most respected centers is profiled under "Institute", apart from the other regular features . "Activities of the Institute" includes a lecture on Taxane Resistance in Breast Cancer, and two workshops on Nutrition & Supportive Care, and Radiotherapy in Pediatric Cancers.

The Institute would be organizing its 8th Annual International Conference "RGCON 2009", having its main theme as "Thoracic Cancers: New Frontiers and Horizons" on March 27-29, 2009 in Delhi. The information on the Conference has been incorporated in the issue.

We express our special thanks to Siemens Medical Solutions for supporting this issue of Cancer News.

The Institute gratefully acknowledges the contributions made by Dr Gauri Kapoor, Dr Sheh Rawat, Dr J.B. Sharma, Dr Pankaj Pande, Mr Triloki Nath and Dr Himesh Gupta. Views and suggestions on 'Cancer News' are welcome from the readers. Wishing our readers a happy, prosperous and healthy New Year 2009.

Dr (Mrs) Ira Ray

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Printed at
Sagar Printers &
Publushers
1880 Udaichand Marg,
Kotla Mubarakpur,
New Delhi - 110 003.

SPECIAL FEATURE

MOLECULAR MARKERS OF CANCER

Introduction

Currently, tumors are diagnosed on the basis of clinical presentation, routine histology, immuno-histochemistry and electron microscopy. However, the histological appearance may not reveal the genetic aberration or underlying biological processes that contribute to the malignancy. Progressive gene mutations, alteration in gene transcription and translation and changes in protein structure and function can often be detected and monitored directly in the tissue of interest (via biopsy) or in surrogate specimens (body fluids) and can be used as molecular markers. Identifying and measuring biomarkers of malignant growth and transformation, potentially have important applications in early detection and diagnosis of cancer, classifying the disease, determining the prognosis and monitoring disease progression, recurrence or response to therapy.

Emerging Molecular Markers

Studies in human cancers and preneoplastic lesions led to the discovery of genetic modifications that occur at early stages of tumorigenesis and which could be used to detect small tumors. Emerging molecular markers are based on the gene expression modifications in chromosomes, DNA, RNA, proteins and mitochondria.

Nucleic acid-based markers: The first genetic analyses were initially carried out on biopsy samples, but the discovery of free DNA in plasma opened new avenues in screening for cancer. Plasma or serum from cancer patients is now analyzed to detect tumor markers, such as oncogene mutations, microsatellite instability, hypermethylation of promoter regions and viral DNA. DNA can also be easily isolated from other body fluids, such as saliva, urine and stools.

Cancer-associated mutations: In 1991 and 1992, TP53 mutations were identified in the urine of patients with bladder cancer and RAS mutations in the stool of patients with colorectal cancer. Initial amplification of the target gene fragment from DNA by PCR followed by mutation- specific ligation of small cDNA strands were developed to identify multiple mutations. Genetic mutation analysis is useful not only in detecting cancer patients, but also in monitoring disease spread and in determining prognosis.

Loss of heterozygosity and microsatellite instability: Loss of heterozygosity (LOH) is a hallmark

Table-1 Selected Molecular Markers of Cancer

Cancer Type	Clinical Sample	DNA Marker	RNA	Protein Marker
Head and Neck	Saliva, serum	TP53, microsatellite alterations, presence of HPV and EBV DNA	Cytokeratins	SCC, CD44 CYFRA, telomerase
Lung	Sputum/BAL serum	RAS and TP53 mutations, microsatellite alterations	Cytokeratins MAGE genes,CEA	CEA, CA 125, telomerase, CYFRA
Breast	Serum	Microsatellite alterations	Cytokeratins, hMAM, MAGE genes, CEA	CA 15-3 (MS-1) CEA, CA 125
Colon	Stool, serum	RAS, APCand TP53 mutations	Cytokeratins, CEA	CEA,CA 19-9, CA 15-3 telormerase
Pancreas	Stool, serum	RAS and TP53 mutations	Cytokeratins, CEA	CA19-9
Bladder	Urine/wash, serum	TP53 mutations, microsatellite alterations	Cytokeratins, survivin uroplakin	CEA, CA 125 CA 19-9, telomerase, survivin, CD44
Prostate	Urine, serum		PSA,MAGE genes, kallikrein	PSA, free PSA, telomerase, kallikrein

Most protein markers in use are not specific enough for routline screening and are used predominantly to monitor response or disease progression. Virtually all genetic markers are still in early stages of development. Prostate-specific antigen (PSA) is widely used to screen men for prostate cancer. Cancer antigens include CA 15-3. CA-125, CA 19-9 and CEA. Telomerase is a riboncleoprotein and usually enzymatic activity is measured; some studies have used direct measurement of the RNA (hTR) component. Most protein markers are measured in serum but other bodily fluids such as urine, saliva and nipple aspirates have been tested for the presence of aberrant proteins. APC, adenomatous polyposis coil; BAL, boncholaveolar lavage; CYFRA, cytokeratin 19 fragment; EBV, Epstein-barr virus; hMAM, mammaglobin; HPV, human papillomavirus; microsatellite alterations loss of heterozygosity (LOH) and/ or instability; SCC, squamous-cell carcinoma antigen.

of cancer that can be detected by various PCR based approaches in most preneoplastic lesions and primary tumors. Some cancers, such as subset of colon cancer, have widespread microsatellite instability due to deficiencies in mismatch-repair proteins.

Hyper methylation: PCR assays have been developed to rapidly and accurately identify methylated regions of DNA. This approach has been used to detect cancer in the saliva of patients with oral cancer, in sputum and bronchoalveolar lavage fluid of patients with lung cancer and in the serum of patients with lung, head and neck and colorectal cancers.

Mitochondrial DNA mutations: Investigators identified mitochondrial mutations in more than 50% of tumor types, including colorectal, lung, head and neck, bladder and breast cancers. High throughput methods need to be developed in order to carry out mitochondrial DNA analysis of clinical samples on a regular basis.

Viral DNA: It is a molecular marker for virus associated cancers, eg hepatocellular carcinoma and cervical cancer.

RNA based approaches: Genetic alterations lead to marked changes in the expression of many genes at the mRNA level. Several mRNA based approaches have been developed to detect caner cells in clinical samples. Reverse transcriptase PCR can be used to quantify mRNA levels of markers and to monitor patient response to anticancer therapies. Cytokeratin mRNA is a common marker of epithelial cancer cells.

Protein markers: Protein based assays typically detect proteins that are over expressed or structurally altered in cancer cells, compared with normal cells. After cancer is diagnosed, expression levels of certain protein markers can be followed to assess therapeutic response and to signal disease recurrence. Telomerase, a ribonucleoprotein, represents a promising molecular marker for cancer.

Biomarker Profiling

Biomarkers can be detected by various methods, including enzyme linked immunosorbent assay, radioimmunoassay, precipitin test, flow cytometry, immunohistochemistry, spectrophotometry, chromatographic techniques, southern analysis, northern analysis, fluorescent in situ hybridization, comparative genomic hybridization, polymerase chain reaction, tissue arrays, serial analysis of gene expression, microarray and proteomic approaches.

Prognostic & Predictive Biomarkers

Biomarkers are classified as risk factors, screening markers, diagnostic markers, prognostic biomarkers, predictive biomarkers. The prognostic biomarkers provide information about the patient's overall cancer outcome, regardless of therapy whilst predictive biomarkers give information on the effect of a therapeutic intervention in a patient.

i) ER/PR in breast cancer: ER and /or PR expression is an independent prognostic factor in breast cancer. High cellular expression of ER and PR predicts benefit from endocrine therapy in the adjuvant and metastatic setting. It now also becomes clear that hormone receptor status in a patient can change during the course of the

Table-2 Biomarkers: Overview of Prognostic and Predictive Value

Biomarker	Tumor Type	Prognostic Value	Predictive Value	Therapy
ER/PR	BRCA	Yes	Yes	Endocrine therapy
HER2/neu	BRCA	Yes	Yes	Trastuzumab
c-KIT	GIST	Yes	Yes	Imatinib
EGFR1	NSCLC	No	Yes	Gefitinib Erlotinib
	CRC	No	Yes	Cetuximab, Panitumumab
Mutated K-ras	NSCLC	Yes	Yes	Gefitinib Erlotinib
	CRC	No	Yes	Cetuximab, Panitumumab
TRAIL receptors	CRC	Yes	Not known	Rh TRAIL: TRAIL receptor antibodies
VEGF	RCC	Yes	No	Angiogenesis inhibitors

ER: oestrogen receptor; PR: progesterone receptor; BRCA: breast cancer; GIST gastrointestinal stromal tumours; EGFR1: epidermal growth factor receptor 1; NSCLC: non-small cell lung cancer; CRC: colorectal cancer; TRAIL: tumour necrosis factor (TNF)-related apoptosis-inducing ligand; VEGF: vascular endothelial factor; RCC: renal cell carcinoma.

disease and may differ across lesions. In addition, PR expression is lost in 40% of previous positive tumors when they metastasize.

ii) HER2/neu in breast cancer: Another relevant biomarker in breast cancer patients is HER2/neu. The HER2/neu gene amplification leads to over expression of its receptor on the cell membrane. This results in increased proliferation and angiogenesis and inhibition of apoptosis. HER 2/neu positive tumors are more aggressive and have, therefore, a worse prognosis compared to negative tumors. HER2/neu is the target for the monoclonal antibody trastuzumab and the EGFR1 and HER2 dual tyrosine kinase inhibitor (TKI) lapatinib. Like ER expression, HER2/neu expression can change over time and can vary between lesions within a patient.

iii)* c-KIT in gastrointestinal stromal tumors (GIST*): The majority of GISTs are characterized by mutations in either the proto-oncogene c-KIT or the platelet-derived growth factor receptor alpha (PDGFRα). With the introduction of imatinib and sunitinib, the outcome of GIST patients improved dramatically. Imatinib and sunitinib are small molecule TKIs, which block signaling via c-KIT and PDGFRα

iv) CD20 in non-Hodgkin's lymphomas (NHL): CD20 is a 33-37 kDa, non-glycosylated phosphoprotein expressed on the surface of almost all normal and malignant B cells. It is also the target for rituximab, the most effective anti-cancer monoclonal antibody developed todate. Since CD20 is not expressed on precursor B-cells, rituximab induces a depletion of only mature B-cells and this effect may be used as biomarkers of prognostic value in treatment of NHL.

v) EGFR1 and K-ras in non small cell lung cancer (NSCLC) and colorectal cancer (CRC): In NSCLC and CRC, biomarkers of interest are EGFR1 and the K-ras oncogene. The prognostic value of EGFR1 protein expression is extensively studied in NSCLC and CRC patients but no definitive association between EGFR1 expression and prognosis was found. The K-ras oncogene controls cell growth via regulation of signal transduction pathways. K-ras mutation results in malignant transformation. In recent years, two small molecule EGFR1 TKIs (gefitinib and erlotinib) and two anti-EGFR1 monoclonal antibodies (cetuximab and panitumumab) have been introduced. In CRC, there is also increasing evidence that mutations in K-ras are predictive of non-response to cetuximab and/or panitumumab.

vi) TRAIL receptors: Tumor necrosis factor (TNF) related apoptosis, inducing ligand (TRAIL or Apo2L), induces apoptosis in a wide variety of tumor cell lines without causing toxicity to normal cells. TRAIL binds the death receptors TRAIL-R1 (DR4) and TRAIL-R2 (DR5) expressed on most tumour cells and initiates the apoptotic pathway to predict which patients might benefit TRAIL receptors targeting therapy, a SPECT imaging study with antibody mapatumumab has been initiated.

vii) VEGF and renal cell carcinoma (RCC): Even very small tumors require angiogenesis to provide nutrients and oxygen for survival. There is a close interaction between tumor cells that produce pro-angiogenic growth factors, like vascular endothelial growth factor (VEGF) and PDGF and endothelial cells expressing growth factor receptors.Targeting the VEGF pathway with TKI sunitinib and sorafenib, the mTOR inhibitor temsirolimus and with the VEGF targeting monoclonal antibody bevacizumab prolongs progression-free survival in metastatic clear cell RCC.

Future of Tumor Profiling

Cancer is a genetic disease and technologies capable of assessing the myriad abnormalities within a malignant cell are essential not only to identify diagnostic and predictive markers but also to optimize drug discovery and therapy optimization. Individual prognostic and therapeutic response markers are rapidly being superseded by genomic, transcriptional and proteomic profiling of malignancies and malignant states.

Conclusion

With current advances in proteomics and genomic technologies, molecular markers would be used in combination with other techniques such as imaging or histological studies to detect, diagnose and monitor cancer. There is a growing need for markers and of tumor profiles that help select patient populations who would be most likely to respond to the novel, specific, molecularly targeted drugs. The clinical researchers should design future trials and molecular biologists should take advantage of the number of tumor samples available in tissue banks to identify new molecular markers and to more fully assess the existing ones.

(The Institute appreciates Dr J.B. Sharma for his contribution to this Special Feature on Molecular Markers of Cancer).

PERSPECTIVE

NATURAL ORIFICE TRANSLUMINAL ENDOSCOPIC SURGERY

Introduction

The current generation of surgical endoscopists is on the verge of witnessing a true paradigm shift, referred to as Natural Orifice Transluminal Endoscopic Surgery (NOTES). NOTES, a scarless surgery, avoids the need for abdominal incisions and accesses the peritoneal cavity via one of the body's natural orifices (mouth, anus, vagina or urethra). A flexible endoscope is advanced into the peritoneal cavity after puncturing one of the viscera (stomach, colon, vagina or bladder). Endoscopic insufflation creates a pneumoperitoneum and the appropriate working space to perform the operation. Conventional endoscopic instruments are advanced through working channels of the endoscope in order to perform the operation. The first report of oral peritoneoscopy done in animals was published by Kalloo et al in 2004. Since then, multiple investigators have used transluminal flexible endoscopy in animal models to perform various intraperitoneal procedures, ranging from tubal ligation to splenectomy. There have been additional reports of unpublished clinical cases in humans.

Advantages Over Current Surgical Techniques

Today, laparoscopy has become a standard approach for most general and oncologic procedures. It has many advantages over open surgery, such as reduced blood loss, reduced post operative pain, lesser need for post operation analgesia, shorter recovery time and a reduced risk of infection of internal organs. NOTES would provide all the advantages of laparoscopic surgery. In addition, the elimination of all abdominal wall incisions might eliminate the risk of wound infection, incisional hernias, postoperative adhesions and small bowel obstruction. Given the portability of NOTES equipment, it will be suited for ICU.

NOSCAR

Recognizing the potential impact of this new technology, expert representatives from the Society of American Gastrointestinal Endoscopic Surgeons (SAGES) and the American Society for Gastrointestinal Endoscopy (ASGE) met in 2005 to identify the potential applications and the challenges facing this novel field. A joint subcommittee between the two societies, Natural Orifice Surgery Consortium for Assessment and Research (NOSCAR) has been set up.

Potential challenges: NOSCAR has identified several potential challenges to safe introduction of NOTES which include peritoneal access, gastric closure, prevention of infection, suturing and anastomosing devices, spatial orientation, developing a multitasking platform, management of complications, understanding untoward physiologic consequences and training.

Guidelines: NOSCAR participants must have a multidisciplinary team that possesses both advanced flexible endoscopic skills and laparoscopic skills; should be member of SAGES and/or ASGE; have animal laboratory facilities in which to perform research and training; must agree to share laboratory results with other NOSCAR members at semi-annual meetings; agree that all human procedures be performed only after obtaining approval from an institutional review board or an equivalent body; and must submit all cases to an outcome registry that will be maintained by the sponsoring societies.

Current Technologic Developments

Issues with current flexible scopes include the lack of a multitasking platform, the number and size of access channels, the inability to position and then fix or "stiffen" the endoscope to allow robust retraction and exposure, the inability to control insufflation pressures, fixed visual horizons that force the surgeon to adjust to tilted or inverted views and inadequate suction/irrigation capabilities. These problems can be resolved to some extent with scope-handling expertise and by altering the surgical approach. Several prototype endoscopes are being tested, including the Transport and Cobra (USGI Medical, San Juan Capistrano, CA), the R scope (Olympus, Center Valley, PA), and the robotic Endovia (Hansen Medical, Mountain View, CA), all designed to resolve these issues.

Conclusion

Surgery is evolving beyond current flexible endoscopic and laparoscopic approaches. The new revolutionary technique, NOTES may, in the near future, establish itself as a viable alternative to open and laparoscopic surgery and may represent the next phase of minimally invasive surgery.

(The Institute appreciates Dr Pankaj Pandey for his contribution to this Perspective on Natural Orifice Transluminal Endoscopic Surgery).

RESEARCH AND DEVELOPMENT

Breakthrough for Cancer Research

A research team at the Ludwig Institute for Cancer Researchers and the Department of Genetics and Pathology, Uppsala University, has discovered an entirely new signal path for a growth factor that is of crucial importance for the survival and growth of cancer cells. This discovery opens up an entirely new landscape for research on breast and prostate cancer, among other types. Signals from various growth factors are critical for normal fetal development. The aggressiveness and capacity for survival in cancer cells are also governed by a number of growth factors with transforming growth factor b (TGF-b) playing a prominent role. TGF-b conveys its signal to the inside of the cell via receptors bound to the cell membrane in a way that is similar in the great majority of animals. TRAF6 is a so-called ubiquitin-ligase, which is used by TGF-to be specifically able to activate a kinase called TAK1, which subsequently activates the other so-called stress-activated kinases, leading to cell death. The discovery that TGF makes use of TRAF6 to activate signal paths in cells opens up an entirely new landscape for future research.

(Uppsala University, Sep 3, 2008)

New Imaging Agent

Scientists have developed a new imaging agent that gives a much clearer and more precise image than the existing methods. The discovery makes use of the anti- cancer drug bevacizumab (Avastin) and Copper-64, a radioactive copper nuclide. Research verifies this new imaging agent for the next generation of tumor detection imaging probes. 64Cu-bevacizumab is highly sensitive in pancreatic, breast and lung cancer models, detecting tumors earlier than 18FDG, with much better contrast between the tumor and the surrounding tissue and with fewer non-tumor-related hot spots. Because it uses different biological mechanisms compared with 18FDG, it could detect a broader range of tumor types than 18FDG. This superior imaging will enable to detect and diagnose tumors at earlier stages, to monitor the effects of therapy on the patients' cancers and will help physicians to decide the size of the tumor and may be able to help the radiation oncologist decide the clinical treatment volume.

(ScienceDaily, Oct 22, 2008)

Potential New Targets in Brain

The Cancer Genome Atlas (TCGA) Research Network has reported the first results of its large scale, comprehensive study of the most common form of brain cancer, glioblastoma (GBM), indicating the discovery of new genetic mutations and other types of DNA alterations with potential implications for the diagnosis and treatment of GBM. Among the TCGA findings are the identification of many gene mutations involved in GBM, including three previously unrecognized mutations that occur with significant frequency and the delineation of core pathways disrupted in this type of brain cancer.

The most exciting finding is that this multipronged study design also enabled the scientists to make a potentially important connection between methylation changes in the glioblastoma cells and which drugs should be used for treatment. Brain tumor that contain a methylated, or silenced, form of a gene, known as MGMT, are also known to be more susceptible to cancer drug temozolomide (Temodar). Therefore, Temodar is routinely given along with radiation to patients with MGMT methylation.

(NCI News, Sep 4, 2008)

Telomerase Structure

Researchers have attempted for more than a decade to find drugs that shut down telomerase, an enzyme that plays a major role in the development of nearly all human cancers. Researchers at the Wistar Institute have deciphered the structure of the active region of telomerase. The landmark achievement opens the door to the creation of new, broadly effective cancer drugs, as well as anti-aging therapies. The study elucidates the active region of telomerase and provides the first full-length view of the telomerase molecule's critical protein component. It reveals surprising details, at the atomic level, of the enzyme's configuration and how it works to replicate the ends of chromosomes-a process critical to both tumor development and the aging process.

The findings should help researchers in their efforts to design effective telomerase inhibitors. Telomerase is an ideal target for chemotherapy because it is active in almost all human tumors, but inactive in most normal cells. Therefore, a drug that deactivates telomerase would likely work against all cancers, with fewer side effects.

(The Wistar Institute, Sep 2, 2008)

NEW TECHNOLOGIES

DIAGNOSTICS

HPV DNA Test

Results of the first study to determine the accuracy of a new rapid screening test for Human Papilloma Virus (HPV) have shown it to be 90% accurate in detecting precancerous cervical disease in China. The results conclude that the test, careHPV, could provide an effective primary screening method for cervical cancer prevention in rural and low-resource settings. Cytologic screening available in North America and Europe has led to 50-80% reduction in mortality, but it was previously not possible to translate this expertise to the developing world where taking smears properly and reading them had been problematic. CareHPV is a signal-amplification assay adapted from the Hybrid Capture test, widely regarded as the gold standard routine HPV DNA test. It requires little space and can be performed by non-technical support staff in approximately two and half hours, allowing testing and clinical follow-up on the same day. The ability of the careHPV test to detect precancerous cells was found to be 90% whilst 84.2% of the women without precancerous disease were identified as negative by the test.

(ScienceDaily, Sep 25, 2008)

Oral Cancer Detection

Researchers at the University of California, Los Angeles School of Dentistry, have demonstrated a new approach for cancer biomarker discovery, using saliva proteomics for detection of oral cancers. This is the first study to globally evaluate saliva protein levels from oral cancer patients. Researchers collected saliva samples from 64 patients with oral squamous cell carcinoma and 64 healthy patients. Five candidate biomarkers were successfully validated using immunoassays: M2BP, MRP14, CD59, profilin and catalase. The presence of these biomarkers confirmed the presence of oral cancer 93% of the times. Since it is very simple to collect and process saliva fluids, the discovery of these biomarkers may lead to a useful clinical tool for noninvasive diagnosis of oral cancer in the future. Researchers are developing point-of-care microfluidic devices to detect these markers that could be used in clinical trials.

(Clinical Cancer Research, Oct 1, 2008)

DRUGS

Amrubicin

Celgene Corporation announced that its drug 'Amrubicin' has been granted Fast Track product designation by the US Food and Drug Administration for the treatment of small cell lung cancer (SCLC) after first-line chemotherapy. A drug designated as Fast Track product is intended for the treatment of a serious or life-threatening condition and demonstrates the potential to provide a therapy where none exists or provide a therapy which may offer a significant improvement in safety and/or effectiveness over existing therapy. This designation is another example of the increasing focus on the clinical potential of Amrubicin as treatment for SCLC. Amrubicin is a third-generation, synthetic anthracyline analogue that has demonstrated substantial clinical efficacy in the treatment of SCLC. Amrubicin is a potent topoisomerase II inhibitor and is being studied as a single agent and in combination with anti-cancer therapies for a variety of solid tumors, including lung cancer. It is currently approved and marketed in Japan for the treatment of lung cancer, and has been granted orphan-drug designation for the treatment of SCLC in both the US and European Union.

(Celgene Corporation, Sep 6,2008)

DAVANAT®

Pro-Pharmaceuticals, Inc. (AMEX: PRW) has submitted supporting clinical and manufacturing data to the US Food and Drug Administration for a New Drug Application registration of DAVANAT®, a new chemical entity for the treatment of advanced colorectal cancer. In pre-clinical studies, DAVANAT has improved efficacy and reduced toxicity of chemotherapy and biologics, such as 5-FU, Irinotecan, Oxaliplatin, Cisplatin, Avastin®, Taxol and Doxorubicin. Data from a completed clinical trial for end-stage colorectal cancer patients showed that DAVANAT®, in combination with 5-FU, significantly extended the median survival. DAVANAT® is a proprietary carbohydrate compound that is administered with chemotherapies and biologics to treat cancer. Its mechanism of action is based on binding to lectins and targeting specific lectin receptors (Galectins) on cancer cells. Current research indicates that Galectins affect cell development and play an important role in tumor cell survival, angiogenesis and tumor metastasis.

(Pro-Pharmaceutical, Inc., Sep17, 2008)

EQUIPMENTS

Microwave Ablation System

The interventional oncology business unit of Covidien Ltd has announced the global release of the Evident^{Tm} microwave ablation system to ablate soft tissue. This major technological advance allows surgical oncologists, interventional radiologists, general surgeons and other medical specialists to perform percutaneous, laparoscopic or open surgical soft tissue ablation and in less time than other forms of ablation. The Evident^{Tm} microwave ablation system typically takes 10 minutes or less. The speed and efficiency of the Evident^{Tm} microwave ablation system may mean less time in the operating or radiology suite and less time that patients will spend under anesthesia.

The system creates heat by generating friction through the vibration of water molecules. Microwave energy is then emanated from the feed point of the radiating portion of the antenna, causing coagulation of the tissue. This technology has shown promising results in ablating soft tissue in patients who are not candidates for surgical resection and have few remaining treatment options.

(Covidien Ltd, Sep 2008)

MRI-Guided Ultrasound

The new treatment, the magnetic resonance imaging (MRI)-guided transurethral ultrasound, uses heat from focused ultrasound to treat cancer in the prostate gland precisely while sparing the delicate non-cancerous tissues around the prostate essential for healthy urinary, bowel and sexual function. Researchers have licensed their innovation and formed Profound Medical Inc., which will develop the technology for clinical use.

The treatment is minimally invasive and takes less than 30 minutes. It reduces the high level of incontinence and impotence associated with the current, invasive treatments. Ultrasound heating applicator works inside a magnetic resonance imager, without the two technologies interfering with each other. A non-invasive therapy for early, localized prostate cancer could improve the quality of life of hundreds of thousands of men. The key to effective non-invasive treatment is accurate imaging of the target organ and of the effects of the treatment on the tissue. MR-guided ultrasound has many potential advantages over transrectal ultrasound-guided focused ultrasound, now approved for use in Canada.

(Sunnybrook Health Sciences Centre, Sep 16, 2008)

Partial Breast Irradiation

The Food and Drug Administration-approved device called SAVI, for partial breast irradiation, made by Cianna Medical. Inc. and offered first by Moores Cancer Center, is aimed at providing customized radiation therapy with reduced treatment time, while minimizing exposure to healthy tissue around the breast after a woman has received a lumpectomy for early stage cancer. A study of the first approximately 100 patients who received partial breast irradiation with this device, inserted inside the breast, has shown that after one year, the device is effective at sparing nearby healthy tissue from the effects of radiation.

The device consists of flexible catheters through which radiation is given. The findings showed that nearly half of the women, because of their anatomy or the location of the tumor, would not have qualified for other such similar internal radiation techniques like mammosite and interstitial irradiation, and would have likely needed a much longer course of therapy. They saw very little radiation burning of the skin and a low infection rate. In addition, it allowed women to have treatment twice daily for five days rather than daily for six weeks.

(Moores Cancer Center, Sep 29, 2008)

Video-Assisted Thoracic Surgery

Conventional or open surgery for lung cancer requires a 6-10 inch incision, cutting the major muscles overlying the chest. With open surgery or video-assisted thoracic surgery (VATS) the surgeon removes either a section of the lung or the affected lobe. VATS is performed with 2-4 small incisions (the main incision is only 2 inches long). Instead of spreading the ribs, the surgeon has a magnified view of the organs on a monitor in the operating room.

For the study, the surgeon analyzed the records of 140 lobectomy patients who underwent VATS (74 patients) and open surgery (66 patients) for stage I non-small cell lung cancer. The post-operative hospital stay was 4 days for VATS patients and 7 days for open surgery patients. VATS patients also had the post-operative chest tube removed sooner than patients with open surgery. Adjusted median chest tube duration was 5 days for open surgery versus 4 days for VATS. The percentage of patients with any complication was 42% for open surgery versus 35% for VATS. This study is important in demonstrating the effectiveness and the reduced impact it can have for patients.

(Fox Chase Cancer Center, Oct 28, 2008)

IN FOCUS

ANTIOXIDANTS AND CANCER

Introduction

Normal human cells produce small amounts of reactive oxygen species (ROS). It is widely accepted that ROS play both positive and negative roles in vivo. The positive roles are related to ROS involvement in energy production, phagocytosis, regulation of cell growth and intercellular signaling and synthesis of biologically important compounds. The negative effects may be very damaging since they oxidise lipids in cell membranes, proteins and DNA in tissues and cause membrane damage, protein modification, including enzymes and DNA damage. This oxidative damage is considered to play a causative role in aging and several degenerative diseases, such as heart diseases, cataracts, cognitive dysfunction and in cancer.

Humans, through endogenous antioxidant system have protective mechanism against free radicals. These systems include some endogenous antioxidants like lipoic acid, ubiquinone etc. and other exogenous systems like alpha-tocopherol, ascorbic acid etc. which are supplied through the diet.

Antioxidants and Cancer

Several mechanisms have been proposed which lead to oxidative stress (OS) in cancer patients: (i) due to anorexia/cachexia the cancer patients nutritional intake is low thereby causing low levels of antioxidants. This accounts for increased OS levels, thereby causing pro- inflammtory process and other damaging oxidation process of lipid and DNA; (ii) a non-specific chronic activation of the immune system accompanied by an excessive production of pro-inflammatory cytokines also increases the ROS production; (iii) use of antineoplastic drugs, such as alkylating agents and cisplatin, may also result in an excess of ROS and may therefore lead to OS.

Several clinical studies have reported modest decrease in treatment-related effects, such as anorexia, tissue wasting, loss of body weight and poor performance status, when supplemental antioxidants, either dietary or pharmaceutical, are administered concurrently with cytotoxic regimens. However, antioxidants also exert their effects on all tissues to some degree, thereby protecting tumor cells as well as healthy ones, thus improving the quality of life and performance status.

Radiation Therapy and Antioxidants

The principal therapeutic effects of radiation occur indirectly via ionization of water molecules in the cytoplasm to increase levels of ROS (superoxide and hydroxyl radicals). It has been observed that those who receive both antioxidants and radiation therapy have a statistically significantly reduced side effects. However, this benefit appears to be offset due to reductions in the local tumor control rates.

Chemotherapy and Antioxidants

The randomised studies reported in literature are confusing as the use of antioxidants and/or chemotherapy has been done on different types of cancers and the results are not uniform to draw any specific conclusions.

Future Directions

As noted above, variations in study design, intervention protocol, eligibility criteria, statistical power, timing of the observation or intervention, malignancy type and anticancer regimens, limit the ability of the authors to make definitive conclusions as to whether the decresed tumor progression is a consequence of administering supplemental antioxidants during chemotherapy and/or radiation therapy.

Importantly, many reports provide a basis for continuing research on the potential for dietary and pharmaceutical antioxidants supplement affecting some cytotoxic regimens and/or decreasing toxicity without interfering with the oncological action.

Conclusion

Much of the evidence to date regarding the effects of antioxidants on tumor control has been derived from experimental research that has little relevance to patients. As these observational studies have been done in phase II trials having no uniformity in selection of patients (like type and size of tumors, site of tumors, number of cases taken in each study) it is difficult to conclude the role of antioxidants in cancer. The phase III studies which will address these variables to get uniformity will bring better understanding of the role of these antioxidants. Further research is required to address these limitations.

(The Institute appreciates Mr Triloki Nath for his contribution to the feature 'In Focus' on Antioxidants and Cancer).

CANCER CONTROL

Apigenin for Cancer Prevention

Study by UC Riverside biochemists reports that ingesting apigenin, a naturally occurring dietary agent found in vegetables and fruits, improves cancer cells' response to chemotherapy. They found that apigenin localizes tumor suppressor p53, a necessary step for killing the cell that results in some tumor cells responding to chemotherapy. The study provides a novel approach to conquer tumor resistance to chemotherapy and suggests an avenue for developing safe chemotherapy via naturally occurring agents.

Apigenin is mainly found in fruits (including apples, cherries, grapes), vegetables (including parsley, artichoke, basil, celery), nuts and plant-derived beverages (including tea and wine). It has been shown by researchers to have growth inhibitor properties in several cancer lines, including breast, colon, skin, thyroid and leukemia cells. It has also been shown to inhibit pancreatic cancer cell proliferation. The study advocates the inclusion of vegetables and fruits in our daily diet to help prevent cancer.

(University of California, Oct 22, 2008)

Chemotherapy Related Nausea

Patients rank nausea and vomiting amongst the most distressing chemotherapy side effects, causing anxiety, depression and sometimes leading to patients stopping potential curative treatment. A recent pilot study in cancer patients showed a 43% reduction in chemotherapy related nausea and vomiting when using acupressure wristbands as opposed to using anti-emetic drugs alone. Worn around the wrist, the Sea-Band® acupressure wrist band exerts a constant, gentle pressure on a point on the inner wrist called the pericardium 6 (P6) acupressure point. Cancer Research UK recognizes the use of Sea-Band® for alleviating post-chemotherapy nausea. Used before or after symptom onset, Sea-Band® acupressure wristbands can reduce nausea within as little as five minutes.

The largest trial worldwide, including four universities and nine regional cancer centers led by the University of Manchester team in UK, will assess the use of Sea-Band® acupressure wrist bands for chemotherapy related nausea. Sea-Band® was granted clearance by the Food and Drug Administration in 2004 for the relief of motion sickness, morning sickness and post chemotherapy and post operative nausea.

(Medical News Today, Sep 23, 2008)

Exercise May Cut Risk of Uterine Cancer

According to the findings of the American Cancer Society's prospective cancer prevention study, in overweight or obese women, physical activity of light or moderate intensities, such as walking, biking aerobics or dancing, equivalent to about 2 hours of moderately paced walking per week, lowers the risk of cancer of the lining of the uterus (endometrial cancer). Researchers at the American Cancer Society in Atlanta identified 466 women who developed endometrial cancer between 1992 and 2003 among approximately 43, 000 older postmenopausal women. They reported that all measures of physical activity and avoidance of sedentary behavior were strongly associated with reduced risk of endometrial cancer in women who were overweight or obese.

(Int. J. of Cancer, Oct 15, 2008)

Massage Therapy

A new study from the National Institutes of Health finds that massage therapy may have immediate benefits on pain and mood among patients with advanced cancer. In a randomized trial of 380 advanced cancer patients at 15 U.S. hospices, improvement in pain and mood immediately following treatment was greater with massage than with simple touch. This study is important because it shows that massage is a safe and effective way to provide immediate relief to patients with advanced cancer. While drug therapies can reduce symptoms, they don't always work and often have troublesome side effects. Researchers think that massage may interrupt the cycle of distress, offering brief physical and psychological benefits. Physically, massage may decrease inflammation and edema, increase blood and lymphatic circulation, and relax muscle spasms. Psychologically, massage may promote relaxation, release endorphins and create a positive experience that distracts temporarily from pain and depression.

Researchers caution that while massage may offer some immediate relief for patients with advanced cancer, the effects do not last over time, hence more effective strategies are required to manage pain at the end of life.

(Annals of Internal Medicine, Sep 17, 2008)

INSTITUTE

MD ANDERSON CANCER CENTER

Introduction

The University of Texas MD Anderson Cancer Center is located in Houston, Texas. It is one of the world's most respected centers devoted exclusively to cancer patient care, research, education and prevention. MD Anderson has ranked first among the nation's cancer hospitals five times in the last eight years. The importance of research was illustrated in 1941 when the Texas Legislature approved the institution's original name: the Texas State Cancer Hospital and the Division of Cancer Research. It became the M.D Anderson Hospital for Cancer Research of the University of Texas in the following year. Cancer care services commenced on March 1, 1944. Since1944, nearly 700,000 patients have turned to MD Anderson for cancer care in the form of surgery, chemotherapy, radiation therapy, immunotherapy or combinations of these and other treatments.

Facilities

i) Adult Oncology Services: Clinicians in all oncologic and supporting specialties work together to plan and implement multimodality therapies. This organization greatly reduces the time needed for initial evaluation, diagnosis and treatment planning and increases convenience for patients.

ii) The Cancer Prevention Center: The cancer prevention center provides comprehensive cancer screening services, including cancer risk assessment, screening exams based on cancer risk, age and gender, personalized risk reduction strategies, genetic testing, chemoprevention, tobacco cessation and nutrition counseling.

iii) Pediatric Oncology Services: Pediatric cancer patients receive treatment through the Children's Cancer Hospital's inpatient facility (where caregivers can room-in with their children), outpatient clinic, day hospital and the pediatric intensive care unit. Full supportive services are provided.

iv) Genetic Counseling and Testing Services: Cancer genetic counseling and testing services are offered through the clinical cancer genetics program. Individuals found to be at high risk for cancer are offered follow up in high risk cancer screening clinics at the center.

Research

At MD Anderson, important scientific knowledge gained in the laboratory is rapidly translated into clinical care. In 2005, the Center invested more than $410 millions in research. MD Anderson ranks first in the number of grants awarded and total amount of grants given by the National Cancer Institute (NCI). It holds ten NCI specialized programs of research excellence grants: bladder, breast, head and neck, leukemia, lung, melanoma, ovarian, pancreatic, prostate and uterine. In September2005, MD Anderson unveiled plans for the Red and Charline McCombs Institute for the early detection and treatment of cancer. The Institute comprises six unique centers focused on genomics, proteomics, screening, diagnostic, imaging and drug development. A Cancer Genomics Core Laboratory at MD Anderson supports research to expand molecular therapeutics and diagnostics. Teams of researchers are devising novel ways to overcome the insidious problem of metastasis. The Institute partners with clinicians to alter key steps in the complex cancer process to improve combination therapies, strengthen diagnostic abilities and design prudent prevention strategies.

Academics

Each year, more than 4,300 students take part in educational programs, which include physicians, scientists, nurses and many health professionals. MD Anderson offers bachelor's degrees in seven allied health disciplines. In addition, more than 1000 clinical residents and fellows come to MD Anderson each year to receive specialized training in the investigation and treatment of cancer. More than 500 graduate students are working on advanced degrees at the Graduate School of Biomedical Sciences, which MD Anderson operates jointly with the University of Texas Health Science Centre at Houston. More than 1300 research fellows are being trained in MD Anderson's laboratories and clinics.

Conclusion

MD Anderson Cancer Center has an international reputation for scientific excellence and outstanding cancer care. Through their exceptional efforts, more effective methods to diagnose and treat cancer are being developed. Research discoveries have been translated and exported far beyond the walls of the Texas Medical Center. The quickening pace of progress against cancer achieved through innovative research will continue to be MD Anderson's gift of better treatment, longer survival and cancers prevented for generations to come.

CLINICAL TRIALS

Colonoscopy

Computerized tomographic (CT) colonography, also known as virtual colonoscopy, is comparable to standard colonoscopy, which uses a long, flexible tube with a camera to view the lining of the colon, in its ability to accurately detect cancer and precancerous polyps and could serve as an initial screening exam for colorectal cancer, according to the results of the American College of Radiology Imaging Network (ACRIN) National CT Colonography Trial. The ACRIN trial is the largest multi-center study to compare the accuracy of state-of-the-art CT colonography with the gold standard of conventional colonoscopy.

CT colonography could be adopted into the mainstream of clinical practice as a primary option for colorectal cancer screening. Colorectal cancer is the third most frequently diagnosed cancer in the United States. CT colonography was found to be highly accurate for the detection of intermediate and large polyps. Ninety percent of the polyps, 1 centimetre or larger, were detected by CT colonography. Since most colon cancers develop from polyps and screening to find and remove these polyps can prevent colon cancer, an opportunity exists to save lives with early detection.

(NCI- News, Sep 17, 2008)

Goserelin in Prostate Cancer

The results from the Phase III EORTC study demonstrate that Goserelin, when used as adjuvant treatment with radiotherapy, improves 10-years overall survival as compared to radiotherapy alone in patients with locally advanced prostate cancer (when the cancer has spread into the capsule of the prostate or through the prostate into the surrounding tissues).

Goserelin is a Luteinizing Hormone-Releasing Hormone agonist (LHRHa) which works in prostate cancer by reducing the levels of testosterone in men, stopping prostate cancer growth. In the study, Goserelin 3.6mg was started on the first day of irradiation and continued for a period of three years. This is called 'medical castration' as opposed to a surgical castration (orchidectomy), the removal of the testes. Goserelin is given as an injectable implant LHRHa, either every 28 days or every 12 weeks, which is implanted into the abdominal wall via subcutaneous injection by nurses or doctors.

(Medical News Today, Sep 23, 2008)

Metastatic Colorectal Cancer

ERBITUX (cetuximab) is a monoclonal antibody (lgG1 Mab) designed to inhibit the function of a molecular structure expressed on the surface of normal and tumor cells called the epidermal growth factor receptor (EGFR, HER, c-ErbB-1).

As reported in 2007, the 1198-patient Phase 3 CRYSTAL (Ceuximab combined with FOLFIRI in first line therapy for metastatic colorectal) study, conducted by Merck KGaA, Darmstadt, Germany, met its primary endpoint of increasing progression-free survival (PFS) and did not, however, demonstrate a statistically significant prolongation of overall survival. The addition of ERBITUX to FOLFIRI in the CRYSTAL study decreased the risk of disease progression by 15% and demonstrated a 21% improvement in the response rate. A preliminary review of the data reveals that a greater proportion of patients randomized to the FOLFIRI-only arm went on to receive ERBITUX following the development of disease progression, compared to patients randomized to FOLFIRI plus ERBITUX.

(ESMOS, Sep 17, 2008)

NauVax

Apthera, Inc. announced the optimized dose and schedule for its lead drug, NeuVax in treating early-stage breast cancer patients to be used in Phase III clinical trials. The proof-of-concept safety and efficacy trial utilized dose escalation with seven different dose groups evaluated in 99 breast cancer patients to determine the optimal biologic dose for NeuVax based on toxicity and immunologic response. At a median follow-up of 30 months, the tumor recurrence rate for patients receiving the optimal dose of NeuVax was much lower than that of patients receiving suboptimal doses.

These results have allowed the investigators to articulate the optimal dose and schedule for the upcoming Phase III clinical trial. Together with the recently published data on preferential activity of NeuVax in patients with low HER2/neu expression, Apthera has identified a patient population with an unmet medical need for NeuVax in the adjuvant therapy setting.

(Cancer, Oct 3, 2008)

WATCH-OUT

Lung Cancer Test

The CD133 marker has been found to be diagnostic of malignant lung cancers. Tests and kits to show cell and used for such cells are disclosed under Patent No. US 2008254488 (A1), published on October 16, 2008 and entitled "Cancer Test". It has now been established that the malignancy of lung cancers is driven by a very small percentage of the cells making up the cancer and that these cells are characterized by the presence of the CD133 marker.

The present invention provides a test for assaying the tumorigenic cells in small cell and non-small cell lung cancer, including the adenocarcinoma, squamous cell carcinoma and large cell carcinoma for the presence of the CD133 marker. They found that lung cancer contains a rare population of CD133+ cancer stem-like cells, able to self-renew and generate an unlimited progeny of non-tumorigenic cells. In another aspect, there is provided a method comprising contacting the sample with an optionally labeled anti-CD133 antibody and establishing the level of binding of the antibody to the sample. A kit is also provided comprising the said antibodies, together with instructions for the use thereof in the establishment of the existence of a cancerous condition.

(European Patent Office, Oct 27, 2008)

Multidrug Resistant Cancer Marker

Nucleophosmin directed diagnostics and therapeutics for multidrug resistant neoplastic disease has been patented under United States patent No. 7,413,851, published on August 19, 2008. Assignee of the patent is Aurelium Biopharma, Inc. (Montreal, Quebec, CA). Some cancer cells in a tumor become multidrug resistant (MDR) to a broad spectrum of chemotherapeutic drugs which is the principle reason for treatment failure in cancer patients. The present invention relates to the detection and treatment of neoplastic and/or damaged cells and for detecting MDR in neoplastic or damaged cells by detecting an increase in the cell surface expression of a nucleophosmin (NPM) intracellular protein marker on the surface of such a MDR neoplastic or damaged cells as compared to the level of expression of the nucleophosmin protein on the surface of a normal cell. NPM is expressed more abundantly on the cell surface of MDR neoplastic cells and MDR damaged cells. NPM is expressed in only negligible amounts on the cell surface of normal cells of the body.

(USPTO, Oct 2008)

NanoXray ™ Anticancer Platform

Nanobiotix, an emerging nanomedicine company focused on cancer therapy, has announced the issue of Patent No. 1744789 by European Patent Office, related to the protection of its NanoXray anticancer platform. NanoXray is designed to allow the precise destruction of cancer cells via the controlled application of an outside-the body energy source as standard X-ray. The patent protects composite particles that can generate free radicals or heat when excited by X-rays and to the uses thereof in health, particularly humans. The patent protection also relates to methods for the production of said particles and to pharmaceutical or diagnostic compositions containing the same. Protecting this intellectual property is the key to long-term commercial success. NanoXray platform technology is now patent protected through the European Union and is expected to receive similar patent protection in the United States as well.

(Nanobiotix, Sep 23, 2008)

Stomach Cancer

Japan based Sysmex Corp. has been assigned a patent No. US2008227094, entitled "Methods for Judging Lymph Node Metastasis of Stomach Cancer," published on Sep 18, 2008. During operation, the diagnosis of lymph node metastasis of cancer cells is very significant and in recent years a genetic test is becoming rapidly widespread in the field of clinical diagnosis. The first step of the present invention relates to a method and the second aspect relates to an apparatus for judging the lymph node metastasis of stomach cancer comprising steps or means for quantifying mRNA of cytokeratin 19 in a detection sample prepared from a lymph node tissue suspected of having stomach cancer metastasis and a means of judging the presence or absence of lymph nodes metastasis of stomach cancer, on the basis of the obtained quantitative value of the mRNA. A third aspect relates to a reagent kit for judging the lymph node metastasis of stomach cancer comprising a pretreatment solution of a lymph node tissue, primer solution for detecting cytokeratin 19 and an enzyme solution for carrying out a nucleic acid amplification method.

(esp@cenet.com, Sep 29, 2008)

GLOBE SCAN

Cancer Probability in Liver Transplant Recipients

According to a new study, cancer incidence is higher among liver transplant recipients in Finland compared to the general population. Researchers sought to describe the cancer risk pattern in Finnish liver transplant patients, hypothesizing that the incidence of specific types of cancer would be higher among the recipients. Among the 540 liver transplant recipients, they found a total of 39 post transplant de novo cancers in 36 patients. The overall standardized incidence ratio (SIR) compared to the general population was 2.59. Non-Hodgkin lymphoma, non-melanoma skin cancer and basal cell carcinoma had significantly elevated SIRs. Interestingly, the authors found lower cancer incidence among patients with history of acute rejections, correlating most strongly with lymphomas. Other reports have noted a significantly increased risk of de novo oropharyngeal and lung cancers amongst liver transplant patients that smoke, which is a potentially preventable condition.

(Finland: *Liver Transplantation, Oct 2008)*

Children's Risk of Brain Cancer

Children and teenagers are five times more likely to get brain cancer if they use mobile phones, a new research from Sweden indicates. Children are more at risk because their brains and nervous systems are still developing and since their heads are smaller and their skulls are thinner. As such the radiation penetrates deeper into their brains. People who started mobile phone use before the age of 20 had more than fivefold increase in glioma, a cancer of the glial cells that support the central nervous system. Those who started using mobiles young, were also five times more likely to get acoustic neuromas, benign but often disabling tumors of the auditory nerve, which usually cause deafness. Children under 12 should not use mobiles except in emergencies and teenagers should use hands-free devices or headset and concentrate on texting. At 20, the danger diminishes because then the brain is fully developed. The hazards to children and teenagers may be greater even than these results suggest, because the results of the study do not show the effect of their using the phone for many years.

(Sweden: *Medical New Today, Sep 21, 2008)*

World Cancer Declaration

To tackle the growing cancer crisis in developing countries, the International Union Against Cancer, the leading international non-governmental organization dedicated to the global control of cancer, hosted world cancer summit in Geneva. More than 60 high-level policymakers, leaders and health experts attended the summit and adopted a global plan. The plan, contained in the World Cancer Declaration, recommends a set of 11 cancer-busting targets for 2020 and outlines priority steps that need to be taken in order to meet them. Targets recommended in the declaration include significant drops in global tobacco consumption, obesity and alcohol intake; universal vaccination programmes for hepatitis B and human papilloma virus to prevent liver and cervical cancer; dramatic reduction in the emigration of health workers with specialist cancer training; universal availability of effective pain medication and the dispelling of myths and misconceptions about the disease.

Adoption of the world cancer declaration is another step in a real commitment, a vision, of how to tackle this huge world health issue. Much can be done to tackle cancer in the developing world. About one-third of cancer cases can be prevented and another third can be cured if detected early and treated properly.

(Switzerland*: Int. Union Against Cancer, Sep 5, 2008*)

Computers Boost Cancer Detection

A computer can safely replace a medical expert in interpreting a breast X-ray, –according to a Cancer Research UK funded study. The study invited around 28,000 women to have their mammograms read both in the conventional way by two radiologists and also by a single radiologist using the computer. Researchers found that computer, aided detection programme, where mammograms were read by a single expert plus the computer, was as good at finding cancers as the standard UK practice where two experts read each mammogram. This is good news for women, particularly those who live in areas where invitations for screening have been late in arriving. In the rare instance when the computer is at odds with the radiologist, the human interpretation takes precedence. Computer can help give more accurate readings and there is bound to be an improvement in the national screening programme which already saves 1400 lives a year through early detection of breast cancer.

(UK: *NEJM, Oct 1, 2008)*

ACTIVITIES OF RGCI&RC

Taxane Resistance in Breast Cancer

Dr Alexander T. Delgado, MD (Regional Disease Area Head-Oncology, Asia Pacific, Bristol-Myers Squibb) delivered a lecture on 'Taxane Resistance in Breast Cancer' on 23rd September, 2008 in the conference hall at Rajiv Gandhi Cancer Institute & Research Centre (RGCI&RC). It was attended by the medical director, consultants, resident doctors, D N B students and research officers of the Institute.

Dr Delgado mentioned that breast cancer is a leading cause of cancer mortality worldwide with more than one million new cases and more than 400,000 deaths occurring annually. Out of newly diagnosed patients, 10% have locally advanced or metastatic disease and out of early breast cancer patients, 20%-85% would develop recurrent or metastatic disease. He mentioned that approved chemotherapy regimens for breast cancer include anthracyclines and taxanes. Despite treatment, most advanced tumors become resistant and relapse/ progress. Chemoresistance is the major cause of treatment failure.

Intrinsic and acquired resistance is a significant cause of non-responsiveness and treatment failure. Instrinsic resistance is related to host factors, and chemotherapy has little or no effect from the outset. Under acquired resistance, chemotherapy selects for drug resistant tumor cell populations, resulting in treatment failure. A study conducted by Thomas, et al showed that 38% patients had progressive disease as their best response to prior taxane-based chemotherapy and another study by Perez E, et al showed that 37% had intrinsic resistance to taxane. All the patients in both studies had metastatic breast cancer.

Under the mechanism for drug resistance, he explained that the major mechanism of chemoresistance is increased expression of P glycoprotein and MRP 1 drug efflux system which recognizes chemo drug as substrate and pump out. Taxanes are microtubule targeting agents which disrupt cellular processes and induce apoptosis. Microtubules are composed of protein tubulin. Decreased influx of drugs by membrane transporters, sequestration of drugs, altered drug targets, activation of DNA repair by cancerous cells and HER 2 amplification, are other reasons responsible for resistance. Tumor cells that have been exposed to one antineoplastic agent, develop cross resistance to that agent as well as other structurally unrelated drugs.

The mechanisms of resistance to chemotherapy are: alterations in cellular transport of cytotoxic agents affect anthracyclines and others, drug sequestration-affects platinums and others, changes in intracellular metabolism-affects nucleoside analogs, alkylating agents and others, modifications in drug targets-affects taxanes and others by reduction in overall tubulin levels and altered expression of subtypes, alterations in cellular responses affects platinums and others by enhanced DNA repair activity, downregulation of apoptotic pathways and defects in P53 activity.

The strategies for addressing chemoresistance include: inhibition or bypass of efflux pumps, and to maintain intracellular accumulation of cytotoxics, blocking transcription of the MDR1 gene with transcription inhibitors which reduce the presence of P glycoprotein and restore chemosenstivity, or altering MDR1 mRNA and blocking post-translational modifications required for a functional P glycoprotein. The second strategy is liposomal encapsulation of drugs for passive diffusion into tumors, inhibition of signaling pathways involved in cell proliferation and to use those drugs which are not a substrate for P glycoprotein efflux pumps such as epothilones. These are novel microtubule targeting agents and are poor substrates for P glycoprotein.

Dr Delgado added that intrinsic and acquired resistance is a significant cause of non-responsiveness and treatment failure, for which strategies are being developed. Now, Ixempra (Ixabepilone, Bristol Myers Squibb) has been approved by the United States Food and Drug Administration as a monotherapy or in combination with capecitabine for the treatment of metastatic or locally advanced breast cancer patients previously treated with anthracyclins and taxanes. It belongs to the class of antineoplastic agents, the epothilones. It binds totubulin and promotes tubulin polymerisation and microtubule stabilization, thereby arresting cells in G2M phase of the cell cycle.

During the concluding session, Dr Delgado answered queries raised by the audience. Dr AK Chaturvedi, Medical Director, RGCI&RC, thanked Dr Delgado for the brainstorming session on behalf of the Institute.

PHOCON 2008

The 11th Pediatric Hematology Oncology Conference (PHO) of PHO chapter of Indian Academy of Pediatrics (PHOCON 2008) was organized in New Delhi from 6th to 9th November 2008. The activities included pre-conference national consultative meetings on 6th November, pre-conference workshops on 7th November and main conference on 8th and 9th November 2008. The Pediatric Oncology Department of Rajiv Gandhi Cancer Institute & Research Centre (RGCI&RC) was actively involved in all of these activities.

Dr Gauri Kapoor, Sr Consultant, Department of Pediatric Oncology, Dr Rajni Mutneja, Dr Amal Roy Choudhury, Dr Rajinder Kumar, Dr Ritesh Sharma, Dr Ajay Sharma and Ms Anita Kumari, represented the Institute in the national consultative meetings on Pediatric Brain Tumors, Pain & Palliative Care and G-CSF.

Two workshops convened by Dr Kapoor were held at the Institute. The workshop on Nutrition & Supportive Care was co-convened by Dr Himesh Gupta, Pediatric Oncosurgeon, while the other on Radiotherapy in Pediatric Cancers was co-convened by Dr Sheh Rawat, Sr Consultant, Radiation Oncology. The workshop on Nutrition & Supportive Care dealt with the various aspects of venous access devices, followed by discussions on nutritional interventions in childhood cancers. The line care workshop started with a very lucid introductory lecture by Dr Himesh Gupta covering different types of central lines and their insertion techniques. A live demonstration of peripherally inserted central catheter line insertion was done by Dr KK Gupta, followed by an interactive panel discussion. The deliberations covered all aspects of line care as well as trouble shooting. Dr Vineet Talwar, Consultant, Medical Oncology, started the next session by giving an in-depth lecture on the importance of nutrition in the treatment of pediatric cancers. Dr Poonam Sidana, Consultant Neonatologist, Max Hospital, made a presentation on the pros and cons of parenteral nutrition. Practical issues on preparing parenteral and enteral nutrition were discussed and the participating delegates were walked through the actual process of calculating the nutritional needs and implementing it.

The workshop on Radiotherapy in Pediatric cancers was chaired by Dr AK Anand, Sr Consultant, Radiation Oncology, RGCI&RC. It began with an introduction by Dr Sheh Rawat who gave a very illustrative presentation describing the evolution in the management of childhood cancers, citing examples of two highly curable cancers, Wilms' tumor and acute lymphoblastic leukemias. He highlighted the importance of liaison between various specialists, including the anaesthesiologists & pathologists in the treatment of pediatric patients. This was followed by panel discussions on pediatric solid tumors moderated by Dr Charu Garg, Associate Consultant, Radiation Oncology, RGCI&RC, and on pediatric hematolymphoid malignancies moderated by Dr Ashish Rastogi from All India Institute of Medical Sciences (AIIMS). The panelists included experts from Batra Hospital, Maulana Azad Medical College, AIIMS and Safdarjung Hospital. The importance of combined modality treatment in pediatric Hodgkins lymphomas and better selection criteria for inclusion of patients for prophylactic cranial irradiation was discussed. These discussions also emphasized the importance of multimodality treatment and precise timing of these modalities in the overall management of pediatric tumors as well as the accompanying concerns on the growth and development of children.

Throughout the course of the workshops, the deliberations remained interactive and lively due to the quiz questions and use of the voting pad system. There were about 40 delegates and 12 faculty who participated in the two workshops. The scientific content and conduct of the workshops was highly appreciated by all the participants and they proposed more such frequent workshops.

The main conference held at India Habitat Centre, witnessed a lot of participation, enthusiasm and suggestions during the scientific sessions. Five original research papers were presented from the Institute, covering topics, such as Ewings Sarcoma, Outcome of Childhood Non Hodgkin's Lymphoma, Emotional and Behavioral Problems in Children undergoing Treatment for Acute Lymphoblastic Leukemia, Improving Nursing Care of Central Lines by Intensive Biweekly Workshop and Assisted Conception & Risk of Childhood Cancer. These papers were presented by Dr Himesh Gupta, Dr Sandeep Jain, Ms Renu Goyal, Sr Sinimol Baby and Ms Rupal Sinha, respectively, and were very well received and appreciated by the delegates and senior faculty.

It is hoped that the knowledge gained by the delegates would be applied in day to day clinical practice to enhance the care of children with cancer.

RGCON 2009 : Programme Overview

The 8th Annual International Conference "RGCON 2009", organised by the Rajiv Gandhi Cancer Institute & Research Centre, is scheduled to be held at New Delhi from 27th to 29th March 2009. RGCON-2009 is designed to highlight recent trends in diagnosis, staging and multidisciplinary treatment of lung and esophageal cancers, emphasizing the molecular oncology, optimal application of newer chemotherapeutic agents and targeted therapy in clinical practice. Special sessions for primary care physicians will concentrate on "partnered care" with emphasis on early diagnosis, emergencies and approach to management of lung and esophageal cancers.

Scientific Sessions

- Live workshop on interventional bronchoscopy, endoscopy, and thoracic surgery
- Stage wise multimodal management of lung and esophageal cancers
- How to choose an appropriate chemotherapeutic agent in lung cancer
- Targeted therapy of lung cancer
- Staging and newer imaging in lung cancer
- Pharmacogenomics and molecular aspects of lung cancer
- Special sessions for primary care physicians

Learning Objectives

After attending **RGCON-2009**, participants will better be able to learn and understand:

- Current trends in therapeutic advances in lung & esophageal cancers
- New molecular biological pathways in lung & esophageal cancers
- Current trends in the multidisciplinary management of lung & esophageal cancers in various stages and situations
- The latest trends in interventional and diagnostic bronchoscopy & upper G I endoscopy
- The role of radiotherapy in the management of lung and esophageal cancers
- Early diagnosis of the lung & esophageal cancers

Who Should Attend?

- Practicing medical oncologists, surgical oncologists and radiation oncologists
- Chest physicians, pulmonologists
- Onco-pathologists, radiologists
- Gastroenterologists and GI surgeons
- PG students in these disciplines
- Surgeons, physicians, general practitioners engaged in community practice
- Research students in lung & esophageal cancers

Accreditations

Organizing committee will get **RGCON-2009** accredited by the Delhi Medical Council with appropriate CME hrs. Application for UICC auspices is in process. Website: **www.rgci.org**

Registration Details

Category	Early bird till 31 Dec 2008	From 01 Jan to 20 Mar 2009	21 Mar 2009 Onwards & Spot
Indian			
Delegates	Rs 1,500/-	Rs 2,000/-	Rs 2,500/-
Residents & PG/UG Students*	Rs 750/-	Rs 1,000/-	Rs 1,250/-
Foreigners			
Delegates	US $ 50	US $ 75	US $ 100
Residents & PG/UG Students*	US $ 25	US $ 40	US $ 50

** Residents/Students must send a certificate to state their status from their Guide/Head of the Department.*

Invitation to RGCON - 2009

Dear Friend,

We are pleased to announce the **8 Annual International Conference - RGCON 2009** on **27- 29 March 2009** with a theme of ***"Thoracic Cancers: New Frontiers and Horizons"*** in pursuit of our efforts of Continuing Medical Education. We, at Rajiv Gandhi Cancer Institute and Research Centre, Delhi, not only strive hard to provide comprehensive cancer care to our patients but also promote academics as well as conduct continuing medical education programme through conferences and updates. A pre conference workshop on 27th March 2009 (Friday) at RGCI&RC will consist of live demonstration of surgical procedures and interventional bronchoscopy/endoscopy in lung and esophageal cancers by renowned national and international faculty along with constant interaction with the attendees.

The scientific sessions are designed to highlight latest advances in multimodal management of lung and esophageal cancers for a practicing oncologists and primary care physicians. A special emphasis will be on early diagnosis of lung cancer in order to improve the cure rates. Around 400 delegates from India and neighboring countries are expected to attend the conference. Scientific sessions would include Orations, Plenary sessions, Symposia and panel discussions to encourage interaction among the delegates. We have a special session with attractive prizes for the PG students for presentation of their works in lung and esophageal cancers.

Rajiv Gandhi Cancer Institute is a 240 bedded exclusive cancer centre located in north-west Delhi providing a comprehensive multidisciplinary treatment to patients of all types of cancers. With state of the art diagnostic and therapeutic equipment, well trained, experienced and renowned faculty members, the institute has excellent training programmes, accredited by National Board of Examination in disciplines of surgical, medical, radiation oncology, imaging, radiation physics and pathology. With its unquestioned unique place in the field of oncology, it has recently acquired the distinction of registering over 1,00,000 patients, indicating the dedication and commitment of the institute to the cause of cancer treatment.

On behalf of the organizing committee, we invite you to **RGCON 2009** and promise you an academic treat. Since the registration would be on first come first serve basis, we would request you to register early. You may contact us through our e-mail: **rgcon2009@gmail.com** or download the registration forms from our website: **www.rgci.org**

We look forward to seeing you in this academic feast.

Yours sincerely

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